Signal molecule

A molecule that moves from one cell to another cell as a way to communicate a message between the cells

- To receive the message, the target cell must have a receptor protein that is specific for binding the signal molecule

- Cellular output response = The response of the target cell to the signal molecule

    √ The response is preprogrammed into the target cell

Fig 11.4

Signal molecule categories:

Paracrines = Signal molecules that diffuse between nearby cells

- Example: Histamine is a paracrine that is released from damaged cells

    - It causes nearby blood vessels to become leaky

Hormones = Signal molecules that are carried in the blood

- Example: Epinephrine is a hormone that is released from the adrenal gland when we are frightened or angry

    - It causes liver cells to release glucose

Fig 11.4

Events in target cell:

1) Reception = A receptor protein on the target cell binds the signal molecule

2) Signal transduction = The receptor activates a protein, which activates another protein, which activates another protein, etc. etc.

√ Relay proteins = The proteins in the signal transduction pathway

3) Cellular output response = The final change in the cell's activity as a result of the signal molecule

√ The response is carried out by the activation of one (or a few) protein (the "cellular response protein")

Fig 11.6

Regulation of enzymes by allosteric molecules

Some enzymes are regulated by molecules that change the shape of the enzyme's active site

• Allosteric activators = Molecules that change the shape of the active site such that substrate molecules can fit into it

Fig 8.20

Regulation of enzymes by phosphorylation

Some enzymes are activated when a phosphate group is added to their amino acids

• Kinase = An enzyme that adds a phosphate group to amino acids

√ ATP is the source of the phosphate group

√ Tyrosine kinase = A protein that adds a phosphate to tyrosine amino acids

√ Serine/Threonine kinase = A protein that adds phosphate to serine and threonine amino acids

There are four major types of receptors for signal molecules

• Tyrosine kinase receptors

• G-protein-linked receptors

• Steroid hormone receptors/Intracellular receptors

• Ion channel receptors

Tyrosine kinase (TK) receptors

Receptors that add a phosphate group to tyrosine amino acids

• TK receptors follow four steps after binding signal molecule:

1) The TK receptors form a dimer (a pair)

2) Dimerizing activates the tyrosine kinase enzymatic activity of the TK receptor dimer

3) The TK receptor dimer phosphorylates its own tyrosine amino acids

4) The phosphates on the receptors act as allosteric activators of the first relay protein

Fig 11.7

How a relay protein can activate the next protein in the signal transduction pathway:

• By phosphorylation of the next relay protein

√ Many relay proteins are either serine/threonine kinases or tyrosine kinases

• By release of second messengers (small non-protein molecules that are allosteric activators of the next relay protein)

Fig 11.8

G-protein-linked receptors

Receptors that activate a G-protein

- The receptor and the G-protein are separate membrane proteins, but are usually in contact with each other

- The receptor always have seven membrane-spanning regions

- The G-protein is a relay protein

    √ It is allosterically inhibited by a GDP nucleotide until the receptor binds signal molecule

    √ Binding of signal molecule to the receptor causes the G-protein to exchange GDP for GTP (an allosteric activator)

    √ The activated G-protein will activate other relay proteins in the membrane

        - The membrane enzyme Adenylyl Cyclase and the membrane enzyme Phospholipase C are the two most common targets of the activated G-protein

Fig 11.7

Adenylyl Cyclase

A membrane relay protein that makes the second messenger cAMP

- cAMP = Cyclic AMP, a nucleotide made from ATP

- The cAMP is an allosteric activator of the next relay protein

Figs 11.9 and 11.10

Phospholipase C

A membrane relay protein that makes the second messenger IP_3

- IP_3 = Inositol triphosphate, a molecule made from the hydrophilic head of a certain membrane phospholipid

- The IP_3 is a second messenger

  - It diffuses to the endoplasmic recticulum (ER)

  - It opens a membrane transport protein that allows Ca^{2+} to diffuse from the ER to the cytoplasm

  - The Ca^{2+} is a second messenger that activates the next relay protein

Figs 5.13 and 11.12

Cells have complex signal transduction pathways with many relay proteins for two reasons:

1) To allow different cells to respond differently to the same signal molecule

- Small differences in the signal transduction pathway can result in very different cellular output responses

- Example: Liver cells respond to epinephrine by releasing glucose; Heart cells respond to epinephrine by beating faster

2) To amplify the signal inside the cell

- Each relay protein can activate several of the next relay protein, resulting in an increase in the signal with each step

Figs 11.13 and 11.15

Steroid hormone receptors/Intracellular receptors

Receptors that are within the cell (not in the membrane)

• Most are receptors for steroid hormones

• Steroid hormones are hydrophobic and reach the receptor by passing through the cell membrane

• Steroid hormone receptors cause the cellular response by causing the cell to make the activated cellular response enzyme

√ The receptor/hormone complex binds directly to the gene for the cellular response enzyme, which increases the level of expression of the cellular response enzyme

Ion channel receptors

Receptors that are membrane transport proteins for ions

• Mostly found on nerve cells

√ The receptor binds neurotransmitter molecules (signal molecules between nerve cells)

• The neurotransmitter causes the ion channel receptor to open, allowing ions to enter the nerve cell

- Na^+ and Ca^{2+} are common transported ions

• The ions change the electrical potential (voltage) of the cell

- The voltage change is used by nerve cells to communicate between body parts