جامعة الانبار

كلية : الصيدلة

قسم : فرع الادوية والسموم

اسم المادة باللغة العربية: فسلجة نظري

اسم المدة باللغة الإنكليزية: **. physiology**

المرحلة: الثانية

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عنوان المحاضرة باللغة العربية: المستقبلات

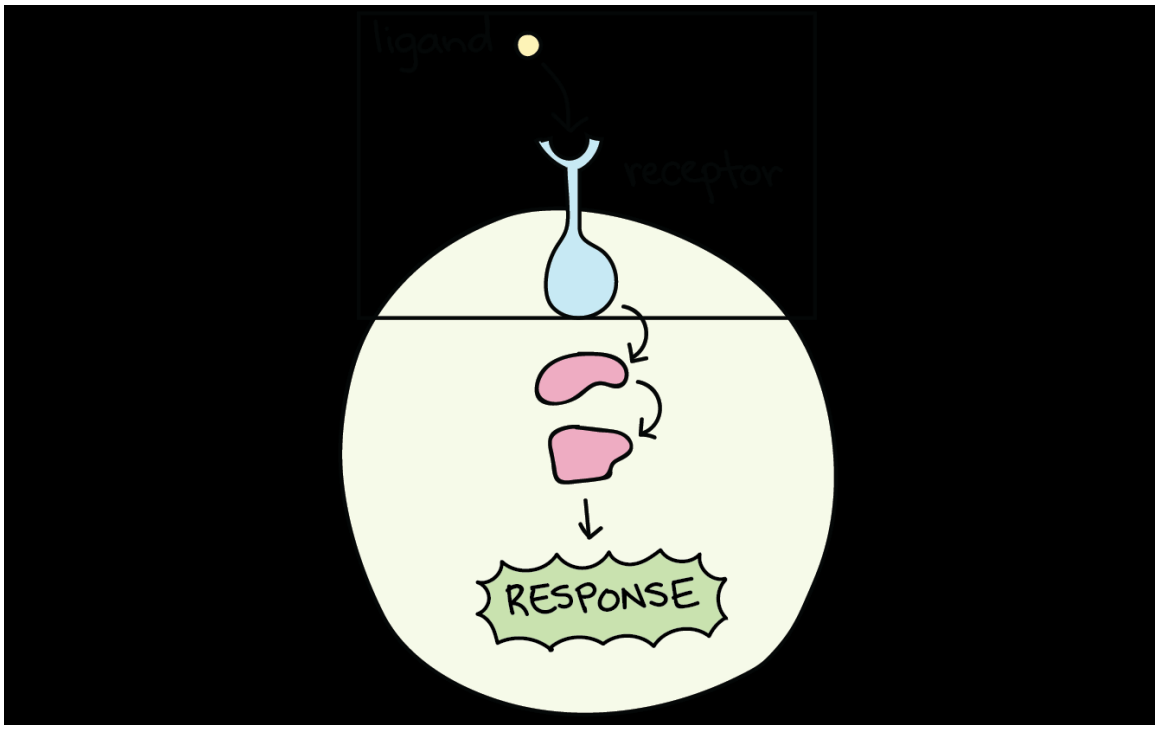
عنوان المحاضرة باللغة الإنكليزية: Receptor

محتوى المحاضرةReceptor

Introduction

Just as a journey of a thousand miles begins with a single step, so a complex signaling pathway inside of a cell begins with a single key event – the binding of a signaling molecule, or **ligand**, to its receiving molecule, or **receptor**.

Receptors and ligands come in many forms, but they all have one thing in common: they come in closely matched pairs, with a receptor recognizing just one (or a few) specific ligands, and a ligand binding to just one (or a few) target receptors. Binding of a ligand to a receptor changes its shape or activity, allowing it to transmit a signal or directly produce a change inside of the cell



In this section, we'll look at different types of receptors, seeing how they interact to turn information from outside the cell into a change inside the cell.

