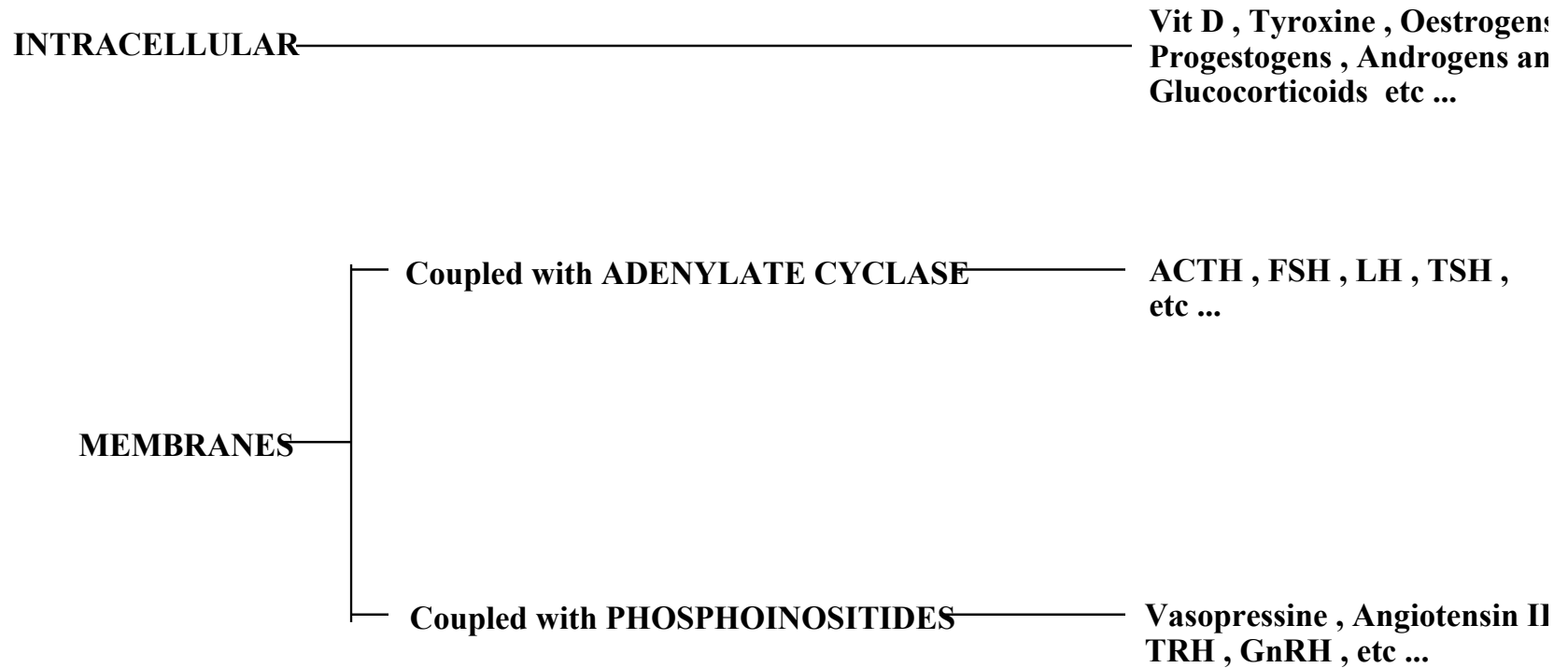
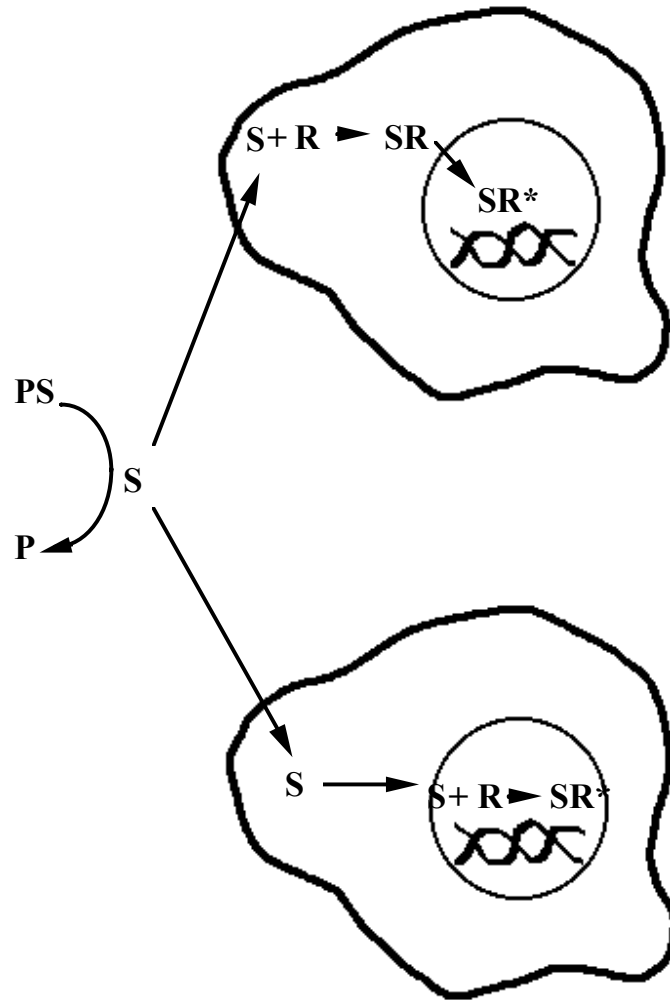


