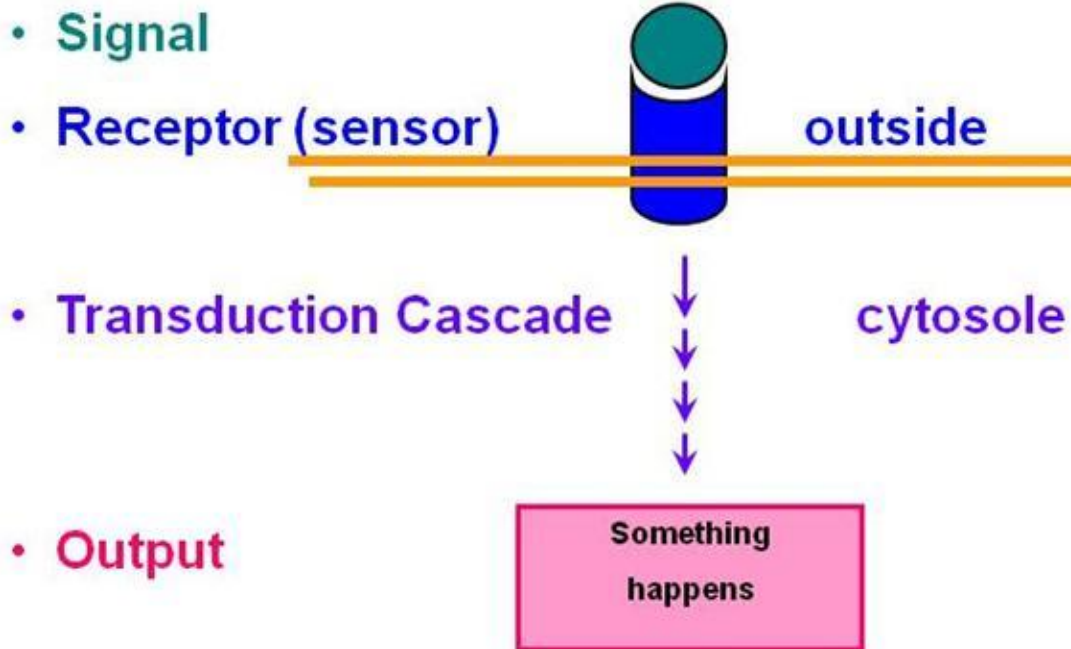


## Cell Signaling

- *Cells sense and send information (signals)*
- *Cells communicate with each other*
- *Cells must sense and respond to changes in the environment*

The signal can come from inside the cell, from another cell, or from the environment.

# Generic Signaling Pathway



## The Cell...

- divides or stops dividing
- differentiates
- commits suicide or kills something
- moves somewhere or stops moving
- alters its metabolism
- passes on the signal

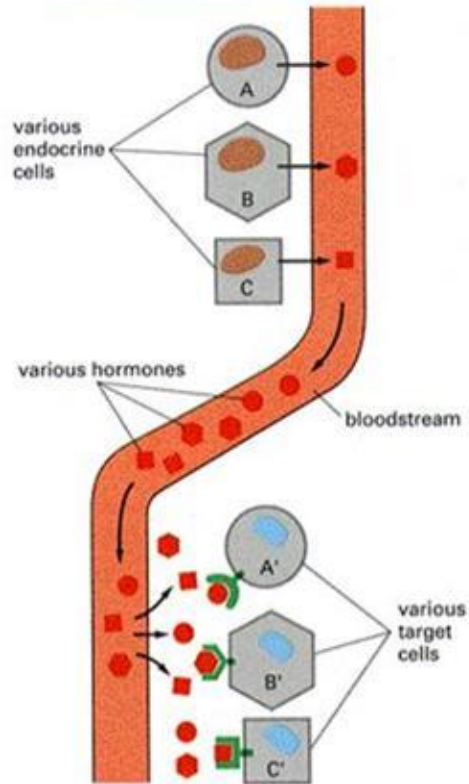
## Responses to cell signaling

- Gene expression is altered at the level of transcription, RNA processing or translation
- Enzyme activities are altered
- Protein-protein interactions are induced or inhibited
- The localization of certain proteins and other stuff is altered

