

Chemical substance
affect bio. system

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Drugs

medication

H₂O, O₂, poisons

dosage form of
Therapeutically use

all medication are drugs
(vice versa No)

الأدوية التي تؤثر على

Pharmacodynamics (1)

medication
surgery
Radiation

بِالْعَرَبِيِّ علم ~~أَخْرَجَ~~ ~~أَخْرَجَ~~ أَخْرَجَ

By

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Definitions

effect = action

- ❑ Drug: any chemical substance that affect a biological system.
- ❑ Pharmacodynamics studies the effects of drugs on the living beings and their mechanisms of action.
- ❑ Drug action, means how the drug works "the mechanism of action".
- ❑ Drug effect, means consequences of drug's action on the body.
- For example: the mechanism of **action** of Aspirin is **inhibition of Prostaglandin synthesis** and its **effects** are **analgesia and anti-pyresis**.

تسكين الألم وخفض الحرارة

Mechanisms of drug actions

A- Non-receptor mediated:

1. Interaction with ^{cellular or extracellular} **enzymes**: e.g. **Neostigmine** inhibits acetyl cholinesterase enzyme.
2. Some drugs act by direct **chemical interaction** such as sodium bicarbonate (antacid) which neutralize gastric acidity.
by direct chemical reaction *Enzyme* *direct chemical reaction*
3. Inhibition of **cellular division**: e.g. some anticancer drugs like **vincristine**
anticancer

4. Other drugs act through their **physical properties**.

Examples:

- ✓ lactulose acts as osmotic laxative. *laxative* ملين
- ✓ *في الجسم* Kaolin and pectin *مثل الاسفنج* can adsorb fluids and treat diarrhea.
- ✓ Radioactive iodine *chemical* emits beta particles which can destroy adjacent thyroid cancer cells.

5. **Nutrients**: e.g. iron, calcium and vitamins.

6. The Vaccines act through **immune modulations**.



B- Receptor-mediated:

- Most drugs act by binding to specific receptors located on the cell membrane (e.g. adrenoceptors) or inside the cells (e.g. steroid receptors).

- "Receptor" means any cellular macromolecule to which a drug binds to initiate its effect.

- Most drug receptors are protein in nature, or nucleic acids (e.g. DNA and RNA).

الشكل المناسب في الفراغ حتى يتحرك

The receptor has two functions:

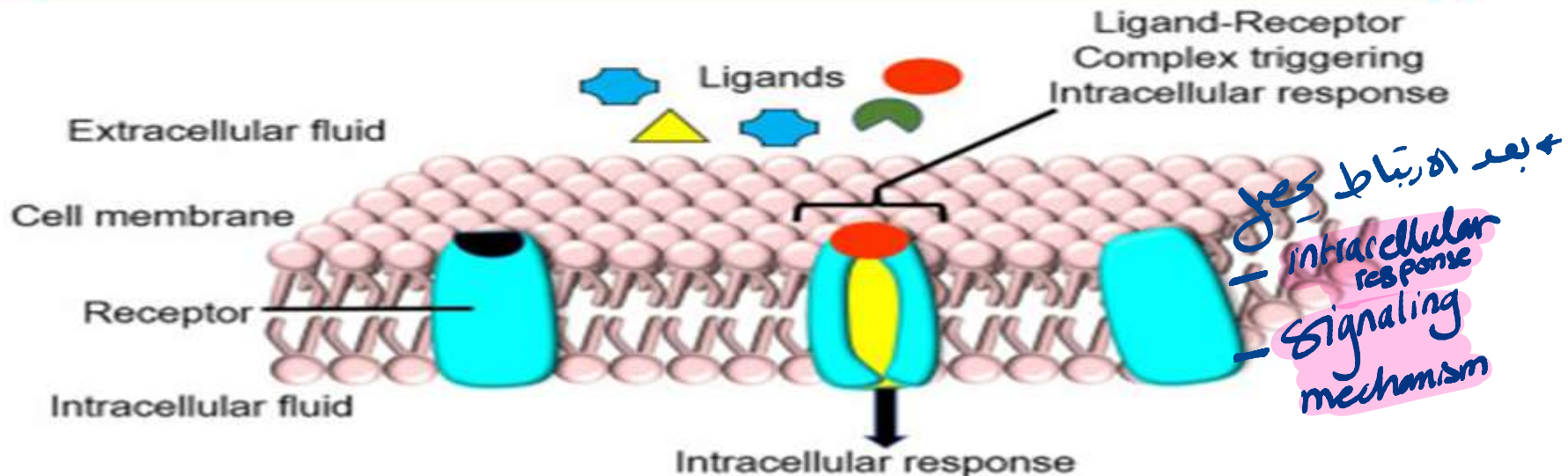
1. Ligand (drug) binding. ^{Hormones من جوار drug من جوار}
2. Message propagation (i.e. signaling) to produce the intended response of drugs. ^{توصيل رسالة}

مثال على message
drug =

Ligands are molecules (e.g. drugs or endogenous hormones or neurotransmitters) that attach selectively to a particular receptor.

