

Unit-2

Secondary messengers

Secondary messengers are small molecules inside the cell that carry signals from a receptor (on the surface) to inside the cell, causing a response.

Cyclic AMP (cAMP)-

Made from ATP by the enzyme adenylate cyclase

Activated by hormones like adrenaline

Activates protein kinase A (PKA) → causes cell response

Involved in: metabolism, heart rate, hormone release

2. Cyclic GMP (cGMP)-

Made from GTP by guanylate cyclase

Activates protein kinase G (PKG)

Helps in: blood vessel relaxation, vision, kidney function

3. Calcium ions (Ca^{2+})-

Stored in the endoplasmic reticulum (ER)

Released into the cytoplasm when needed

Activates many proteins, like calmodulin

Controls: muscle contraction, secretion, nerve signals

4. Inositol 1,4,5-triphosphate (IP_3)-

Made when a membrane lipid (PIP_2) is broken by an enzyme (PLC)

Opens calcium channels in ER $\rightarrow \text{Ca}^{2+}$ is released

Works together with DAG

5. Diacylglycerol (DAG)-

Also made from PIP_2 by PLC (along with IP_3)

Stays in the membrane

Activates protein kinase C (PKC) → leads to cell response

6. Nitric Oxide (NO)-

A gas that works as a secondary messenger

Made from arginine by NO synthase

Activates guanylate cyclase → increases cGMP

Helps in: blood vessel relaxation, brain signals

Messenger	Made From	Main Function
cAMP	ATP	Activates PKA, regulates metabolism
cGMP	GTP	Relaxes blood vessels, activates PKG
Ca^{2+}	ER stores	Muscle, nerve signals, secretion
IP_3	PIP_2	Releases Ca^{2+} from ER
DAG	PIP_2	Activates PKC
NO	Arginine	Increases cGMP, blood flow

cGMP Signaling Pathway -

1. Signal molecule binds to receptor

A signal like nitric oxide (NO) or atrial natriuretic peptide (ANP) binds to a receptor.

The receptor can be soluble guanylate cyclase (for NO) or a membrane-bound receptor (for ANP).

2. Activation of guanylate cyclase

The receptor activates the enzyme guanylate cyclase.

3. Guanylate cyclase makes cGMP

Guanylate cyclase converts GTP (guanosine triphosphate) into cGMP (cyclic GMP).

cGMP acts as a secondary messenger.

4. cGMP activates protein kinase G (PKG)

cGMP binds to and activates PKG (protein kinase G).

PKG adds phosphates to target proteins to cause changes in the cell.

5. Cell response happens

cGMP causes different responses depending on the cell type:

Relaxes smooth muscle (helps lower blood pressure)

Improves blood flow

Helps vision in the retina

6. Signal ends

The enzyme phosphodiesterase (PDE) breaks down cGMP.

This stops the signal.

Summary Flow:

Signal (e.g. NO or ANP)

→ Guanylate cyclase activation

→ cGMP production

→ PKG activation

→ Cell response (like muscle relaxation)

Mitogen-Activated Protein Kinase (MAPK) pathway:

The MAPK pathway is a chain of proteins inside the cell that passes signals from the cell surface to the nucleus.

It helps the cell grow, divide, survive, or respond to stress.

1. Signal binds to a receptor

A growth factor (like EGF) binds to a receptor tyrosine kinase (RTK) on the cell membrane.

2. Receptor activates Ras protein

Ras is a small G-protein that starts the MAPK pathway.

3. Ras activates Raf (MAPKKK)

Raf is the first kinase (MAP kinase kinase kinase).

4. Raf activates MEK (MAPKK)

MEK is the second kinase (MAP kinase kinase).

5. MEK activates ERK (MAPK)

ERK is the final kinase (MAP kinase).

ERK enters the nucleus.

6. ERK turns on specific genes

ERK activates transcription factors that turn on genes for growth, division, or survival.