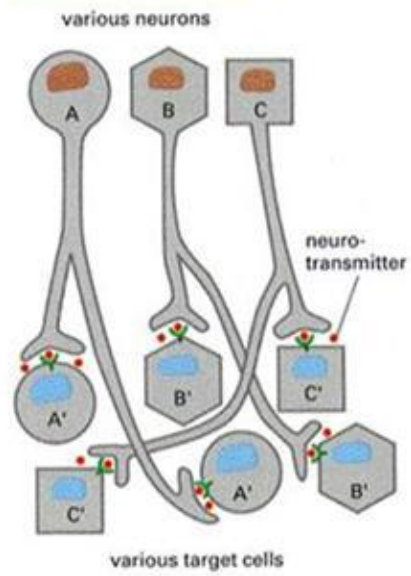
## What can be a signal?

- Peptides - insulin, glucagon...
- Proteins
- Amino acid derivatives - epinephrine, histamine
- Other small biomolecules - ATP
- Steroids, prostaglandins
- Gases - Nitric Oxide (NO)
- Photons
- Damaged DNA
- Odorants, tastants

(A) ENDOCRINE SIGNALING



(B) SYNAPTIC SIGNALING



# Types of Cell Signaling

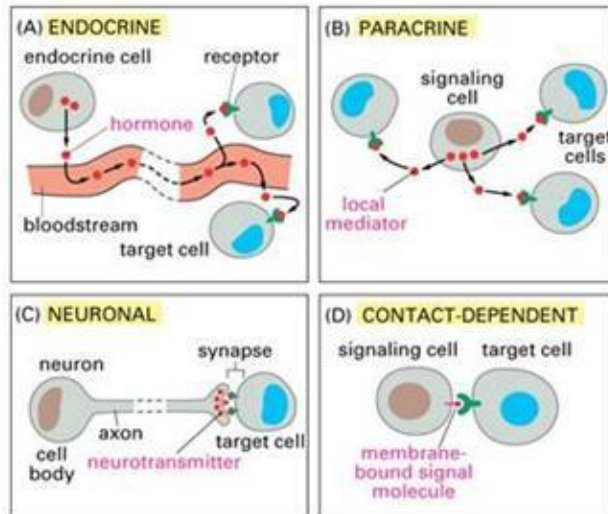


Figure 16-3. Essential Cell Biology, 2/e. (© 2004 Garland Science)

# The same signal can produce different effects in different cells

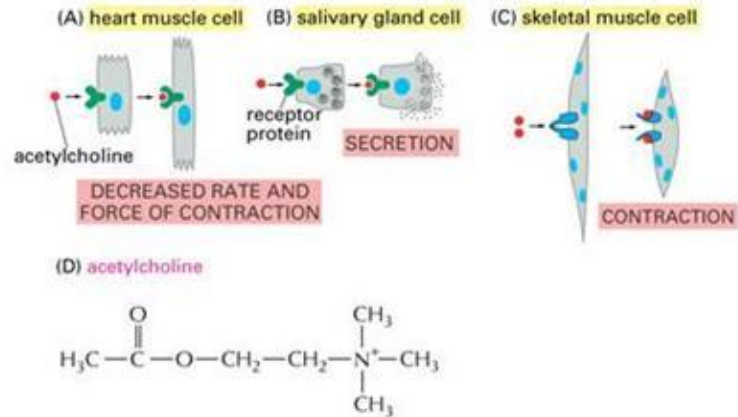


Figure 16-5 Essential Cell Biology, 2/e. (© 2004 Garland Science)

- **Types of Signals based on Where they Bind**
  - To an intracellular receptor:  
e.g. Steroid hormones
  - To a cell-surface receptor: G-protein linked, enzyme-linked, or ion channel-linked

# Cell Signaling

- A. Ligand gated ion channel
- B. Cell Surface Receptors: G-protein linked receptors
- C. Tyrosine kinase linked type
- D. Intra cellular steroidal type