The interaction of the drug with the receptor is analogous to "lock and key" where the drug would fit properly into the receptor and activate it.

- Following this binding, the receptor exerts its regulatory actions directly on its cellular targets, effector proteins or intermediate cellular signaling molecules.

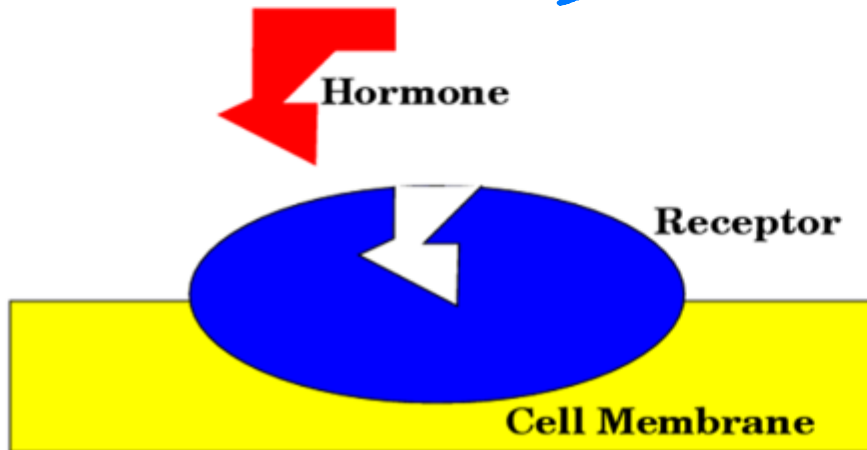


Drug receptor interaction (Lock and key mechanism)

The chemical structure of a drug makes it suitable to bind to a specific receptor and not suitable to bind to other receptors (**specificity**) like the key and the lock.

- The ability of a drug to bind to a specific receptor is called "**affinity**".
- The cellular changes occurring due to drug receptor binding is called "**efficacy or intrinsic activity**".

لو الارتباط سبب تفاعلات كيميائية



maybe one ligand has affinity to many receptors:
 1- Adrenaline → α & β receptor
 but insulin Just with insulin receptor
 2- male sex hormone → male sex hormone receptor and Glucocorticoid receptors



KEYS



Drug receptor coupling and signaling mechanisms

When a receptor becomes bound to a ligand (hormone or a drug, etc.), it undergoes a conformational change which allows it to interact productively with other components of the cells, leading to an alteration in the physiologic state of the cell.

Binding of hormone to receptor initiates a series of events which leads to generation of so-called second messengers within the cell (the hormone is the first messenger).
أو يمكن علاوة

The second messengers then trigger a series of molecular interactions that alter the physiologic state of the cell. Another term used to describe this entire process is *signal transduction or coupling*.

Pharmacological basis of drug-receptor interaction

➤ When a drug binds to a receptor and produces an action like the action of an endogenous regulatory substance already present in the body such as hormones or neurotransmitters,

the drug is called “**Agonist**” *دواء بوي تفاعل مع مستقبل مثل هورمون طبيعي او ناقل عصباني
انه يتفاعل عكس
كارتيك (100%) اذخ ...*

➤ When a drug binds to a receptor and leads to inhibition of the action of a regulatory substance on that receptor, it is called

“**Antagonist**” *no any conformational change → no cellular change
→ most drug are antagonist → physiology change*

➤ Some drugs bind to a receptor but activate it partially and not fully. They are called “**Partial Agonist**” *هناك بعض receptor كوني
effect من 1 و بعض
للصفر*

➤ If a full agonist has an intrinsic activity = 1, that of pure antagonist is = 0 and that of a partial agonist is between 0 and one.

Agonists and Antagonists

Agonists Drugs that occupy receptors and activate them.

Antagonists Drugs that occupy receptors but do not activate them.
Antagonists block receptor activation by agonists.

