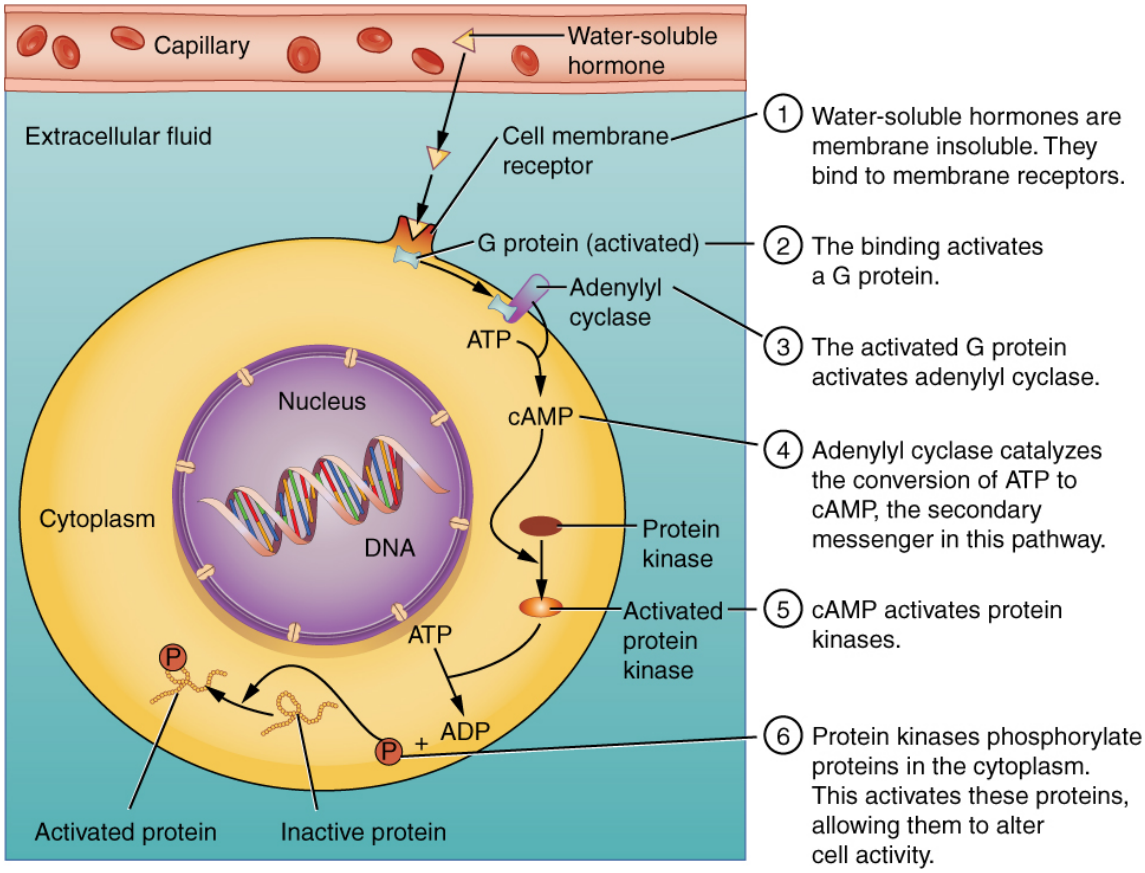
5.4.2

Hormone Receptors

Hormones act by binding with **specific receptors** on the target cells. Receptors associated with cells are located in three areas:

