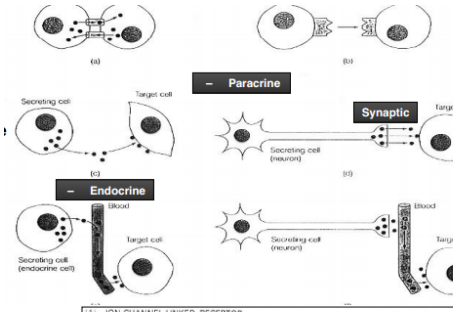
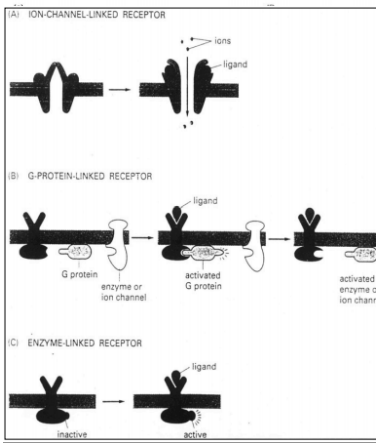
Lecture 2– Cell Signalling Overview



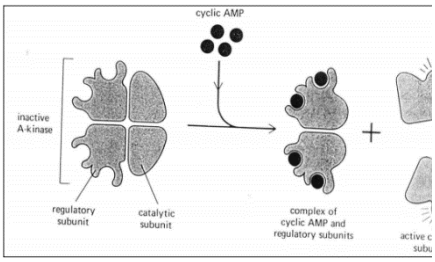
Types of Signals

- **Endocrine signals** involve a cell releasing a substance into the *bloodstream that eventually reaches the target cell (e.g. insulin is released from pancreatic cells to reach liver cells via hepatic bloodstream).* Endocrine signals are slow, diffuse, have a longer response time and take longer to turn off *(e.g. release of sex hormones during puberty).*
    - They have a lower hormone concentration at target but have a high affinity receptor
- **Paracrine signals** involve a cell releasing a *substance onto an adjacent cell (e.g. the synaptic terminal).* These signals are fast, precise and have a sharp on/off switch *(e.g. calcium acting on Ryanodine Receptors for muscle contraction).*
    - They have a high transmitter concentration and low affinity receptor
- **Autocrine signals** involve the release of transmitter that acts on the cell itself. Signals include *proteins/peptides, amino acid derivatives (histamine & thymine), fatty acids and their derivatives (prostaglandins), cholesterol derivatives (steroids), gases (NO, CO) and ions (Ca2+).*



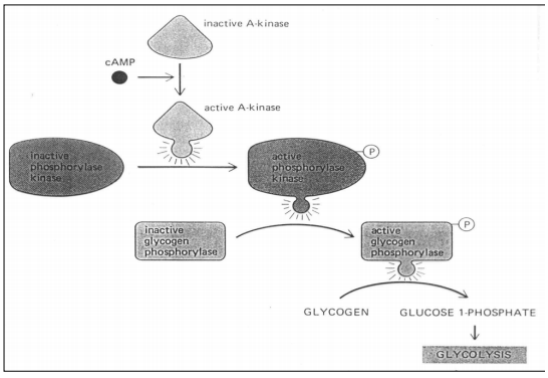
Receptors

- Intracellular: Intracellular receptors have hormone or gas ligands that can diffuse through the cell wall. They are usually enzyme linked (cGMP or NO).
- Surface: Surface receptors can be channel or enzyme linked, or can be G Protein Linked (the activation of which opens a channel or activates an enzyme through phosphorylation).
    - Ligand binding or phosphorylation in a G Protein alters the shape and confirmation of the protein, which causes a change in function. This allows for the opening of an ion-gated channel.
    - One example is the C Terminal of the Beta Adrenergic Receptor.



Adrenaline Example

- **Adrenalin** binds to the **Adrenergic Receptor.** The activated receptor-ligand complex binds to and activates **G-Protein** which activates **Adenylyl Cyclase** and allows for the synthesis of **Cyclic AMP** from **ATP.**
- Cyclic AMP binds to **Protein Kinase-A** via the *Regulating Subunit.* This stops it from binding to the **Catalytic Subunit** and becomes active.
- Active PKA the binds to **inactive Phosphorylase Kinase** to activate it via *phosphorylation* and converts *Glycogen to G1P.* This induces **Glycogenolysis.**



Other Examples

- **Cyclic AMP** activates **PKA.** PKA phosphorylates **CREB** *(cAMP response element binding protein – which binds to the promoter region of DNA).* Transcription of genes is increased. This leads to altered levels of particular proteins.
- **TGF-b** ligand binds to receptors **I & II** to attract 2 & 3 **SMAD proteins.** This causes **3 & 4 SMAD** to bind to *co-factors* to form **SBE complex** and allows for protein production.