Agonist alone



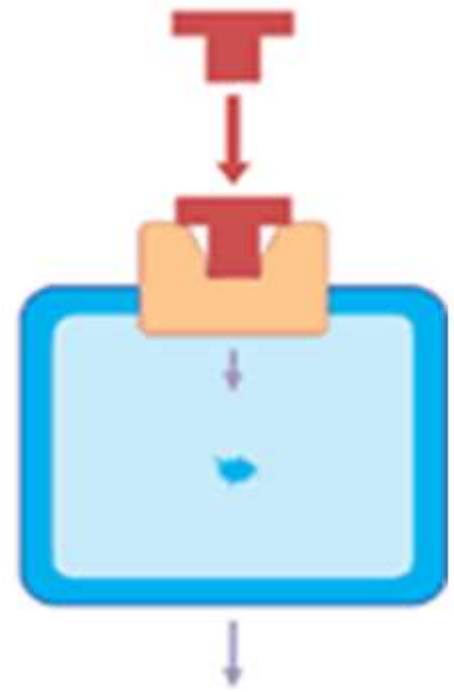
Full activation

Agonist + antagonist



Less activation

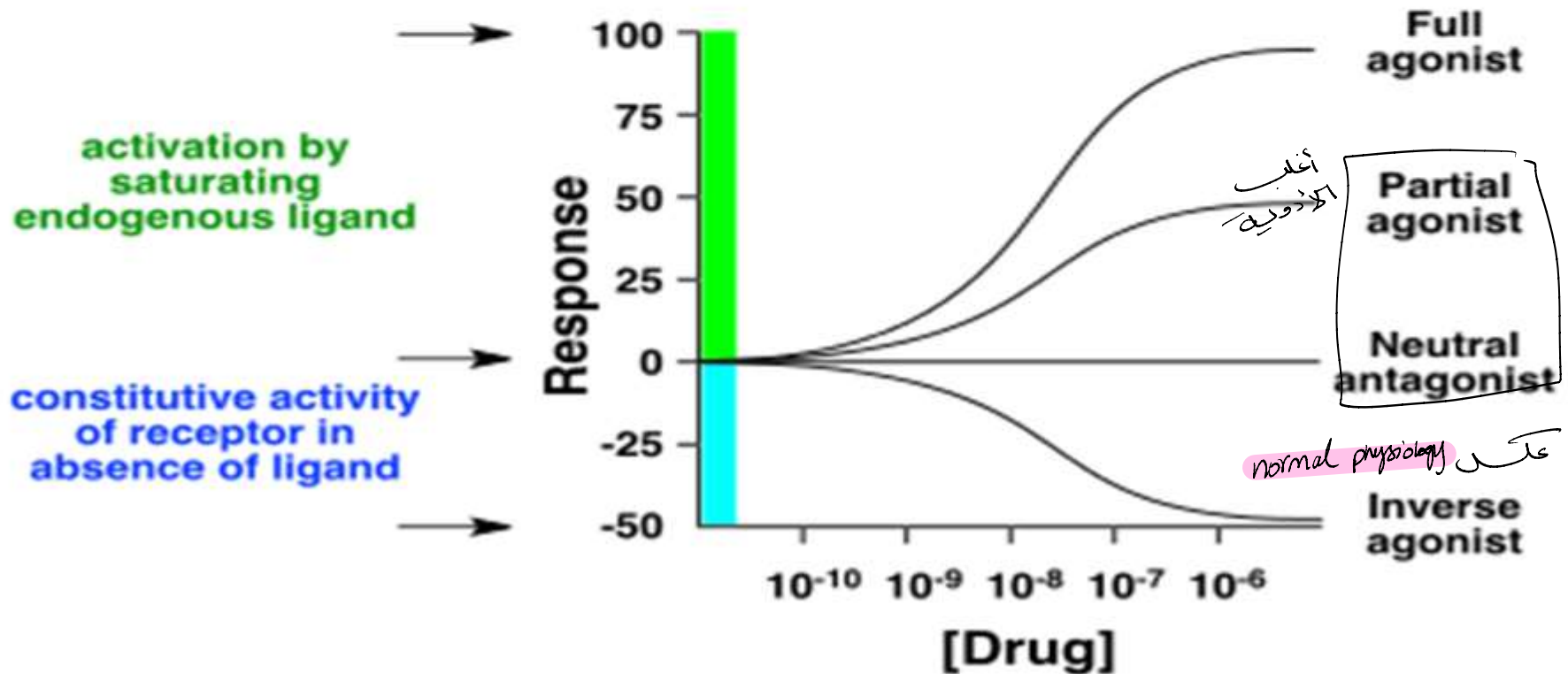
Antagonist alone



No activation

Inverse agonists: drugs that bind to the receptors but has *negative efficacy*.