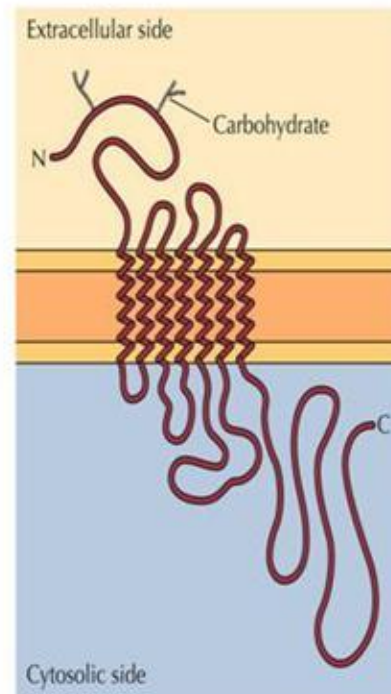


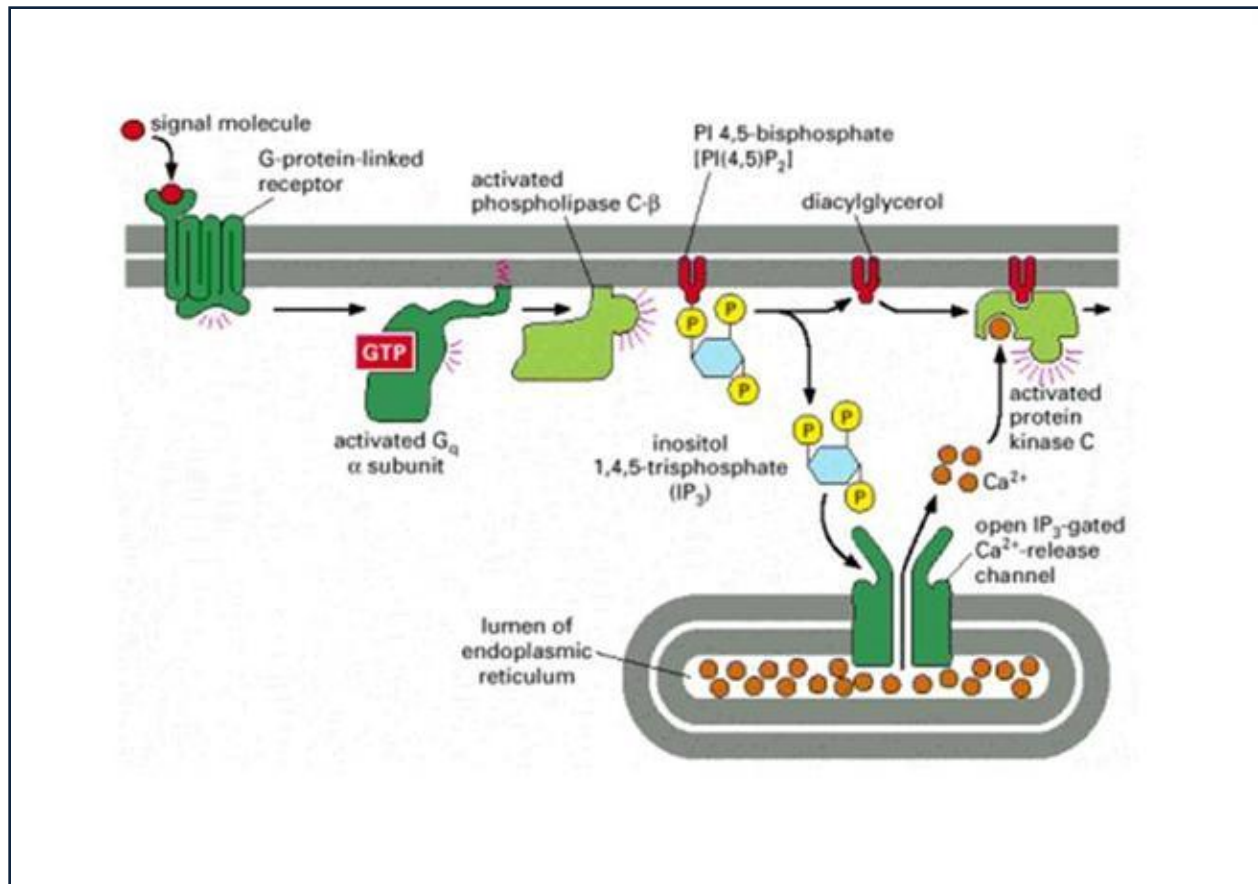
## Cell Surface Receptors: G-protein linked receptors

