






# Receptor Families



If you didn't  
understand any part  
from this lecture  
Click here!

-  **Important**
-  **In male and female slides**
-  **Only in male slides**
-  **Only in female slides**
-  **Extra information**

# Objectives



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

Any Future corrections will be posted  
on the editing file.  
make sure to check it **frequently**

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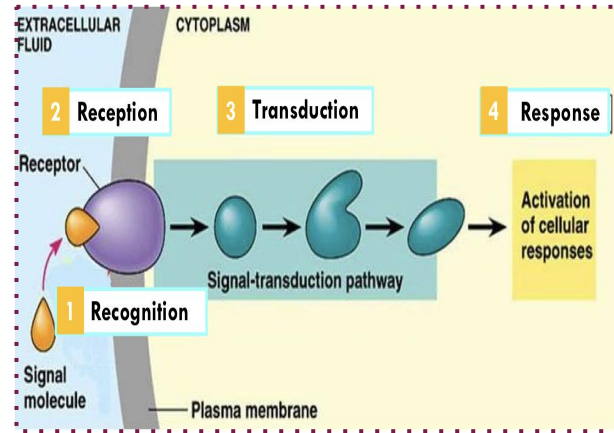
## Main Receptor classes ( Receptor Families)

Effect persistency of drugs

Cellular mechanism of the drugs

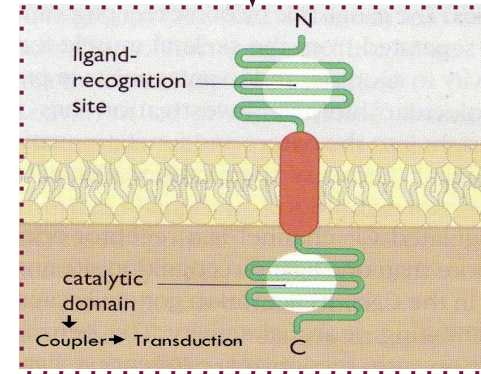
selectivity of drugs

Development of new drugs



### Receptor Structure:

- Ligand recognition site
- Inner catalytic domain



Type 1

Ion channel-linked receptor

Type 2

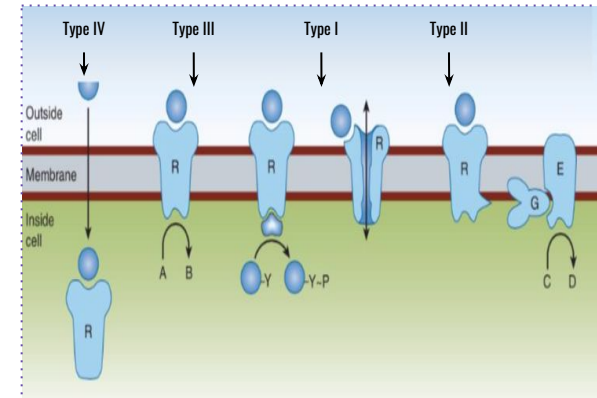
G-protein coupled receptor

Type 3

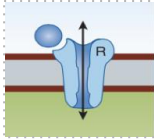
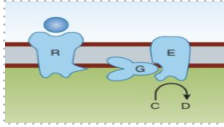
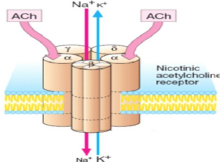
Enzyme-linked receptor

Type 4

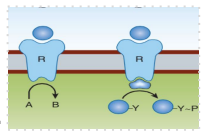
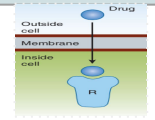
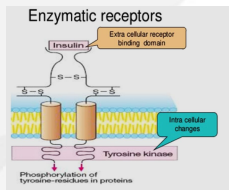
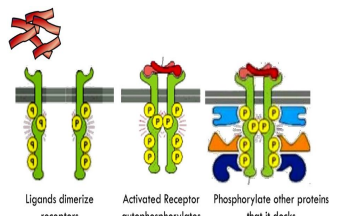
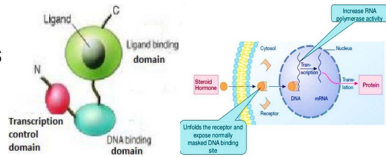
Receptors linked to gene transcription