Example: **Agonists** for the **GABA_A** receptor (such as benzodiazepines) open chloride channels while beta-carbolines actively close the chloride channels



Types of receptors and signaling mechanisms

	Type 1 Ligand gated ion channels or ionotropic receptors	الأشهر والأكثر انتشاراً Type 2 G-protein coupled receptors or metabotropic receptors	Type 3 Tyrosine -kinase linked receptors receptor enzyme	قادرة على صناعة نوعاً جديداً female breast Type 4 Nuclear receptors
Location	Trans membrane	Trans membrane	Trans membrane	Intracellular
Effectors	Ion channel Ligand	Channel or enzyme	Enzyme	Gene transcription لا تترك الدواء على ن lipid soluble
Coupling	Direct no drug needed	G-protein	phosphorylation	Via DNA
Example	Nicotinic receptor and GABA type A receptors Chlore	Muscarinic receptor and adrenoceptors adenoRc	Insulin growth factor and cytokine receptors tyrosine kinase	Steroid & thyroid hormone receptors vitamine D
Response	Very fast (fraction of millisecond)	Fast (few milliseconds)	Long lasting glucose transporter	Long lasting

لا يتطلب الاستقبال بالحدود مبادئ في تنشيط سلسلة من عمليات الخسفة التي تنقل الإشارة

و عليكم السلام حين قال انه تأخذ حوالي ثوانى قليلة فمصدق فيها انه ارتباط الأنسولين أو عوامل النمو Growth Factor على الجزء الخارجي من المستقبل فتنشيطه فإضافة الفوسفات على التايروسين وذلك البروتين للنواة وتفعيله ال Glucose Transporter وخروج هذا الناقل لسطح الخلية وسحب الجلوكوز من السائل المحيط بالخلية وانخفاض مستوى السكر في الدم حتى يعود إلى هنا يكون الوقت عبارة عن ثوان بسيطة

أما عبارة Long Lasting فهي تخص تأثير Glucose Transporter فعمليتها تطول على سطح الخلية وهي بتسحب في الغلو كوز لأن لها عمر طويل فحكما هنا على التأثير بحكم أن هذه النواقل تبقى على سطح الخلية وتطول مددها وليس كم تأخذ من وقت لتفعيل هذه النواقل هذا حسب كلام الدكتور