- **Largest family of cell surface receptors**
  - Different ones respond to a wide variety of mediators including different hormones, neurotransmitters, local mediators
  - Examples: Receptors to epinephrine, acetylcholine, serotonin

# Functions of Cell Surface Receptors

- G proteins are **guanine nucleotide-binding proteins** that assist in transmitting signals to intracellular targets.
- **G protein-coupled receptors** are structurally and functionally related proteins characterized by seven membrane-spanning  $\alpha$  helices.
- **cAMP** is an important second messenger that mediates cellular responses to a variety of hormones.

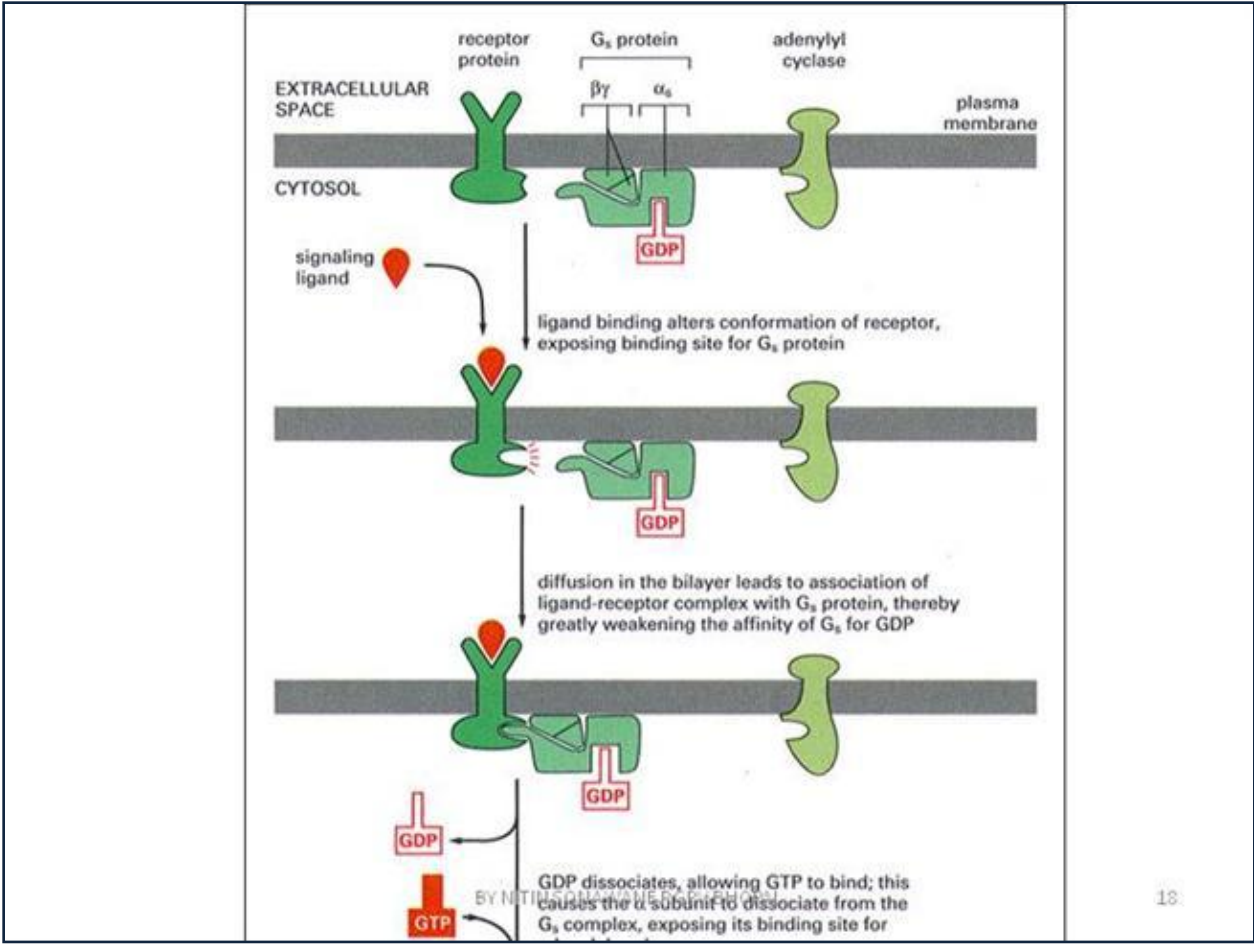


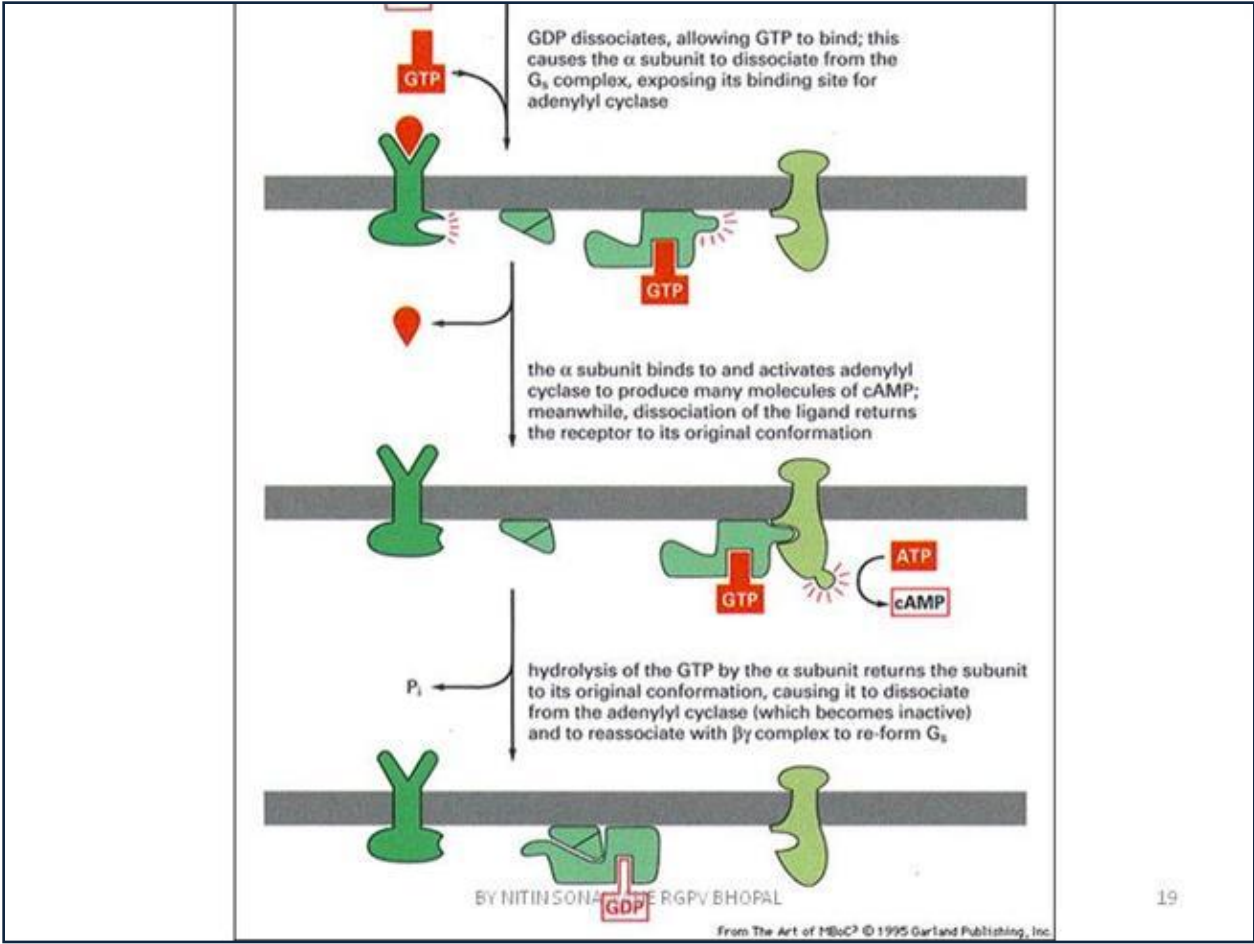


- What do G-protein receptors do?
  - G-protein receptors activate trimeric G-protein
  - Activated G-protein alters the cellular concentration of a “second messenger”: usually cyclic AMP or Ca $^{2+}$
  - The second messenger activates a protein kinase enzyme
  - The protein kinase phosphorylates another enzyme and alters its activity

- Trimeric G-proteins disassemble when activated
  - Three chains:  $\alpha$ ,  $\beta$ , and  $\gamma$
