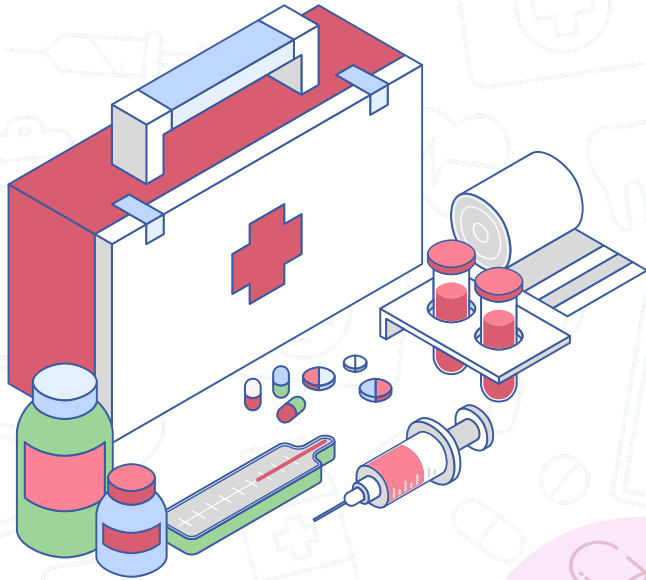


RECEPTORS FAMILIES

442



EDITING FILE



Important
Main text

Male slide

Female slide

Extra info

Doctor notes

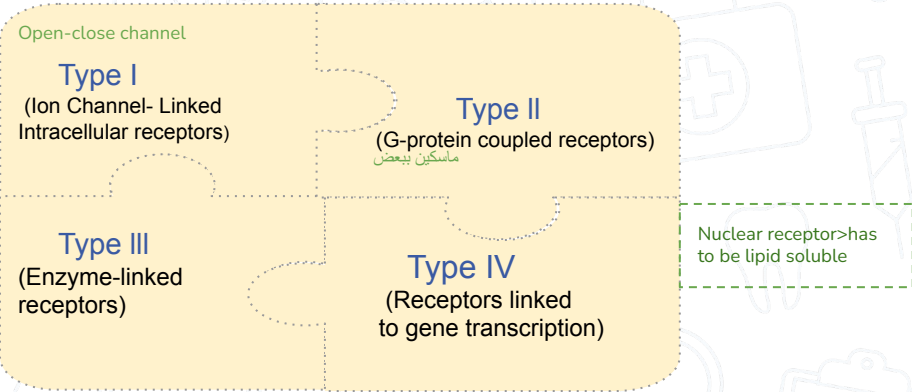
OBJECTIVES

- Classify receptors into their main superfamilies
- Recognize their different transduction mechanisms
- Identify the nature & time frame of their response

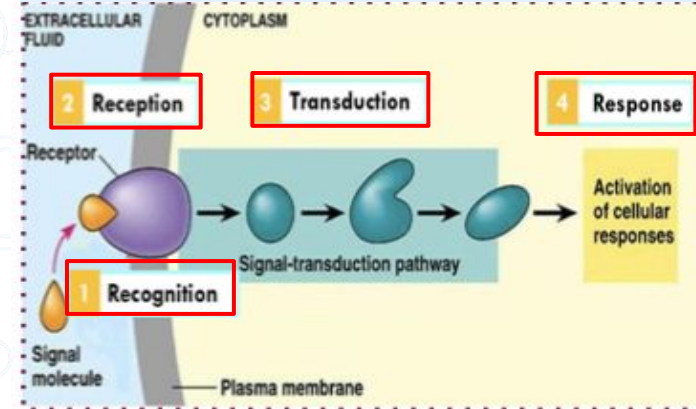
helping
video!!
1 hour (:

Note :the next lecture depend on it try to understand best luck (:

RECEPTOR FAMILIES



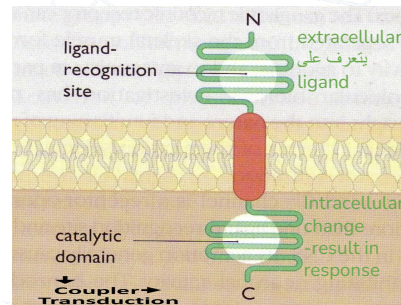
THE DRUG WILL PRODUCE ITS ACTION IN 4 STEPS:



3-intracellular change *how many steps required to reach response? it differs from receptor to another*

A RECEPTOR STRUCTURE :

- Ligand(signal molecule) recognition site.
- Inner catalytic domain (catalysis>break cell)