هذه مصاحبة ارتباطه
intrinsic activity
تأثيره على activity
سريع

عبر الارتباط بجملها فتتميز
ارتفعت دفقة مباشرة

ارتباطا برعي G-protein وهو الذي يقوم بدوره بتفعيل انزيمات والتاثير على مستقبلات

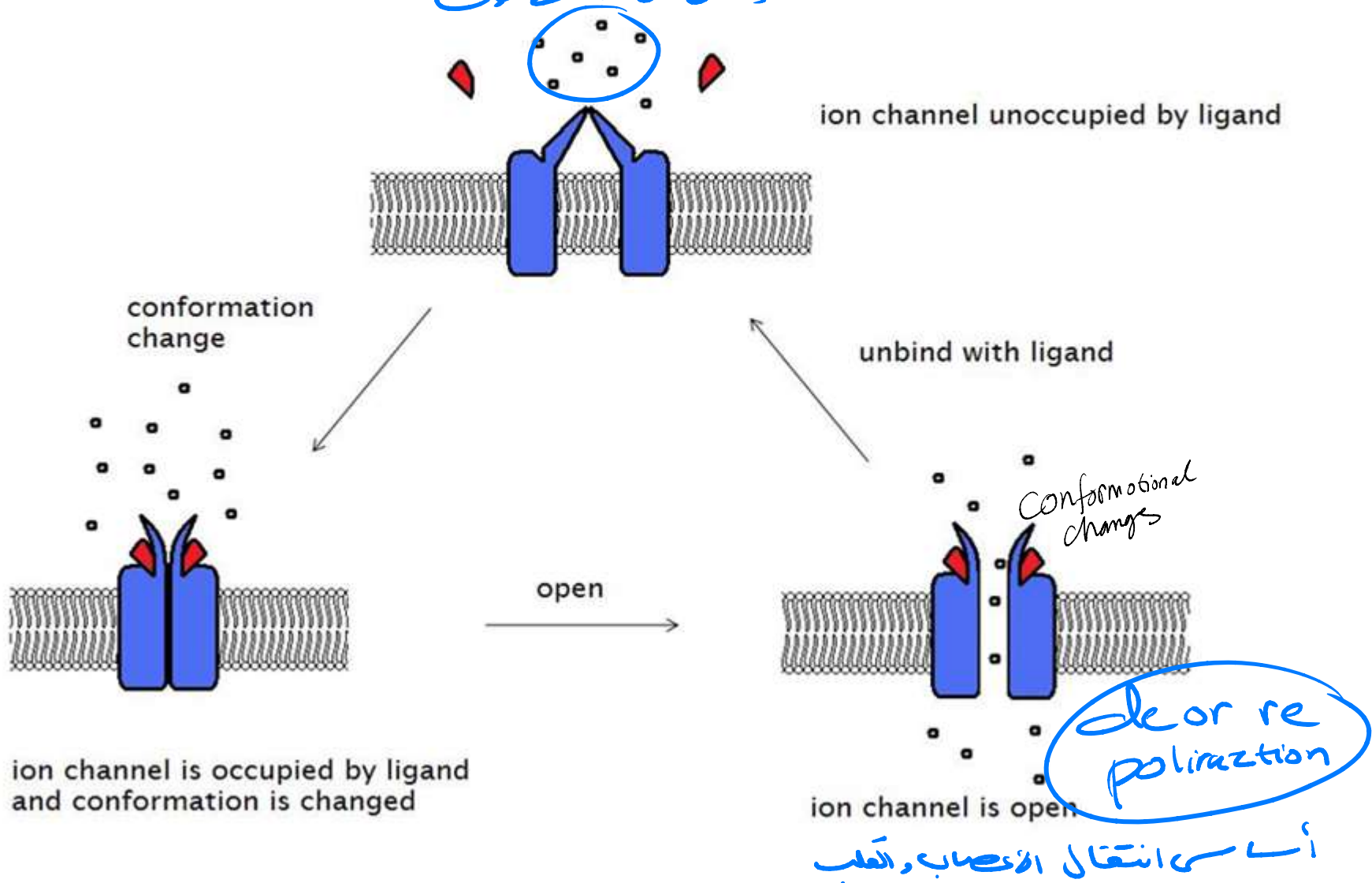
تدخل مساعف اى DNA وتؤثر على الخيس الجين (استجابة بطوية المدى)

كورتيزون

Type 1

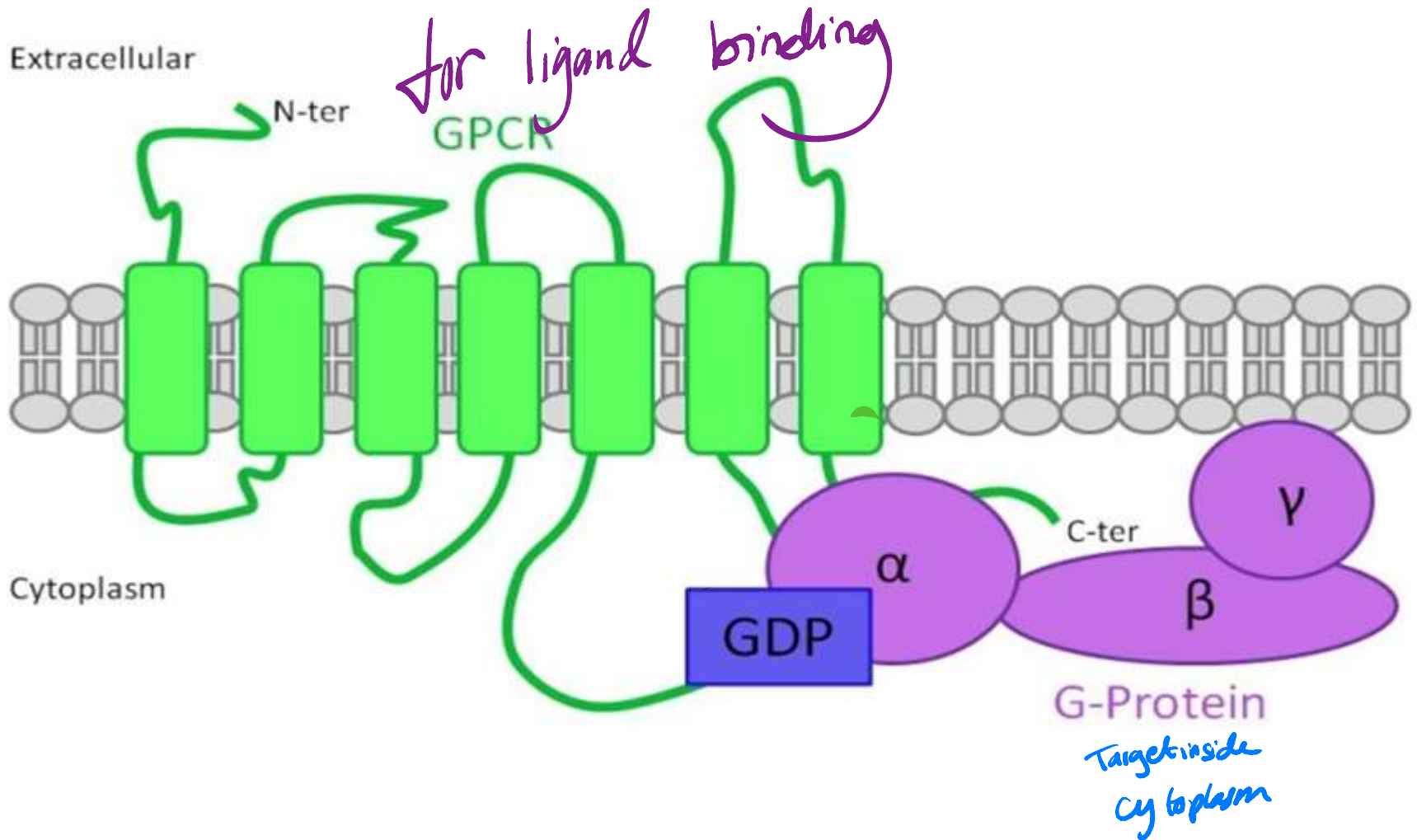
Ligand gated ion channels or Ionotropic receptors