# Receptors Families

	Type I	Type II
Known as	<ul style="list-style-type: none"> <li>• <b>Ion channel-linked receptors</b></li> <li>• Ligand gated ion channels</li> <li>• Ionotropic receptor</li> <li>• Ionotropic receptors</li> </ul> 	<ul style="list-style-type: none"> <li>• <b>G-Protein coupled receptors</b></li> <li>• Metabotropic Receptor</li> </ul> <p>The <b>largest</b> Family that accounts for many known drugs</p> 
Location	Located at <b>cell membrane</b>	Located at all <b>cell membranes</b>
Coupling	<ul style="list-style-type: none"> <li>• Directly activated by ligand binding</li> <li>• Directly related to ion channels.</li> </ul>	<ul style="list-style-type: none"> <li>• Response through ion channels or enzymes</li> <li>• Coupled to G-protein</li> </ul>
Synaptic transmission	<b>very fast</b> (milliseconds)	Involved in rapid transduction, <b>response occurs in seconds</b>
Example	<p><b>nicotinic receptors</b> (activated by occupancy of a ligand as acetylcholine)</p> 	<ul style="list-style-type: none"> <li>• <b>Muscarinic receptors</b> of Ach (M)</li> <li>• <b>Adrenergic receptors</b> of Noradrenaline (Alpha and Beta)</li> </ul>

# Receptors Families

	Type III	Type IV
Known as	<ul style="list-style-type: none"> <li>Enzyme-Linked receptors</li> <li>Tyrosine Kinase-linked receptor</li> </ul> <p>They control many cellular functions as metabolism and growth.</p> 	<ul style="list-style-type: none"> <li>Receptors linked to gene transcription</li> <li>Nuclear receptors</li> </ul> <p>Their natural ligands are lipophilic hormones; steroids, thyroids, Estrogen.</p> 
Location	Located at <b>cell membrane</b> (with intrinsic enzymatic activity)	Located <b>intracellularly</b>
Activation of receptors results in:	<ol style="list-style-type: none"> <li>Activation of protein kinases as tyrosine kinase with phosphorylation of tyrosine residue on their substrates.</li> <li>activation of many intracellular signaling pathways in the cell.</li> </ol>	Could either increase or decrease Protein synthesis.
Direct/Indirect	Involved in response to: growth factors, hormones ( controls metabolism)	Directly related to DNA (Gene transcription).
Synaptic transmission	<b>Response occurs in minutes to hours.</b>	<b>Response occurs in hours or days and persists longer.</b>
Example	<b>Insulin receptors.</b>	<b>Estrogen Steroid receptors</b>
	<p>Enzymatic receptors</p>  	<p>-They possess an area that recognizes specific DNA sequence in the nucleus which can bind it. This sequence is called a <b>Responsive Element [RE]</b>.</p> <p>-This means that the activated receptors are acting as <b>TRANSCRIPTION FACTORS [TF]</b> (i.e. expressing or repressing target genes.)</p> <p>Prof not : (مش عيزاكم تعرفوها :)</p> 

- GTP binding regulatory proteins
- Regulate guanine nucleotides GTP,GDP
- Comprise of 3 subunits (Alpha,Beta,Gamma), Alpha subunit possess GTPase activity