Types of receptors

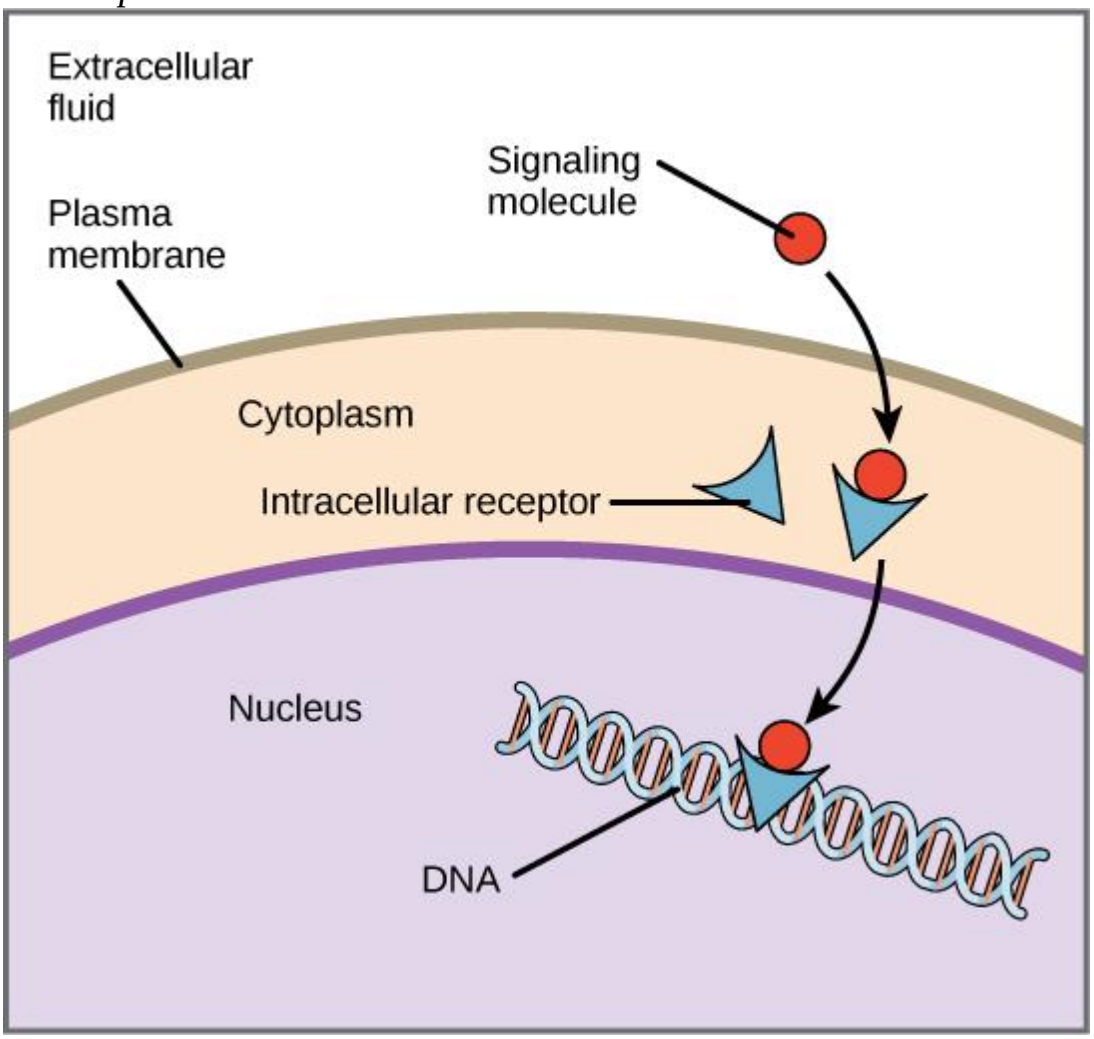
Receptors come in many types, but they can be divided into two categories: intracellular receptors, which are found inside of the cell (in the cytoplasm or nucleus), and cell surface receptors, which are found in the plasma membrane.