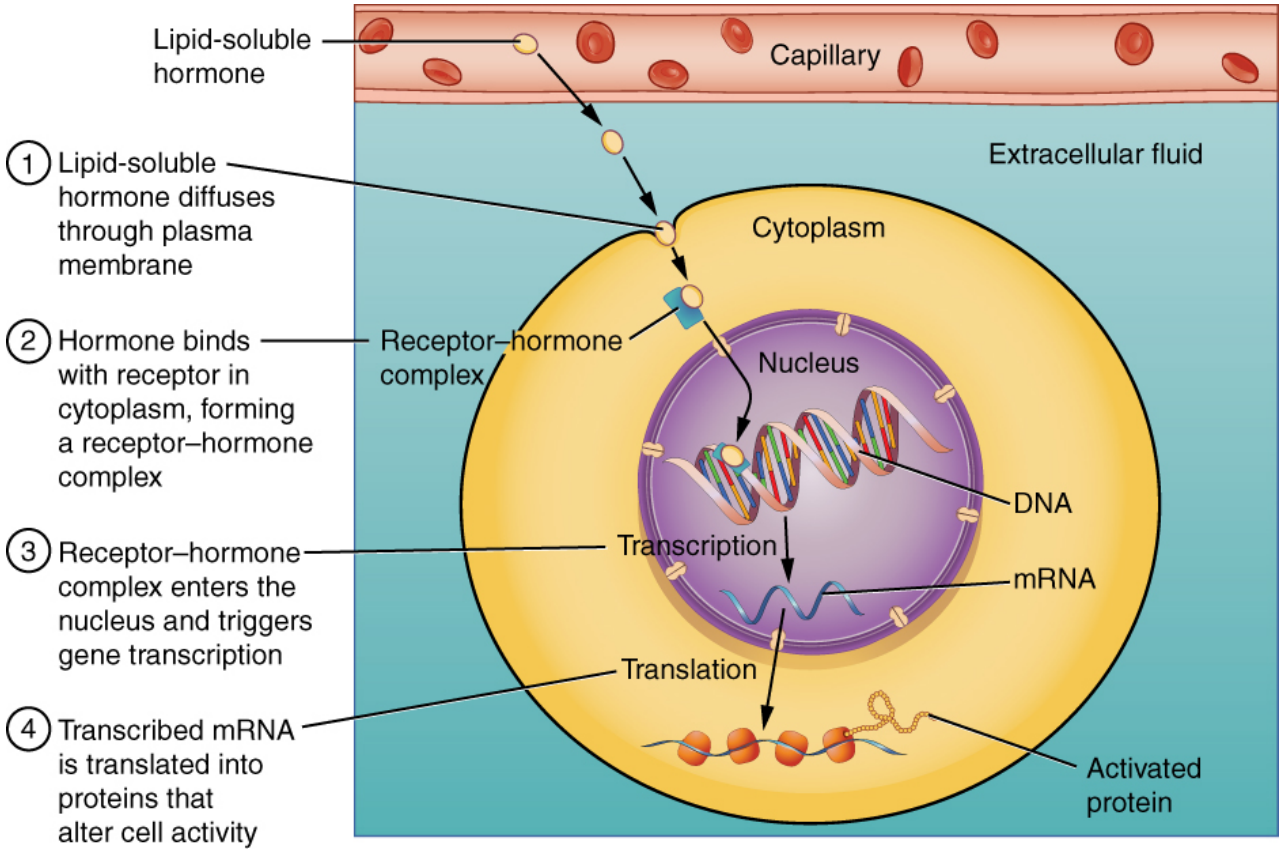
- On the plasma membrane
- In the cytosol of the cell
- In the nucleus.

The majority of plasma membrane receptors are **G-protein-coupled receptors**. Other types include **receptor tyrosine kinases** and **receptor serine/threonine kinases.** Activation of these receptors leads to an intracellular cascade that produce second messengers like cAMP, cGMP, or inositol triphosphate (IP3). These second messengers activate other enzymes such as those that phosphorylate or dephosphorylate proteins. Adding a phosphate to an enzyme is like flipping a light switch, sometimes that switch turns off the enzyme (inactive) and sometimes the switch turns on the enzyme (active). Additionally, the second messenger may increase intracellular calcium. Calcium can also act as a messenger that turns on events in the cell. Remember the role of calcium in muscle contraction.



Water-Soluble (Hydrophilic or Amino Acid Derived) Hormone Receptors: G-protein-coupled receptors. Synthesized by cell receptors on cell surface. Examples include Insulin, Growth Hormone, and Epinephrine

Intracellular and nuclear receptors interact with DNA and affect mRNA synthesis. Nuclear receptors, or receptors on the nucleus of the cell, when activated stimulate transcription of various genes, resulting in the production of new proteins. The new proteins result in a change in the cell. Having different kinds of receptors such as membrane receptors and intracellular receptors accommodates both hydrophilic and hydrophobic hormones. Hydrophilic hormones easily dissolve in water, but do not easily enter the cell due to the phospholipid bilayer of the cell membrane and therefore act via membrane bound receptors, while nonpolar or hydrophobic hormones like testosterone that can easily cross the plasma membrane bind to cytosolic and nuclear receptors. In addition, membrane receptors typically induce short term and rapid responses, while intracellular receptors tend to produce slower but prolonged responses.