## G-protein classes

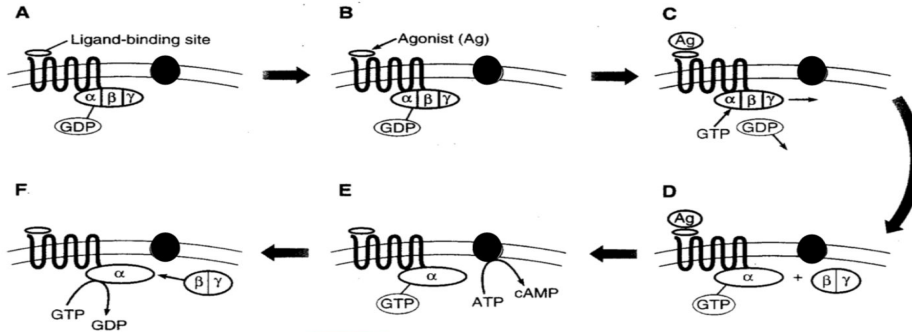
### (Guanine nucleotide-binding proteins)

are divided according to their  $\alpha$ -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).**



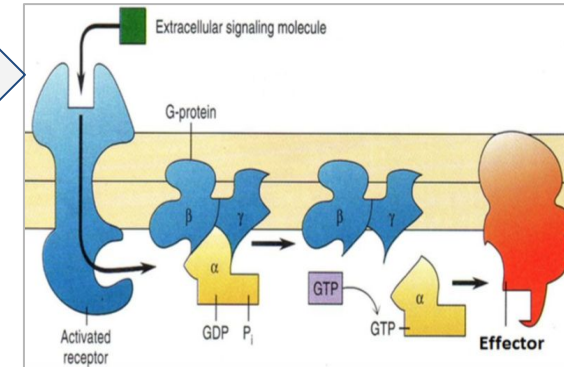
Receptors in this family respond to agonists:

By promoting the binding of GTP to the G protein alpha subunit.

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

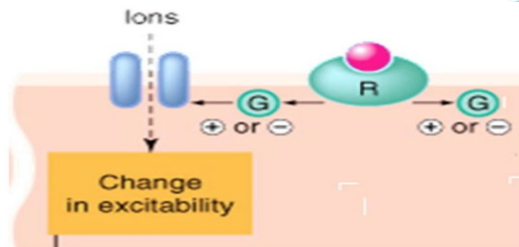
The G protein remains active until it hydrolyzes the bound GTP to GDP and returns to its ground (inactive) state.

- When the G-protein trimer ( alpha, beta, gamma ), binds to agonist-occupied receptor , the a-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 a-subunit to recombine with (beta, gamma) and returns to its inactive state.



## Ion channels

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



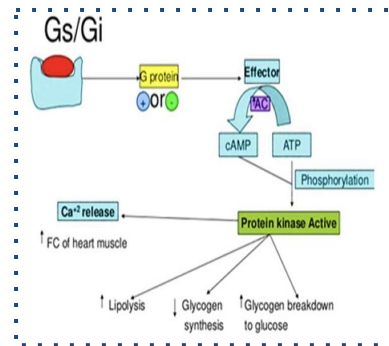
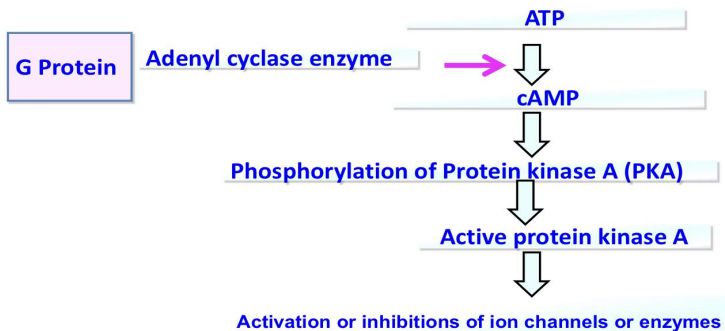
## Type II receptors Targets for G-protein

## Enzymes

(To give  
Second  
messengers)