MAIN RECEPTOR CLASSES (RECEPTOR FAMILIES)

- Effect Persistency of drugs
- Cellular mechanism of the drugs
- Selectivity of drugs
- Development of new drugs

Receptor Families

1, 2 and 3 are surface receptors (on the cell membrane). Type 4 is intracellular receptor

Overview <small>Will discuss in details Next slides</small>	Type I (ion channel-linked)	Type II (G- PCR) 	Type III (Enzyme - linked R)	Type IV (intracellular R)
Location	Membrane	Membrane	Membrane	Nucleus
Coupling	Direct	G-protein Indirect	Direct	Via DNA Indirect
Synaptic transmission	Very fast	Fast	Slow	Very slow
Response	Milliseconds	seconds	Minutes	Hours or days
Examples	Nicotinic receptors	Muscarinic receptors Adrenergic receptor	Insulin receptors	Estrogen steroid receptors
Effectors	Channels	Channels/ enzymes	Enzymes	DNA

Type I : ion channel-linked receptor (ligand gated ion channel)-(ionotropic receptor)

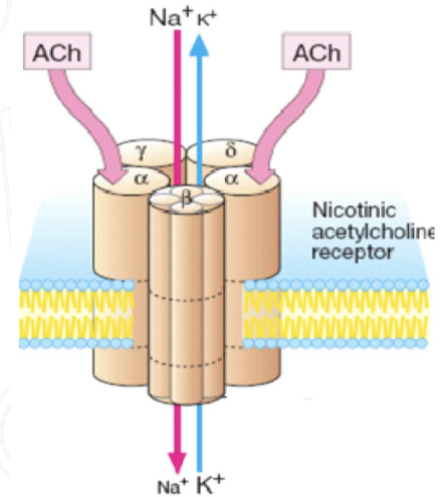
-**Located at cell membrane** (as it's on the cell membrane, it doesn't require to be lipid soluble).

Directly activated by ligand binding. (no second messenger needed)

-**Directly related to ion channels** (when the drug starts produce its effect, the effect will directly change the ion channel, open or close the channel).

- **Involved in very fast synaptic transmission - Response occurs in milliseconds.**

- **E.g: nicotinic acetylcholine** receptor that is activated by occupancy of a ligand as **acetylcholine**



Ion is a
key word
for type 1

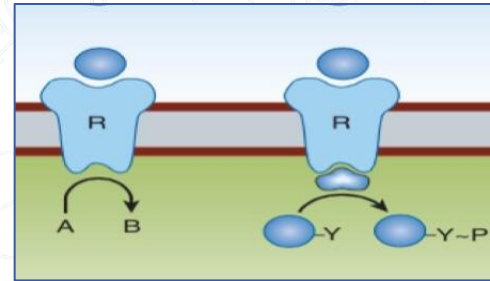
Extra explanation

Nicotinic receptor only found inside ganglia for parasympathetic so it could activate any action related to parasympathetic system the process simply will be
Neuron transmission (Ach) is a ligand -> bind to the receptor ->the receptor will open channel-> High Na intracellular
->depolarisation ->parasympathetic response such as heart relaxation

Type III (Enzyme-Linked receptors) (Tyrosine Kinase-linked receptor)

- Located at **cell membrane**
- Linked to enzyme (with intrinsic enzymatic activity)
- Involved in response to hormones, growth factors.
- They control many cellular functions as **metabolism and growth**.
- **Response occurs in minutes to hours.**

