

Introduction to Cellular Signaling

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Fundamentals, components, and major pathways

1. Why Cells Need Signaling

- **Coordination:** Enables single-cell organisms to respond to the environment and multicellular organisms to synchronize tissue/organ function.
 - **Homeostasis:** Maintains internal conditions (e.g., glucose level, calcium concentration).
 - **Development & Differentiation:** Directs cell fate, migration, and organogenesis.
 - **Adaptation & Survival:** Triggers stress responses, apoptosis, or proliferation as needed.
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2. Core Concepts

Term	Definition
Ligand	Extracellular molecule (hormone, growth factor, neurotransmitter, cytokine, etc.) that initiates a signal.
Receptor	Protein (membrane-bound or intracellular) that specifically binds a ligand and converts the binding event into a cellular response.
Signal Transduction	Sequence of molecular events that convey the signal from the receptor to downstream effectors.
Second Messenger	Small intracellular molecules (cAMP, Ca ²⁺ , IP ₃ , DAG) that amplify and propagate the signal.
Effector	Protein or enzyme that executes the final cellular response (e.g., kinase, transcription factor).
Feedback	Positive or negative regulation that modulates signal strength/duration.
Crosstalk	Interaction between distinct signaling pathways, allowing integration of multiple cues.

3. General Steps in a Signaling Pathway

1. **Reception** – Ligand binds to its receptor.

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2. **Transduction** – Conformational change ? activation of intracellular proteins (often via phosphorylation).
 3. **Amplification** – One activated receptor can generate many second?messenger molecules, increasing signal strength.
 4. **Response** – Activation/inhibition of target proteins, changes in gene expression, cytoskeletal rearrangement, secretion, etc.
 5. **Termination** – Signal is turned off by ligand degradation, receptor internalization, phosphatases, or feedback inhibitors.
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4. Major Types of Receptors

Category	Location	Typical Ligand	Signal?Transmission Mechanism
Ion?channel (Ligand?gated)	Plasma membrane	Neurotransmitters (e.g., GABA, acetylcholine)	Ligand binding opens channel ? ion flux (Na?, Cl?, Ca ²⁺) ? rapid depolarization/hyperpolarization
G?protein?coupled receptors (GPCRs)	Plasma membrane	Hormones, photons, odorants	Ligand ? conformational change ? G? protein activation ? downstream effectors (adenylyl cyclase, PLC, ion channels)
Receptor tyrosine kinases (RTKs)	Plasma membrane	Growth factors (EGF, insulin)	Dimerization ? autophosphorylation ? recruitment of adaptor proteins ? MAPK, PI3K pathways
Serine/Threonine kinase receptors	Plasma membrane	TGF?? family	Ligand?induced heteromeric complex ? serine/threonine phosphorylation ? SMAD signaling
Intracellular (Nuclear) receptors	Cytoplasm or nucleus	Steroid hormones, thyroid hormone, retinoic acid	Ligand diffuses in ? receptor?ligand complex binds DNA ? transcriptional regulation
Cytokine receptors (non?kinase)	Plasma membrane	Interleukins, interferons	