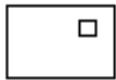
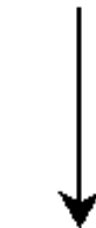
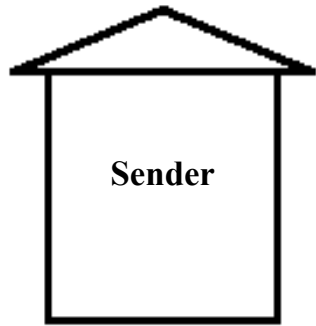
# RECEPTOR TYPE AND SECOND MESSANGERS



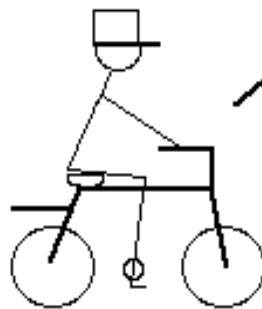
# CYTOPLASMIC AND/OR NUCLEAR RECEPTORS



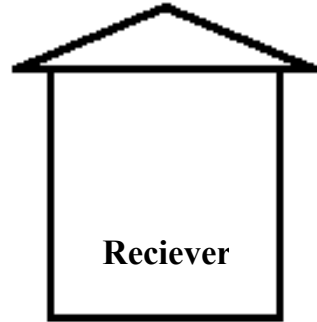
Genetically engineered receptors with a HRE from the Glucocorticoid receptor and a hormone binding domain from the Oestradiol receptor induce Glucocorticoid-like activities !