Lipid-Soluble (Hydrophobic or Cholesterol-derived) Steroid Hormone Receptors: Cytosolic and Nuclear Receptors. Synthesized inside the nucleus of the cell. Examples are Testosterone and Estrogen

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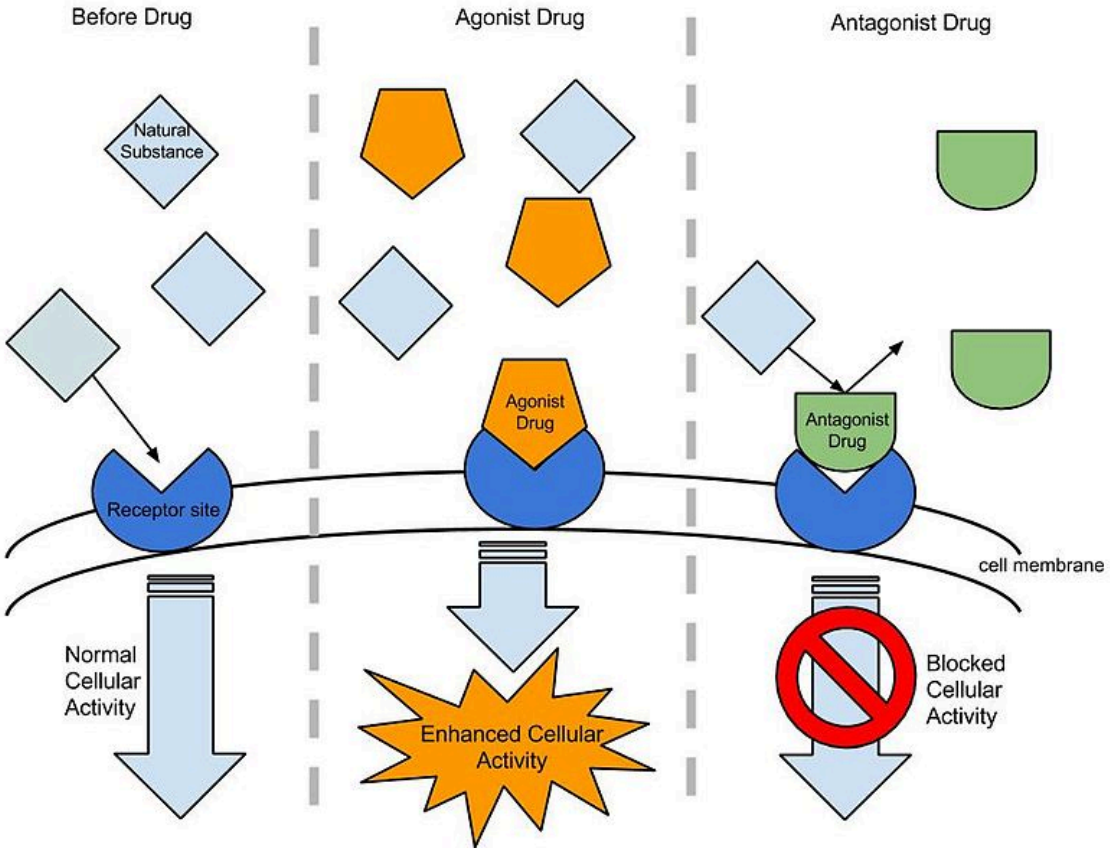
It is truly the receptor, not the hormone that ultimately determines the cellular response. Most receptors are highly selective to their particular hormone, that is, even similar hormones don't bind to the receptor with the same affinity. The receptor recognizes subtle differences in hormone structure which allows the receptor to distinguish between hormones. This concept has allowed pharmaceutical companies to design drugs (hormone analogs) that can interact with specific receptors to provide medicinal intervention. Drugs that bind to and stimulate a receptor are called **agonists**, while those that bind to a receptor and block its effects are called **antagonists**.



Agonist and Antagonist Ligands. Agonists fit hormone receptors and activate them. Antagonists occupy hormone receptors and do not activate them but block them from activation.

Approximately 60% of prescription drugs act by either activating or blocking specific receptors. The term **ligand** is a general term used to describe any substance that interacts with a receptor. The specificity of receptors allows hormones to be released at any site in the body and circulate throughout, but only affect the tissue that contains the particular receptor for the hormone.

Receptor numbers are constantly being changed within a given cell, thus, depending on the number of receptors present, a cell may become less or more responsive to a given hormone. These receptor numbers can be regulated by hormones in a positive (**up-regulation**, more) or negative (**down-regulation**, less) manner.

For example, an increased blood level of the hormone prolactin induces an up-regulation of prolactin receptors in the cells of the liver.

In contrast, prolonged exposure of cells to the hormone insulin results in a down-regulation of the insulin receptor. In some instances, a hormone binding to its receptor may enhance the actions of a separate hormone on a different receptor of the same cell, a process called **synergism**.