الصورة للتوضيح



Activation of type III receptors

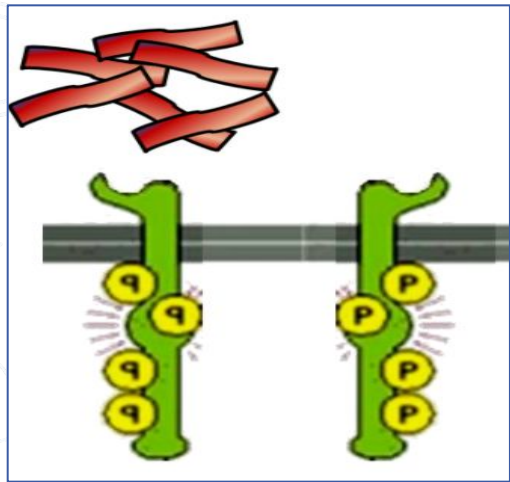
results in

- E.g. **Insulin receptors**

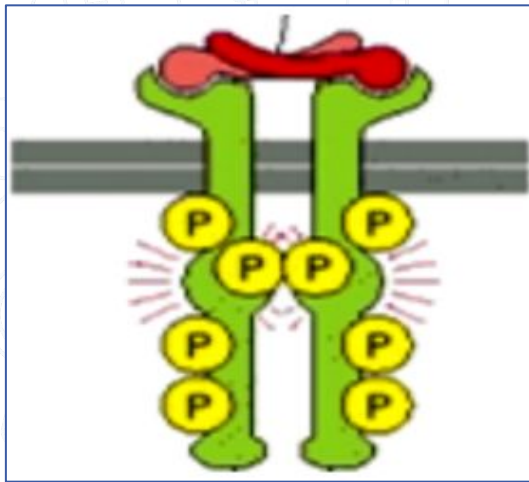
- Dimerization of receptors
- Auto-phosphorylation
- Activation of kinases as tyrosine kinase with phosphorylation of tyrosine residue on their substrates and activation of many intracellular signaling pathways in the cell.

437 TEAM: Kinase enzyme make phosphorylation (adding phosphate) to the tyrosine. Tyrosine located in the intracellular protein, like enzyme

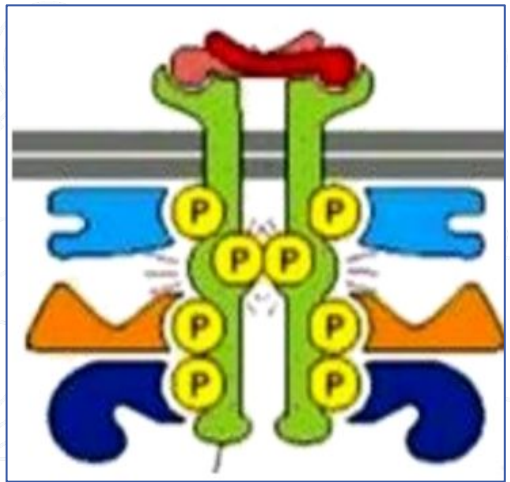
Type III (Enzyme-Linked receptors) (Tyrosine Kinase-linked receptor)



Ligands dimerize receptors
يمسكون مع بعض



Activated Receptor
autophosphorylates



Phosphorylate other proteins
that it docks
Intracellular activity-response-

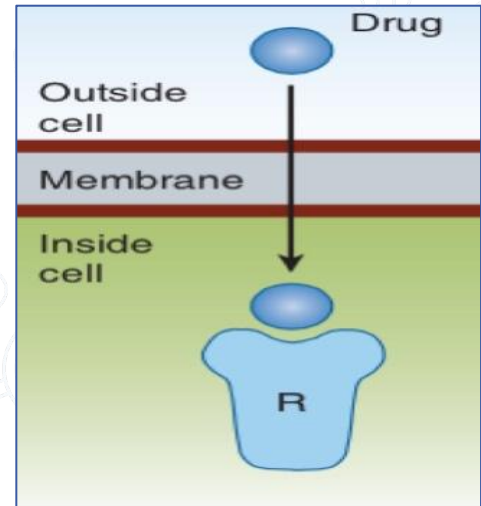
Type IV: Nuclear receptors

Gene transcription receptors

- Located **intracellularly**. (lipid soluble)
- Directly related to DNA (Gene transcription).
- Activation of receptors either **increase** or **decrease** protein synthesis.
- Response occurs in hours or days and **persists longer**.
- Their natural ligands are **lipophilic hormones**; **steroids, thyroids, estrogen**.
- They possess an area that recognizes specific DNA sequence in the nucleus which can bind it. This sequence is called a **Responsive Element [RE]**.
- This means that the activated receptors are acting as: **TRANSCRIPTION FACTORS [TF]** → expressing or repressing target genes.

اعرفوا انه التأثير يكون داخل النواة. Dr.