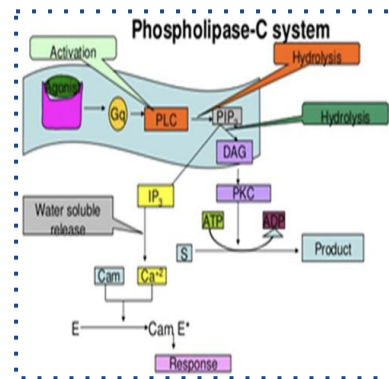
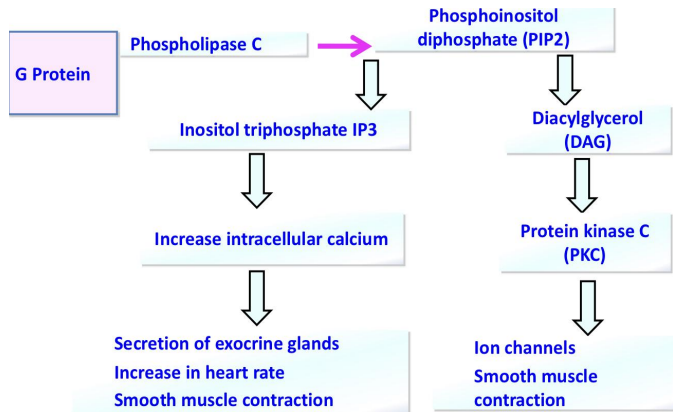
- Adenyl cyclase enzyme (AC)  
Cyclic AMP system  
(cAMP)