ایونان کی خانگی کھول



Type 2

G-protein coupled receptors or metabotropic receptors



□ Activation of G-protein coupled receptors leads to:

- 1- Activation or inhibition of adenylyclase
- 2- Activation of phospholipase C
- 3- Activation of ion channels (e.g. calcium channels)

Drug is the first messenger

Second messenger

- Activation of adenylyclase by (Gs) ^{stimulate} would increase cellular cAMP
- Inhibition of adenylyclase by (Gi) ^{inhibit} would decrease cellular cAMP → contraction of smooth ms
- Activation of phospholipase C (Gq) would increase cellular inositol triphosphate (IP3) and diacylglycerol (DAG)
- Activation of calcium channels would increase cellular calcium. →

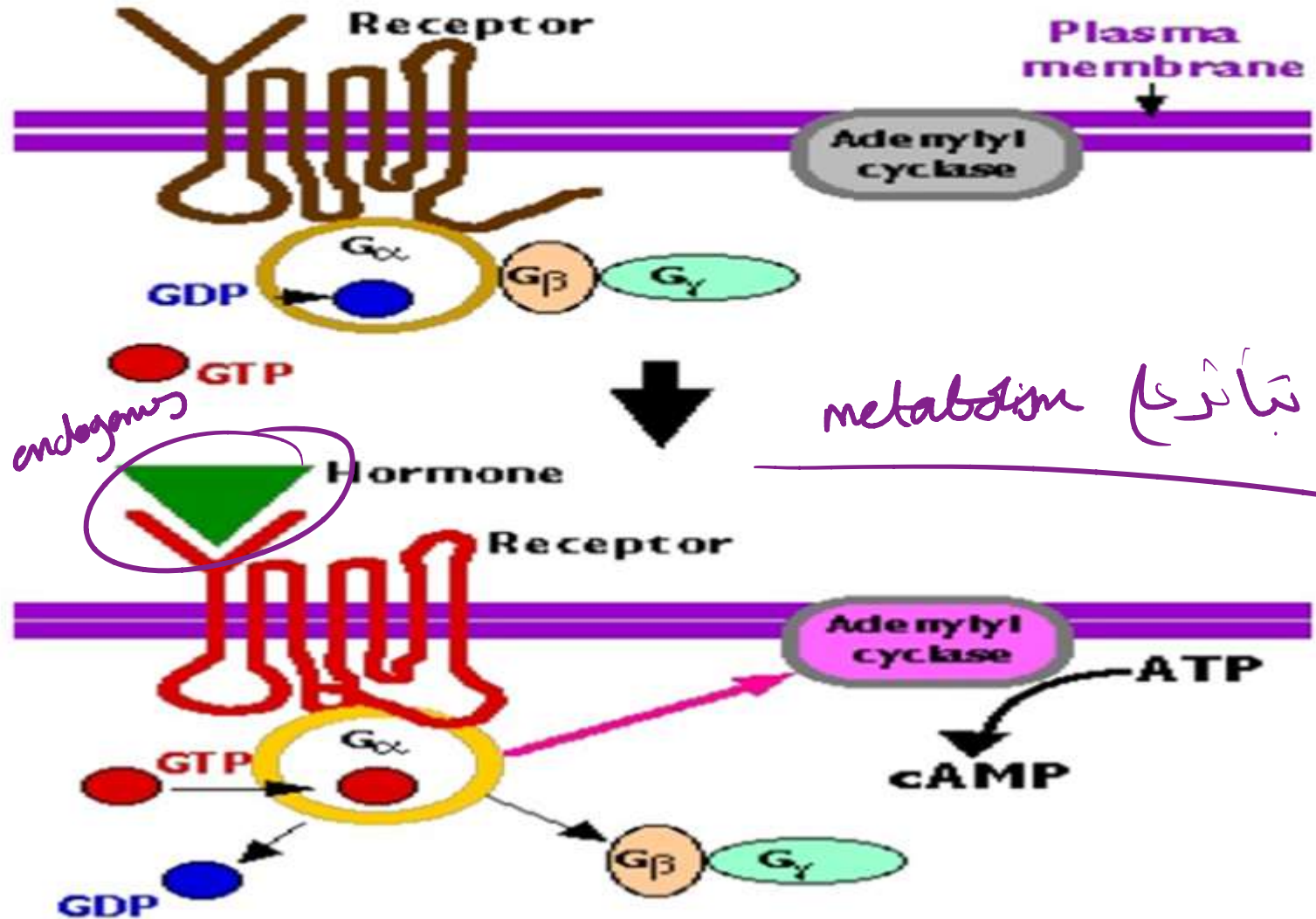
بفتحها من جوا

□ Secondary messengers produce the final cellular response (e.g. contraction, relaxation, secretion, etc).

1. cAMP → relaxation of smooth ms.
2. IP3 contraction
3. DAG contraction
4. Calcium contraction or release or secretion