•E.g. **Estrogen Steroid receptors**

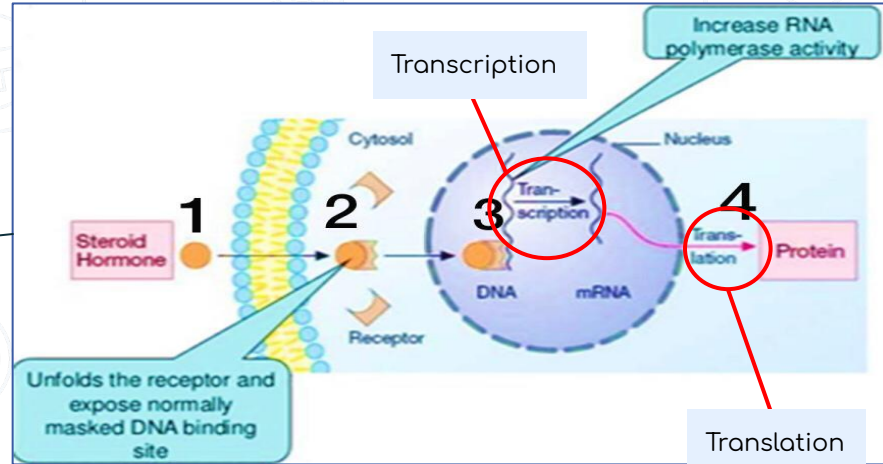


Type IV: Nuclear receptors Gene transcription receptors

فقط للتوضيح

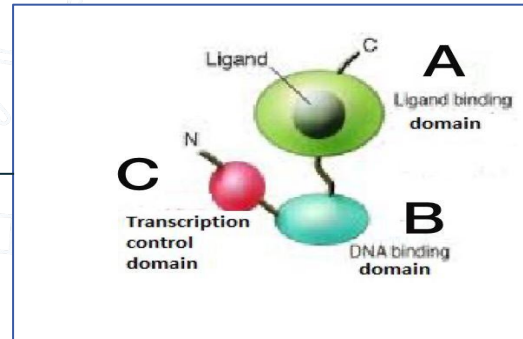
Med 441

- 1- Ligand must be lipophilic hormones so it can pass through the cell membrane.
- 2- When ligand bind to the receptor, ligand's shape will change so it can enter the nucleus.
- 3- Lies on Responsive Element, it either increases or decreases the gene transcription
- 4- The produced protein is either good or not



Med441

- A- where Ligand will bind.
- B- where DNA will bind.
- C- responsible for increasing or decreasing the gene transcription.



Male slides only

Type II Is the Most Abundant Type

(G-Protein coupled receptors)

Metabotropic-metabolism - receptor

- The **largest** family that accounts for many known drug targets.
- Located at **cell membrane**.
- Coupled to intracellular effect via G-protein Response through **ion channels** or **enzymes** (**not direct**)
- Involved in **rapid** transduction Response (α & β) occurs in **seconds**.
- Eg:
 - 1- **Muscarinic** receptors of Ach (M)
 - 2- **Adrenergic** receptors of Noradrenaline (α & β)

1-Muscarinic is receptor for both para and sympathetic system
-Which means it can activate response for both
2-Adrenergic is a receptor only for sympathetic
-which means it can only activate response for sympathetic in this scenario

G-protein coupled receptors

Metabotropic Receptor

-will be discussed in details next slides-

(Guanine nucleotide-binding proteins)

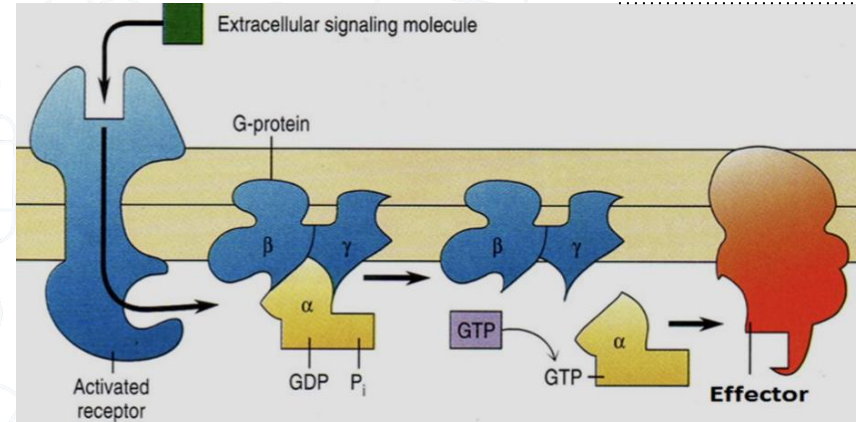
- Regulatory proteins (regulation for intracellular events)
- Comprise of three subunits ($\alpha\beta\gamma$), **α subunits possess GTPase activity.**
- G proteins belong to the larger group of enzymes called **GTPases.**
- Regulate guanine nucleotides GDP, GTP.
- They bind and hydrolyze **guanosine triphosphate** (GTP) to **guanosine diphosphate** (GDP).
- They are active '**on**' when they are bound to **GTP.**
- They are inactive '**off**' when they are bound to **GDP.**

Receptors in this family respond to agonists by:

promoting the binding of GTP to the G protein **alpha (α) subunit.**

GTP activates the G protein and allows it, in turn to activate the effector protein

The G protein remains active until it hydrolyzes the bound GTP to GDP and returns to its ground (inactive) state.