cAMP = cyclic adenosine monophosphate



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

IP3 = inositol triphosphate  
DAG = diacylglycerol



## Type II receptors (G-Protein coupled receptors classes)



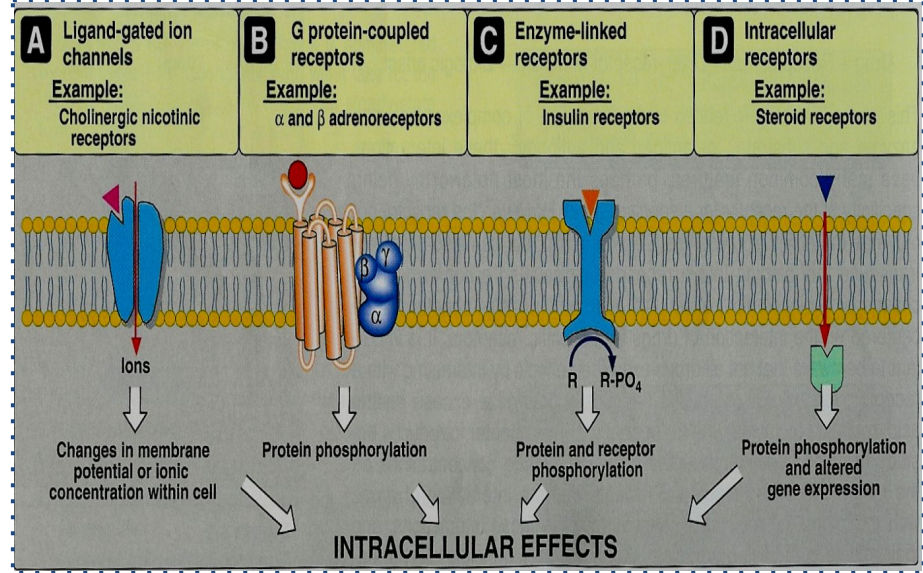
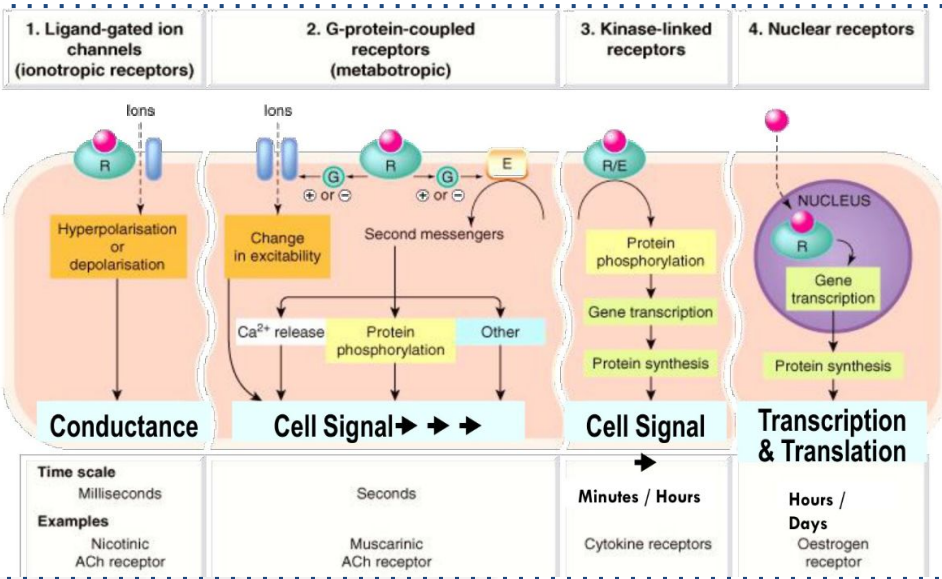
Adrenoceptors (Alpha & Beta)	Cholinergic receptors (M)															
<p><b>a<sub>1</sub></b> Adrenoceptors couple to <b>Gq</b> to stimulate <b>PLC</b> = Contraction of smooth muscles</p> <p>◀ second messenger is inositol phosphate system (IP3+DAG)</p>	<p>◦ <b>M1 &amp; M3</b> Ach receptors couple to <b>Gq</b> to stimulate <b>PLC</b>.</p> <p>◀ second messenger is inositol phosphate system (IP3+DAG)</p> <p style="text-align: right; color: green;">ملاحظة: الأعداد الفردية من M مرتبطة ب Gq</p>															
<p><b>a<sub>2</sub></b> Adrenoceptors couple to <b>Gi</b> to inhibit AC.</p> <p>◆ Second messengers is cyclic AMP system (cAMP)</p>	<p><b>M<sub>2</sub> &amp; M<sub>4</sub></b> Ach receptors couple to <b>Gi</b> to inhibit AC</p> <p>◆ Second messengers is cyclic AMP system (cAMP)</p>															
<p><b>b<sub>1&amp;2</sub></b> Adrenoceptors couple to <b>Gs</b> to stimulate AC</p> <p>◆ Second messengers is cyclic AMP system (cAMP)</p>	<div style="text-align: center;"> <table border="1" style="margin: 0 auto; border-collapse: collapse;"> <tr> <td style="text-align: center;"></td> <td style="text-align: center;"></td> <td style="text-align: center;"></td> <td colspan="2"></td> </tr> <tr> <td style="text-align: center;"></td> <td style="text-align: center;"></td> <td style="text-align: center;"></td> <td style="text-align: center;"></td> <td style="text-align: center;"></td> </tr> <tr> <td style="text-align: center;"></td> <td style="text-align: center;"></td> <td style="text-align: center;"></td> <td style="text-align: center;"></td> <td style="text-align: center;"></td> </tr> </table> </div>															
<p>- Adrenaline binds to <b>a<sub>2</sub></b> Adrenoceptors that will activate Gi (Inhibitory) protein. <b>Gi</b> protein will inhibit (AC) that will decrease cAMP Concentration = <b>Decrease contraction.</b></p> <p>- Adrenaline works on heart muscles by binding to <b>b2</b> Adrenoceptors, that will activate <b>Gs</b> (Stimulatory) protein. <b>Gs</b> protein will activate (AC), that will increase cAMP Concentration = <b>Increase muscle contraction (tachycardia)</b></p>	<p>- Acetylcholine works on bronchi by <b>M<sub>3</sub></b> Ach receptor that will activate <b>Gq</b> proteins and <b>Gq</b> proteins will activate (PLC) phospholipase c that will increase Ca concentration = <b>Increase contraction of smooth muscles</b></p> <p>- Adrenaline works on smooth muscles by <b>a<sub>1</sub></b> receptor that will activate Gq proteins and Gq proteins will activate (PLC) that will increase Ca concentration = <b>Increase contraction</b></p>															