لو فتحها
الدواء من جوا
من الصبغ في الماء لكن
بفتحها
second messenger

Type 2 G-protein coupled receptors (Gs) signaling



Type 3

receptor enzyme
نفس
نفس

Tyrosine-kinase linked receptors

إضافة phosphate ك اي

Tyrosine

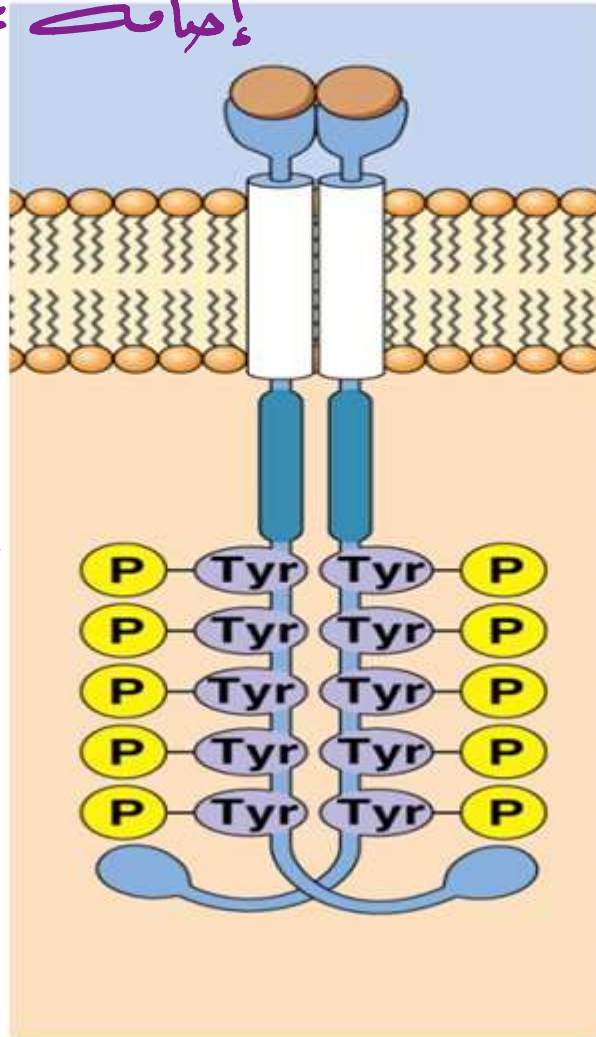
الجليك بنوعه انه

insulin

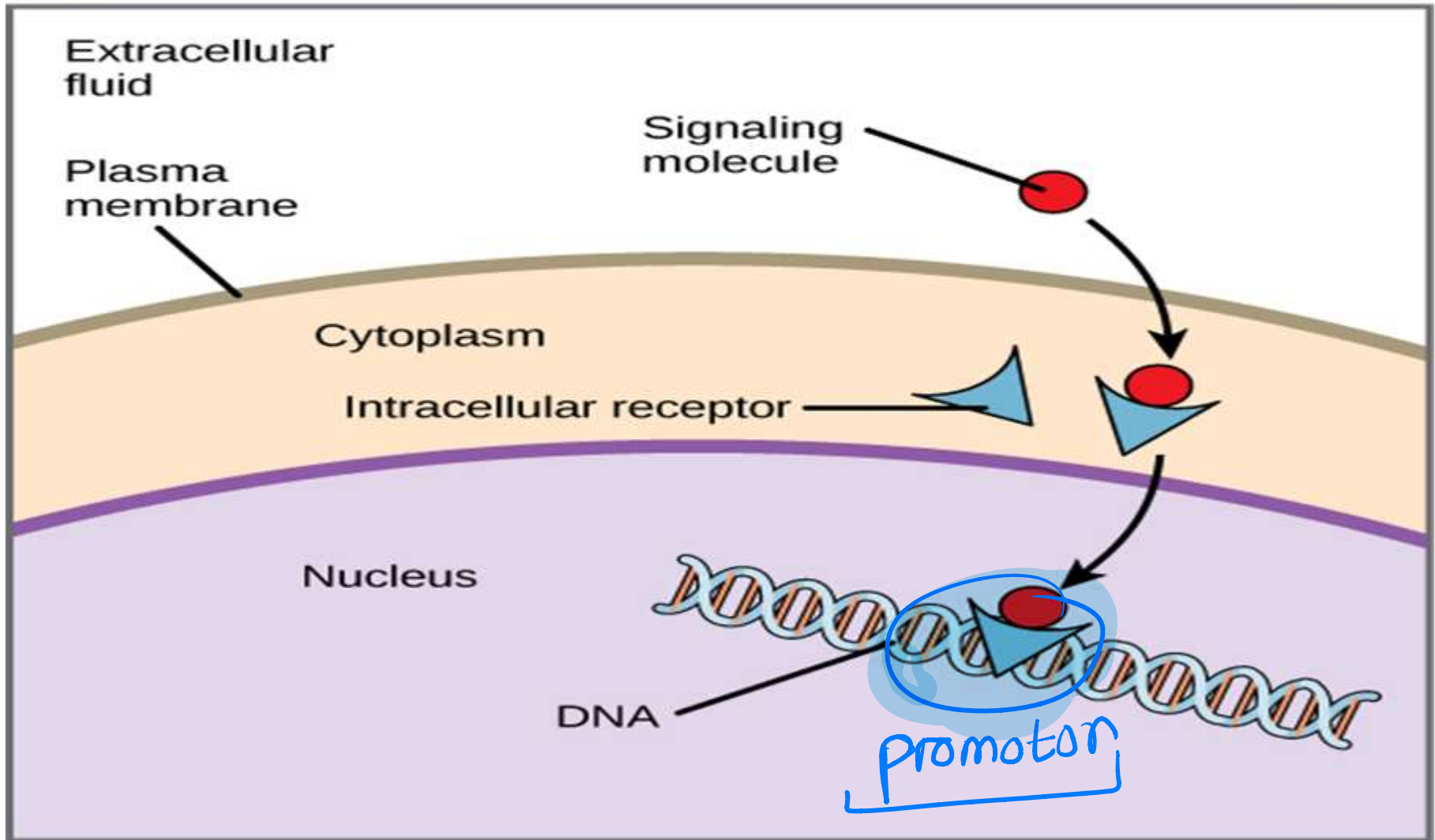
و بتوي

Glucose Carrier

← بيا خذ few seconds



Type 4 Nuclear receptors



Thank
you

The image features the words "Thank you" in a 3D, blocky font. The letters are light yellow with a blue outline and are arranged in two lines: "Thank" on top and "you" below it. The text is set against a light pink background and casts a soft red shadow. Scattered around the text are several colorful stars in shades of cyan, yellow, purple, and red, each with a red shadow beneath it.