Intracellular receptors

Intracellular receptors are receptor proteins found on the inside of the cell, typically in the cytoplasm or nucleus. In most cases, the ligands of intracellular receptors are small, hydrophobic (water-hating) molecules, since they must be able to cross the plasma membrane to reach their receptors. For example, the primary receptors for hydrophobic steroid hormones, such as the sex hormones estradiol (an estrogen) and testosterone, are intracellular.

When a hormone enters a cell and binds to its receptor, it causes the receptor to change shape, allowing the receptor-hormone complex to enter the nucleus (if it wasn't there already) and regulate gene activity. Hormone binding exposes regions of the receptor that have DNA-binding activity,

meaning they can attach to specific sequences of DNA. These sequences are found next to certain genes in the DNA of the cell, and when the receptor binds next to these genes, it alters their level of transcription. *[What's transcription?*



Many signaling pathways, involving both intracellular and cell surface receptors, cause changes in the transcription of genes. However, intracellular receptors are unique because they cause these changes very directly, binding to the DNA and altering transcription themselves.

Cell-surface receptors

Cell-surface receptors are membrane-anchored proteins that bind to ligands on the outside surface of the cell. In this type of signaling, the ligand does not need to cross the plasma membrane. So, many kinds of molecules (including large, hydrophilic or "water-loving" ones) may act as ligands.

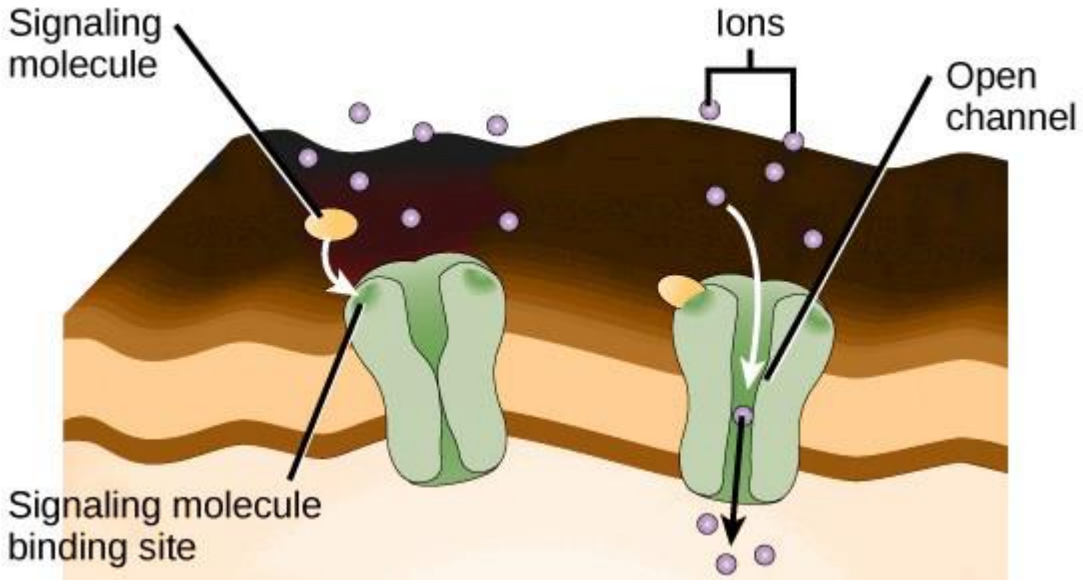
A typical cell-surface receptor has three different **domains**, or protein regions: a extracellular ("outside of cell") ligand-binding domain, a hydrophobic domain extending through the membrane, and an intracellular

("inside of cell") domain, which often transmits a signal. The size and structure of these regions can vary a lot depending on the type of receptor, and the hydrophobic region may consist of multiple stretches of amino acids that criss-cross the membrane.

There are many kinds of cell-surface receptors, but here we'll look at three common types: ligand-gated ion channels, G protein-coupled receptors, and receptor tyrosine kinases.