  - $\alpha$  chain binds and hydrolyzes **GTP**
  - $\beta$  &  $\gamma$  chains form a tight complex  $\beta\gamma$  that anchors G-protein to the plasma membrane

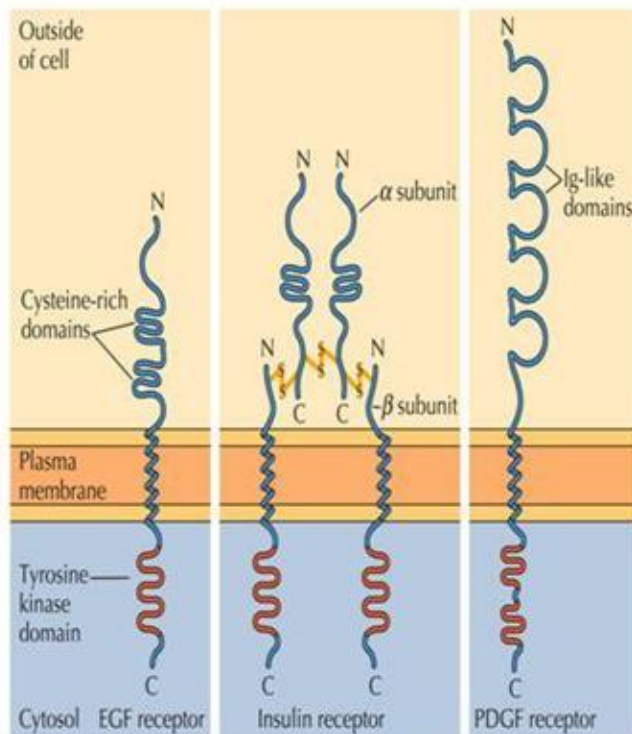
- Trimeric G-proteins disassemble when activated
  - Inactive G-protein has a bound GDP
  - When activated: GDP dissociates, new GTP is bound
  - This causes  $\alpha$  to dissociate from  $\beta\gamma$
  - $\alpha$  binds to adenylate cyclase, altering its activity
  - $G_s$  protein stimulates activates adenylate cyclase,  $G_i$  inhibits it