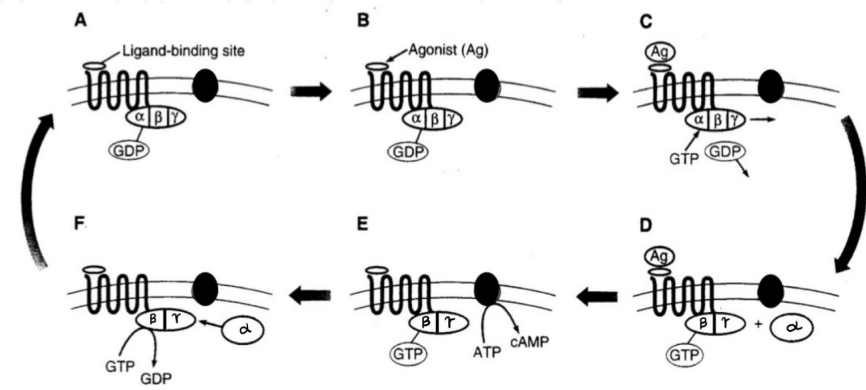


إذا طلعت الفاتصير هي اکتف و البيتا والجاما
اكتف (طلعت وسوت خير لهم ولها)

G-protein classes

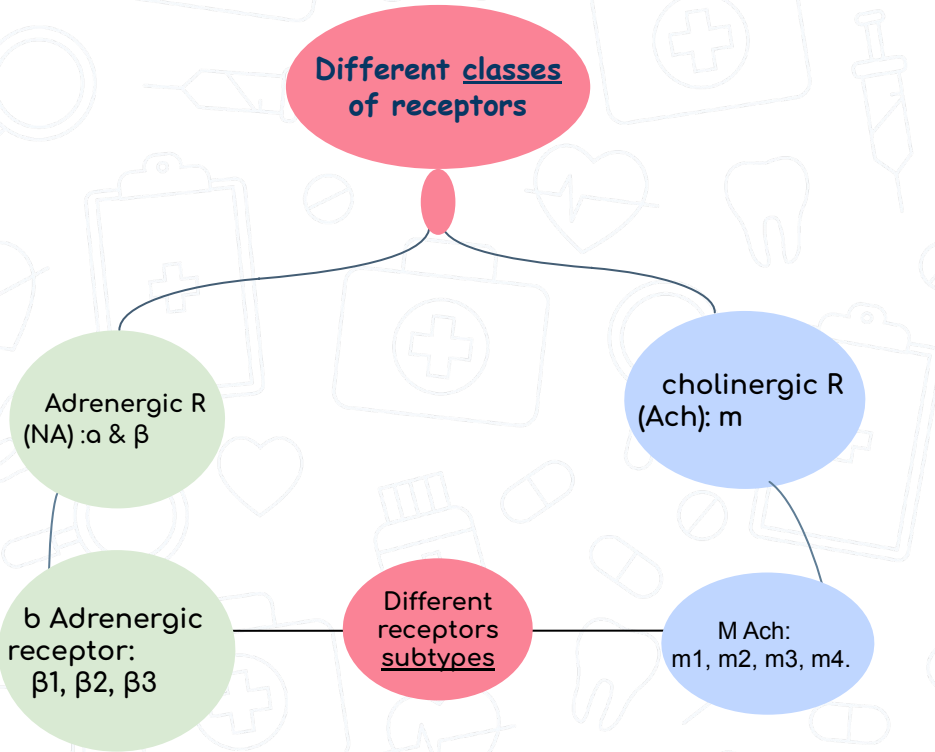
When the G-protein trimer ($\alpha\beta\gamma$), binds to agonist-occupied receptor, the α -subunit dissociates & is then free to activate an effector.

-Activation of the effector is terminated when the bound GTP molecule is **hydrolyzed** to GDP which allow α -subunit to recombine with ($\beta\gamma$) and returns to its inactive state.



Type II receptors (G-Protein-Coupled Receptors)

helping video!!



(Guanine nucleotide-binding proteins) are divided according to their **α-subunits** into:

Gs:
stimulation of the effector
Linked to the CAMP-dependent pathway

Gi: Inhibition of the effector
Linked to the CAMP-dependent pathway

Gq:
(activation, linked to Inositol phosphate system).

