

ENDOCRINOLOGY

Mechanisms of Hormone Action

Hormone: chemical substance classified as peptide/steroid/amine; synthesized and secreted by endocrine cells commonly found in endocrine glands (hypothalamus; anterior + posterior lobes of pituitary; thyroid; parathyroid; adrenal cortex; adrenal medulla; gonads; placenta; pancreas; kidney)

Affinity: ability of the receptor to bind to ligand

Specificity: hormone can act at more than one receptor

Modes of cytokine action:

- **Autocrine:** cytokine act on cell which produces it
- **Paracrine:** cytokine act on adjacent cells
- **Juxtacrine:** cytokine released from cell by exocytosis and docks onto receptors on adjacent cells
- **Endocrine:** cytokine enters circulation to reach distant targets

Second Messenger Action

Major mechanisms of hormone action and associated second messengers

- **Adenylyl cyclase mechanism: cAMP**
 - Hormone binds to a receptor; coupling by Gs/Gi protein; activation/inhibition of adenylyl cyclase; increases/decreases in intracellular cAMP; cAMP amplifies hormonal signal
 - Hormone binds to receptor → conformational change in α -subunit which is replaced by GTP → α s-GTP complex migrates and binds to/activates adenylyl cyclase which then converts ATP to cAMP → activation of PKA by cAMP → phosphorylation of intracellular proteins
 - cAMP degraded to inactive 5' AMP by phosphodiesterase
- **Phospholipase C mechanism: IP3/Calcium**
 - Hormone binds receptor → conformational change in α -subunit → GDP released from α -subunit and replaced by GTP; α q subunit detaches from Gq protein → α q-GTP complex migrates, binds and activates PLC → PLC frees DAG and IP3 from PIP2 → IP3 increases intracellular calcium via release of calcium from intracellular ER/SR stores → calcium and DAG activate PKC → protein phosphorylation
- **Steroid hormone mechanism: insulin and IGFs** (via tyrosine kinase mechanism)
 - Steroid hormone diffuses across cell membrane and binds close to C-terminus of target receptor protein in cytosol/nucleus at steroid responsive elements (SREs; found at 5' region of target genes); hormone-receptor complex = transcription factor regulating rate of gene transcription; new mRNA is transcribed, leaves nucleus, is translated to new proteins
- **Guanylate cyclase: cGMP**
 - Extracellular domain of guanylyl cyclase receptor domain has binding site for ANP; intracellular domain has guanylyl cyclase activity
 - ANP binds → activates guanylyl cyclase → GTP converted to cyclic GMP → cGMP activates cGMP-dependent kinase → protein phosphorylation