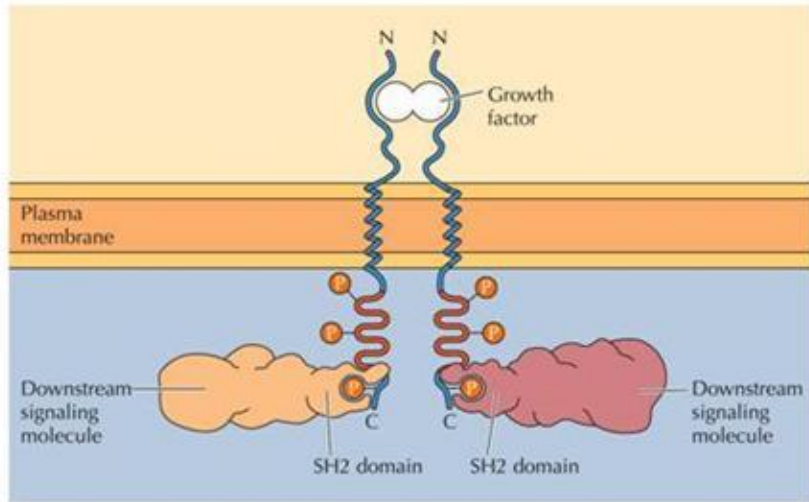




# Receptor Protein-Tyrosine Kinases

- **Receptor protein-tyrosine kinases** phosphorylate their substrate proteins on tyrosine residues.
- The human genome encodes **59 receptor protein-tyrosine kinases**, including the receptors for EGF, NGF, PDGF, insulin, and many other growth factors.







## Intracellular Receptor Signaling: Steroid Hormones

- Overview of Steroid Hormone Action:
  - Steroid hormone (small, hydrophobic) is secreted by glandular cells and released into bloodstream (usually transported via shuttle proteins)
  - The hormone enters the cytoplasm of cells
  - In the cytoplasm of target cells, the hormone binds to steroid hormone receptor protein

## Intracellular Receptor Signaling: Steroid Hormones

- Overview of Steroid . . . (cont.):
  - The steroid-receptor complex is translocated into the nucleus, where it activates the transcription of the primary response genes
  - Transcription of the primary response genes, followed by translation, results in the production of primary response proteins

## Intracellular Receptor Signaling: Steroid Hormones

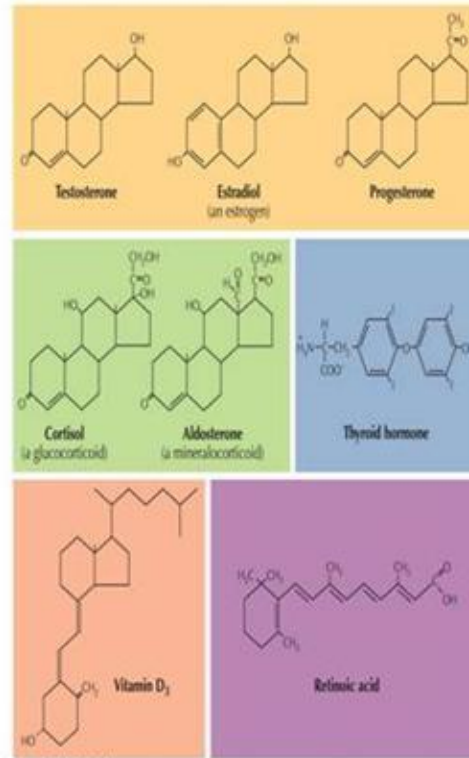
- Overview of Steroid . . . (cont.):
  - The primary response proteins usually inhibit further transcription of their own genes, and they may activate transcription of secondary response genes.

# Steroid Hormones and the Nuclear Receptor

- **Hormones** are signaling molecules that are produced by endocrine glands that act on cells at distant body sites.

- **Steroid hormones** are a group of hydrophobic hormones that are derivatives of cholesterol.

- **Testosterone** is a steroid hormone produced by the testis.



# Steroid Hormones and the Nuclear Receptor Superfamily

- **Estrogen and progesterone** are steroid hormones produced by the gonads.
- **Corticosteroids** are steroid hormones produced by the adrenal gland.
  - **Glucocorticoids** are steroids produced by the adrenal gland that act to stimulate production of glucose.
  - **Mineralocorticoids** are steroid hormones produced by the adrenal gland that act on the kidney to regulate salt and water balance.
- **Thyroid hormone** is synthesized from tyrosine in the thyroid gland and it plays important roles in development and regulation of metabolism.
- **Vitamin D<sub>3</sub>** regulates Ca<sup>2+</sup> metabolism and bone growth.
- **Retinoic acid** is a signaling molecule synthesized from vitamin A. Retinoids play important roles in vertebrate development and are synthesized from vitamin A.
- The **nuclear receptor superfamily** is a family of transcription factors that includes the receptors for steroid hormones, thyroid hormone, retinoic acid, and vitamin D<sub>3</sub>.