Difference in their related G-Protein Classes

Type II : G-Protein Coupled receptors

Enzymes
(To give Second messengers)

Ion channels

• Phospholipase C enzyme Inositol phosphate system (IP3+DAG)

Adenyl cyclase enzyme (AC)
-for ATP-
Cyclic AMP system (cAMP)

E.g. Ach acts on **muscarinic** receptors in heart (opening of K-channel), to decrease heart rate

• Inositol phosphate system (IP3+DAG)

• M1 & M3 Ach receptors couple to Gq to stimulate PLC.

• α_1 Adrenoceptors couple to Gq to stimulate PLC.

Will discuss in detail next slides

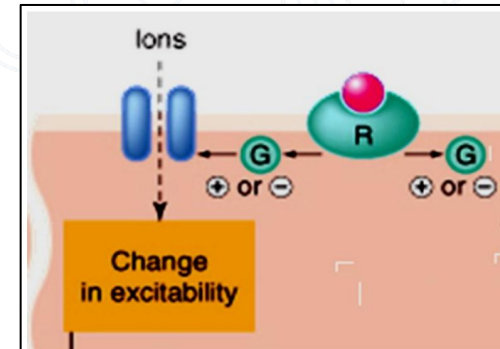
Cyclic AMP system (cAMP):

• M2 & M4 Ach receptors couple to Gi to inhibit AC.

• α_2 Adrenoceptors couple to Gi to inhibit AC.

• β_1 & β_2 Adrenoceptors couple to Gs to stimulate AC

الصورة للتوضيح



IP3 = inositol trisphosphate
DAG = diacylglycerol

cAMP = cyclic adenosine monophosphate

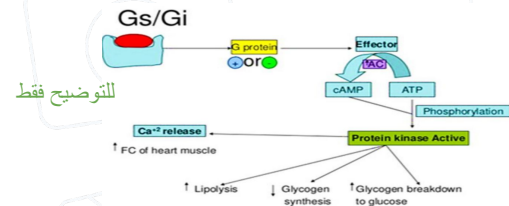
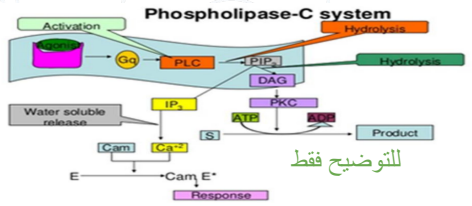
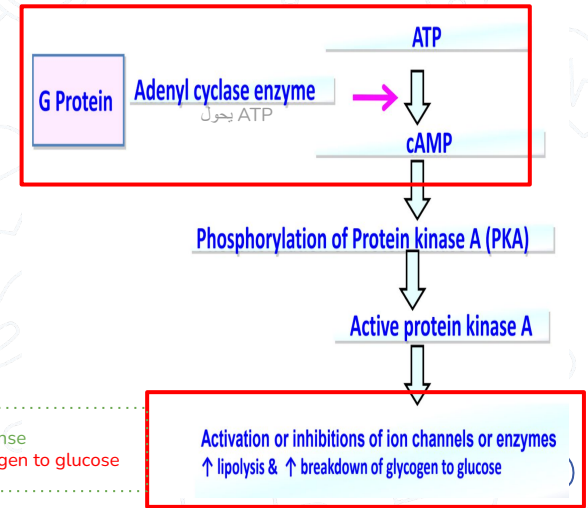
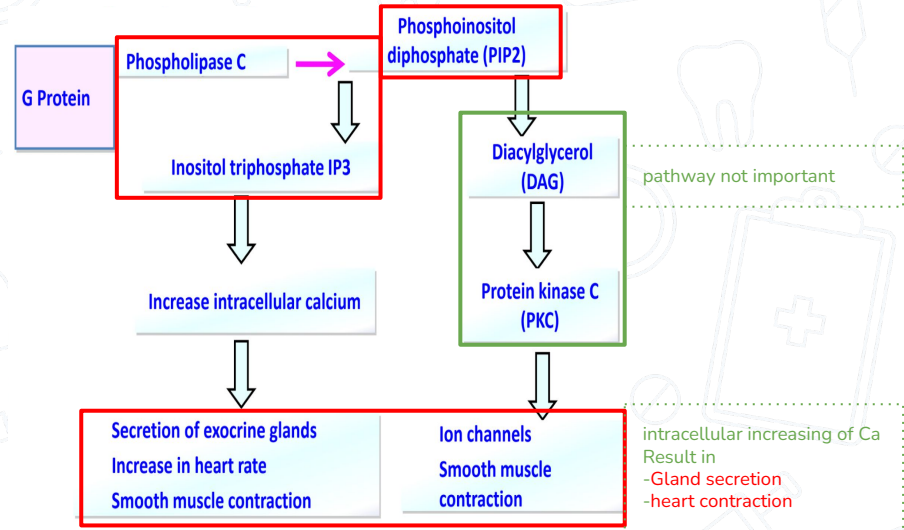
Must understand **all** the pathway
 -red box is the most important