Ach receptors	Couple to		
M <sub>1</sub> stimulatory	Gq	stimulate PLC	stimulation
M <sub>2</sub> inhibitory	Gi	Inhibit AC(↓ cAMP) Opening of K-channels	:Heart (Bradycardia (slow heart rate
M <sub>3</sub> stimulatory	Gq	stimulate PLC	Contraction of Smooth muscles (bronchoconstriction)
M <sub>4</sub> inhibitory	Gi	Inhibit AC (↓ cAMP)	Inhibition

Adrenoceptors	Couple to		
b <sub>1</sub> stimulatory	Gs	stimulate AC	Stimulation (tachycardi Increase heart rate ( Because ↑ Ca
a <sub>1</sub> stimulatory	Gq	stimulate PLC	Contraction of smooth muscles

# Signaling Mechanisms



# Receptor Families

	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	Direct	Via DNA
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

Check out the questions made by MQ Team439 about this lecture [here!!](#)



**1) Located at cell membrane with intrinsic enzymatic activity...**

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

**2) Its Response occurs in hours or days and persists longer...**

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

**3) All types of receptors are located at cell membrane except type :**

- |      |       |        |       |
|------|-------|--------|-------|
| A) I | B) II | C) III | D) IV |
|------|-------|--------|-------|

**4) which of the following receptors is coupled with Gq protein ?**

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

## ANSWERS

1	C
2	B
3	D
4	A



**5) The largest Family that accounts for many known drugs:**

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

**6) Which one of these G-Protein classes work as an inhibitor of the effector?**

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

**7) which one of the following is a target for G-protein?**

- |                               |            |        |            |
|-------------------------------|------------|--------|------------|
| A) Adenyl cyclase enzyme (AC) | B) nucleus | C) Ach | D) a and c |
|-------------------------------|------------|--------|------------|

**8) Insulin receptors are an example of which type?**

- |           |            |            |             |
|-----------|------------|------------|-------------|
| A) Type I | B) Type IV | C) Type II | D) Type III |
|-----------|------------|------------|-------------|

## ANSWERS

5 B

6 B

7 A

8 D

1) What are the two structures of the receptors ?

2) Which system gets activated when acetylcholine binds to M1 or M3 via Gq receptor ?

3) What response happens in the body when calcium level increases by the activation of inositol phosphate system ?

4) Inositol phosphate system activates which protein?

5) Give an example of type 2 receptor family

## ANSWERS

1) Ligand recognition site & Inner catalytic domain

2) Inositol Phosphate system

3) If the receptor is in heart then the heart contracts more-(tachycardia), if receptor in gland then the gland secretes more, if the receptor is in smooth muscles then muscles contracts more

4) Protein Kinase C

5) Adrenergic receptors of Noradrenaline (Alpha and Beta)

# GOOD LUCK!



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## Girls team members

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رانيا المطيري  
نورة الدخيل  
اسيل الشهري  
الجوهرة النبيان  
شادن العبيد  
سديم آل زايد  
روان باقادر  
ميس العجمي  
نورة السالم  
نوف السبيعي   
ندى بابلي   
دانة نائب الحرم

## Team leaders

- طرفة الشريدي
- حمود القاضب

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عبداللطيف المشاط  
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عبدالرحمن الدويش  
حمد الموسى   
راكان الدوهان  
فيصل العتيبي  
محمد القهيدان  
يزيد القحطاني