Ligand-gated ion channels

Ligand-gated ion channels are ion channels that can open in response to the binding of a ligand. To form a channel, this type of cell-surface receptor has a membrane-spanning region with a hydrophilic (water-loving) channel through the middle of it. The channel lets ions to cross the membrane without having to touch the hydrophobic core of the phospholipid bilayer. When a ligand binds to the extracellular region of the channel, the protein's structure changes in such a way that ions of a particular type, such as Ca or Cl can pass through. In some cases, the reverse is true: the channel is usually open, and ligand binding causes it to close. Changes in ion levels inside the cell can change the activity of other molecules, such as ion-binding enzymes and voltage-sensitive channels, to produce a response. Neurons, or nerve cells, have ligand-gated channels that are bound by neurotransmitters.



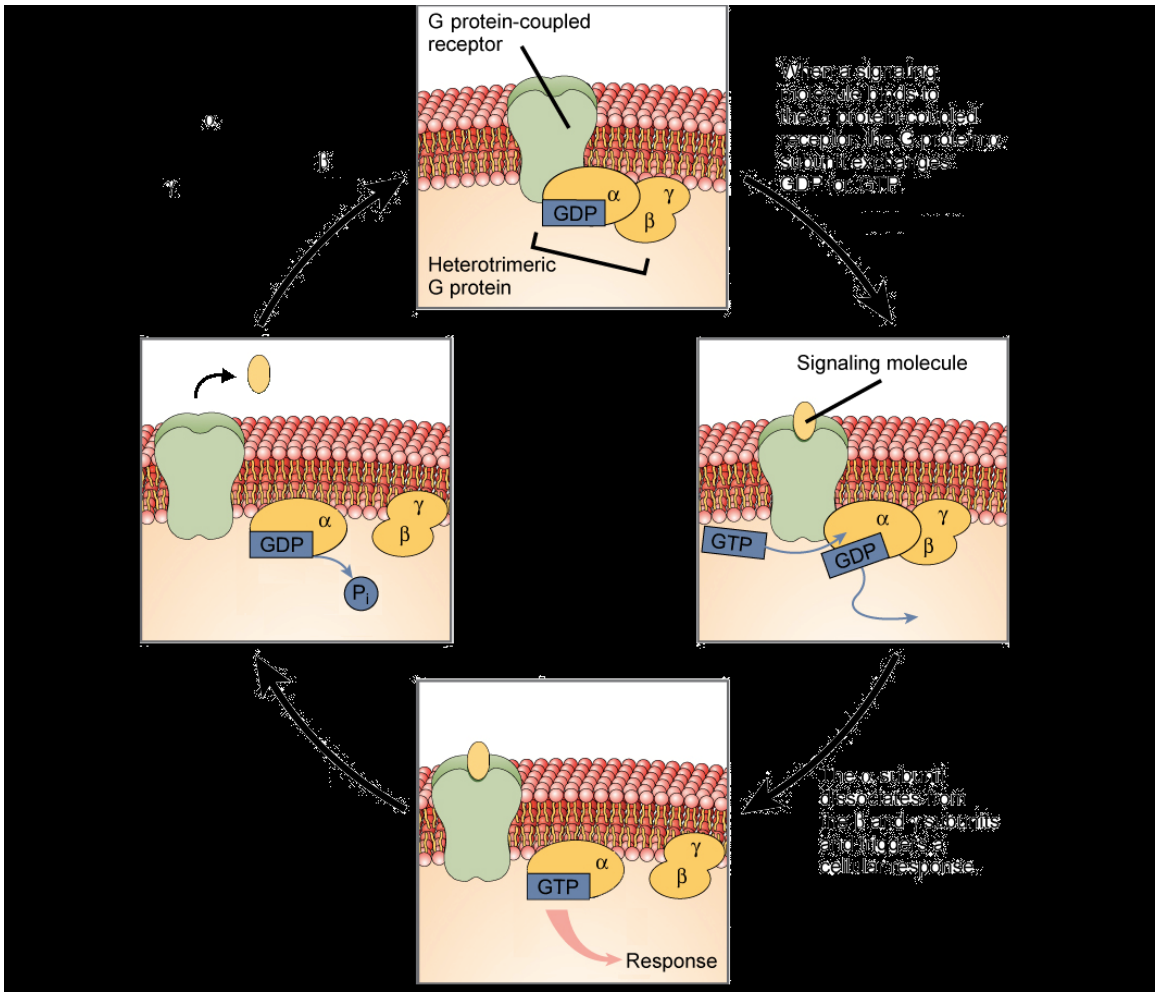
G protein-coupled receptors

G protein-coupled receptors (**GPCRs**) are a large family of cell surface receptors that share a common structure and method of signaling. The members of the GPCR family all have seven different protein segments that cross the membrane, and they transmit signals inside the cell through a type of protein called a G protein (more details below).

GPCRs are diverse and bind many different types of ligands. One particularly interesting class of GPCRs is the odorant (scent) receptors. There are about 800 of them in humans, and each binds its own "scent molecule" – such as a particular chemical in perfume, or a certain compound released by rotting fish – and causes a signal to be sent to the brain, making us smell a smell.

When its ligand is not present, a G protein-coupled receptor waits at the plasma membrane in an inactive state. For at least some types of GPCRs, the inactive receptor is already docked to its signaling target, a **G protein**.

G proteins come in different types, but they all bind the nucleotide guanosine triphosphate (GTP), which they can break down (hydrolyze) to form GDP. A G protein attached to GTP is active, or "on," while a G protein that's bound to GDP is inactive, or "off." The G proteins that associate with GPCRs are a type made up of three subunits, known as **heterotrimeric G proteins**. When they're attached to an inactive receptor, they're in the "off" form (bound to GDP).