Enzymes (To give Second messengers)

الفكرة بشكل عام
 G first messenger -> activate enzymes
 ->enzymes second messengers
 ->response

Inositol phosphate system

Cyclic AMP system (cAMP)



Adrenoceptors (Alpha & Beta)	Cholinergic receptors (M)
<p>α1 Adrenoceptors couple to G_q to <u>stimulate</u> PLC = Contraction of smooth muscles ◀ second messenger is inositol phosphate system (IP3+DAG)</p>	<p>M1 & M3 Ach receptors couple to G_q to stimulate PLC ◀ second messenger is inositol phosphate system (IP3+DAG)</p>
<p>α2 Adrenoceptors couple to G_i to <u>inhibit</u> AC. ◆ Second messengers is cyclic AMP system (cAMP)</p>	<p>M2 & M4 Ach receptors couple to G_i to <u>inhibit</u> AC ◆ Second messengers is cyclic AMP system (cAMP)</p>
<p>β1 & 2 Adrenoceptors couple to G_s to <u>stimulate</u> AC ◆ Second messengers is cyclic AMP system (cAMP)</p>	 <p>The diagram illustrates five types of cholinergic receptors (M1-M5) and their associated G proteins. Each receptor is shown as a multi-subunit protein with a stem connecting to a G protein. M1, M2, and M3 are coupled to Gq (blue). M4 and M5 are coupled to Gi (orange). M2 is also coupled to Gs (green).</p>
<p>- Adrenaline binds to α2 Adrenoceptors that will activate Gi (Inhibitory) protein. Gi protein will inhibit (AC) that will decrease cAMP Concentration = Decrease contraction.</p> <p>- Adrenaline works on heart muscles by binding to β2 Adrenoceptors, that will activate Gs (Stimulatory) protein. Gs protein will activate (AC), that will increase cAMP Concentration = Increase muscle contraction (tachycardia)</p> <p style="text-align: center;">Thx for #438</p>	<p>- Acetylcholine works on bronchi by M3 Ach receptor that will activate Gq proteins and Gq proteins will activate (PLC) phospholipase c that will increase Ca concentration = Increase contraction of smooth muscles</p> <p>- Adrenaline works on smooth muscles by a 1 receptor that will activate Gq proteins and Gq proteins will activate (PLC) that will increase Ca concentration = Increase contraction</p>

Important slide

Ach receptors	Couple to	Intracellular mechanism	
M1 stimulatory	Gq	stimulate PLC	stimulation
M2 inhibitory	Gi	Inhibit AC (cAMP) Opening of K-channels	:Heart (Bradycardia) (slow heart rate)
M3 stimulatory	Gq	stimulate PLC	Contraction of Smooth muscles (bronchoconstriction)
M4 inhibitory	Gi	Inhibit AC (cAMP)	Inhibition

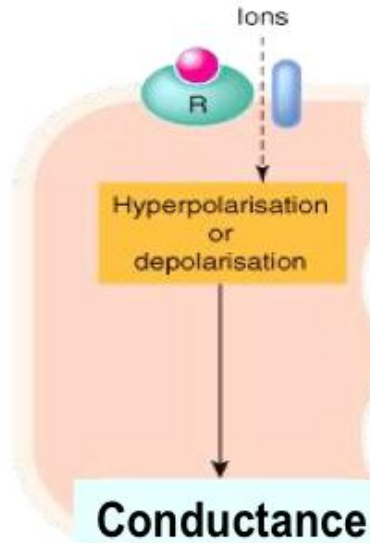
الأعداد الفردية :
stimulate
الأعداد الزوجية:
Inhibit

Adrenoceptors	Couple to	Intracellular mechanism	Sympathetic system response
β 1 stimulatory	Gs	stimulate AC	Stimulation (tachycardia Increase heart rate Because \uparrow Ca)
α 1 stimulatory	Gq	stimulate PLC	Contraction of smooth muscles

Signaling mechanism



1. Ligand-gated ion channels (ionotropic receptors)



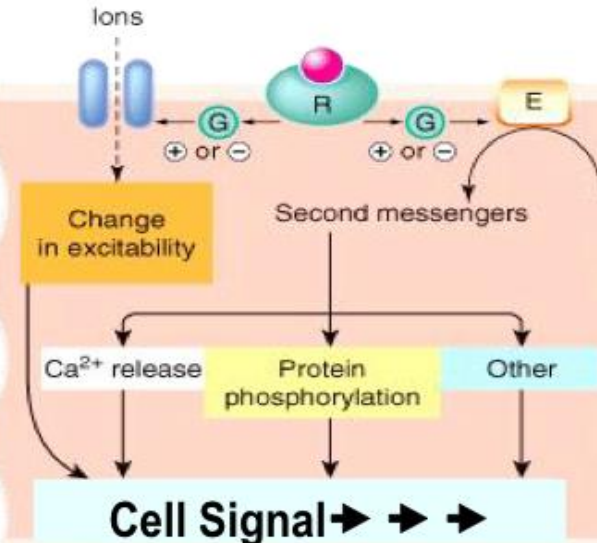
Time scale

Milliseconds

Examples

Nicotinic ACh receptor

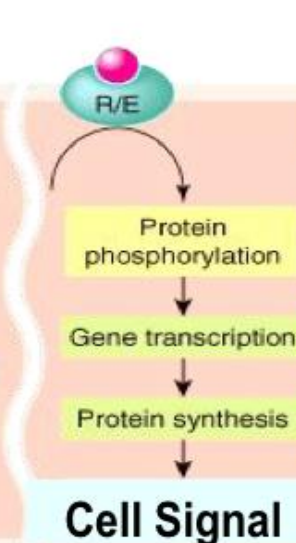
2. G-protein-coupled receptors (metabotropic)



Seconds

Muscarinic ACh receptor

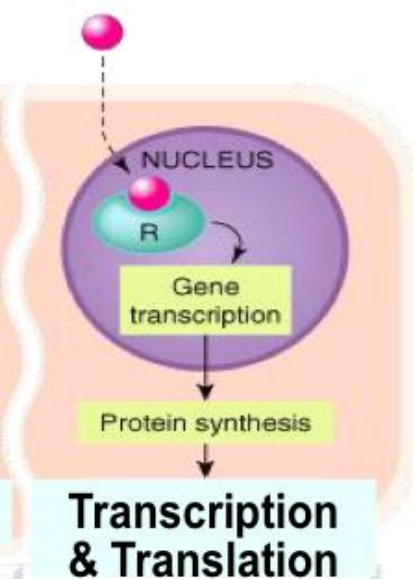
3. Kinase-linked receptors



Minutes / Hours

Cytokine receptors

4. Nuclear receptors



Hours / Days

Oestrogen receptor

RECEPTORS FAMILIES

Summary	Type I	Type II	Type III	Type IV
Location	Membrane	Membrane	Membrane	Nucleus
Coupling	Direct	G-Protein	Direct	Via DNA
Synaptic transmission	Very Fast	fast	slow	Very slow
Response	milliseconds	Seconds	minutes	Hours or days
Examples	Nicotinic receptor	-muscarinic Receptors -adrenergic receptors	Insulin receptors	Estrogen Steroid receptors
Effectors	channels	Channels/enzymes	Enzymes	DNA

MCQ

Q-1 Which one of these G-Protein classes work as an inhibitor of the effector?

- A) Gs. B) Gi. C) Gq. D) Both A&B

Q-2 Their natural ligands are lipophilic

- A-Type I Receptors B-Type II Receptors C-Type III Receptors D-Type IV Receptors

Q-3 which of the following receptors is coupled with Gq protein ?

- A) Alpha 1. B) Alpha 2. C) Beta 1. D) Beta 2

Q-4 When a ligand / Molecule comes near to a receptor, the first action will occur is

- A-Reception. B- Transduction C- Recognition D- Response(effect)

Q-5 Its Response occurs in hours or days and persists longer

- A) Type 2. B) Type 4. C) Type 1 D) Type 3

1-B

2-D

3-A

4-C

5-B

The logo for 'SAQ' (Short Answer Question) is positioned at the top left. It features the letters 'SAQ' in a bold, blue, sans-serif font. To the left of the text are several medical icons: a syringe with red liquid, a white pill with a blue line, and a green pill with a white line. The background of the entire slide is a light blue pattern of various medical icons, including first aid kits, pills, syringes, hearts, and magnifying glasses.

SAQ

Q-1 Which system gets activated when acetylcholine binds to M1 or M3 via Gq receptor ?

Q-2 Inositol phosphate system activates which enzyme ?

Answers

1- Inositol phosphate system

2- Phospholipase C enzyme

You GOT
THIS!

Special thanks to 441 team



DONE BY THE AMAZING TEAM

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