Ligand binding, however, changes the picture: the GPCR is activated and causes the G protein to exchange GDP for GTP. The now-active G protein separates into two pieces (one called the α subunit, the other consisting of the β and γ subunits), which are freed from the GPCR. The subunits can interact with other proteins, triggering a signaling pathway that leads to a response.

Eventually, the α subunit will hydrolyze GTP back to GDP, at which point the G protein becomes inactive. The inactive G protein reassembles as a three-piece unit associated with a GPCR. Cell signaling using G protein-coupled receptors is a cycle, one that can repeat over and over in response to ligand binding.

G protein-coupled receptors play many different roles in the human body, and disruption of GPCR signaling can cause disease.

[GPCR signaling and cholera]

Receptor tyrosine kinases

Enzyme-linked receptors are cell-surface receptors with intracellular domains that are associated with an enzyme. In some cases, the intracellular domain of the receptor actually *is* an enzyme that can catalyze a reaction. Other enzyme-linked receptors have an intracellular domain that interacts with an enzyme^55start superscript, 5, end superscript.

Receptor tyrosine kinases (**RTKs**) are a class of enzyme-linked receptors found in humans and many other species. A **kinase** is just a name for an enzyme that transfers phosphate groups to a protein or other target, and a receptor tyrosine kinase transfers phosphate groups specifically to the amino acid tyrosine.

How does RTK signaling work? In a typical example, signaling molecules first bind to the extracellular domains of two nearby receptor tyrosine kinases. The two neighboring receptors then come together, or dimerize. The receptors then attach phosphates to tyrosines in each others' intracellular domains. The

phosphorylated tyrosine can transmit the signal to other molecules in the cell

Receptor tyrosine kinases are crucial to many signaling processes in humans. For instance, they bind to **growth factors**, signaling molecules that promote cell division and survival. Growth factors include platelet-derived growth factor (PDGF), which participates in wound healing, and nerve growth factor (NGF), which must be continually supplied to certain types of neurons to keep them alive. Because of their role in growth factor signaling, receptor tyrosine kinases are essential in the body, but their activity must be kept in balance: overactive growth factor receptors are associated with some types of cancers