**Information**



**Carrier**



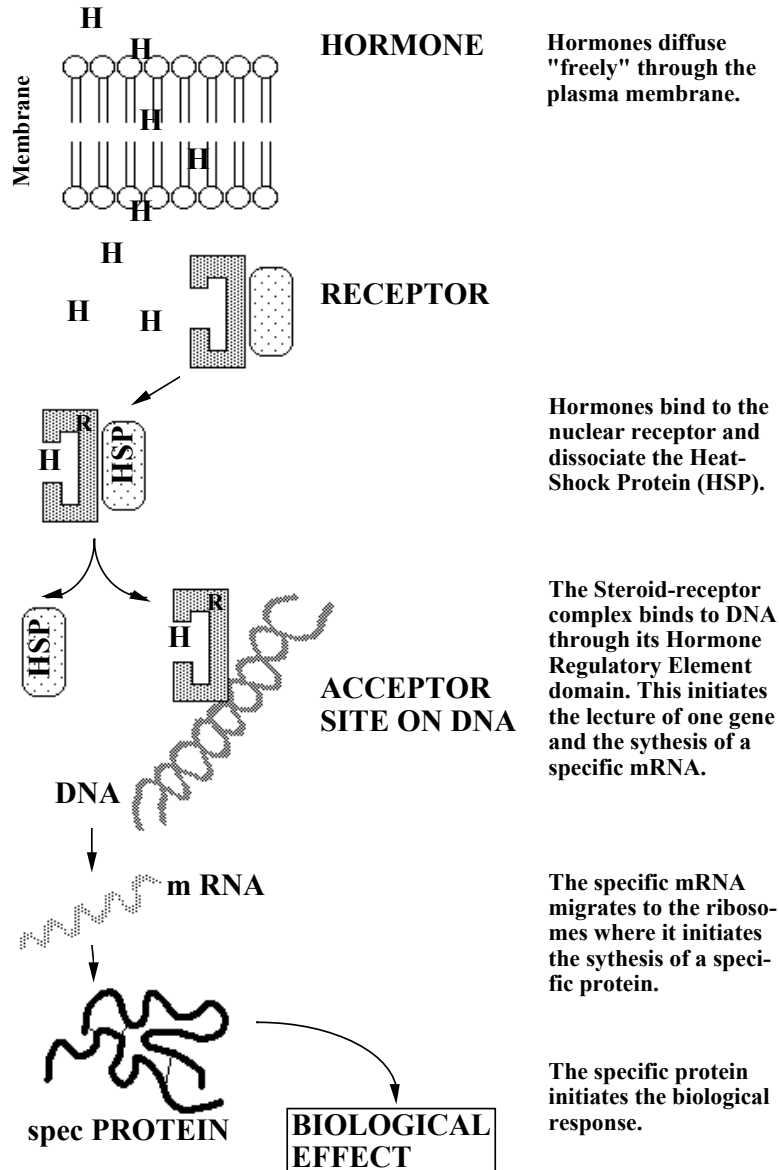
**Receiver**



**Action**



# INTRACELLULAR RECEPTORS



Hormones diffuse "freely" through the plasma membrane.

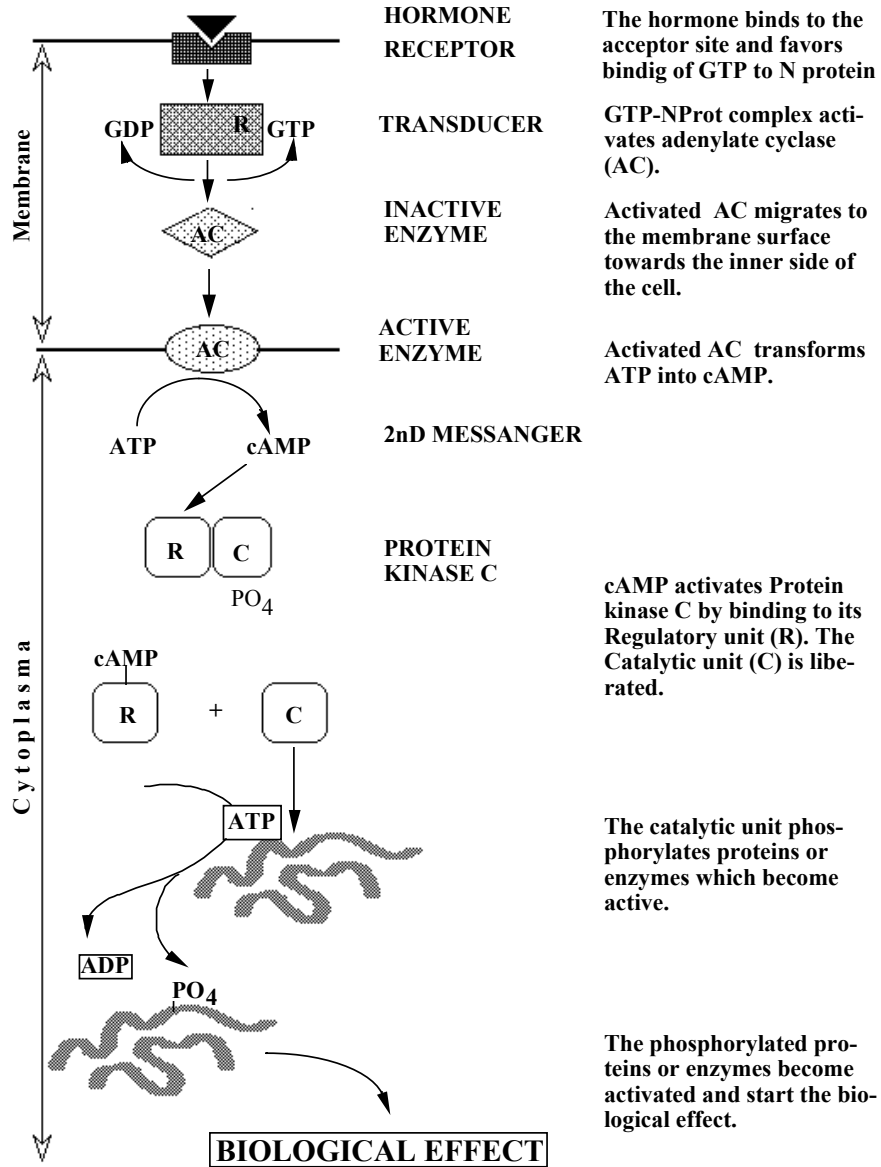
Hormones bind to the nuclear receptor and dissociate the Heat-Shock Protein (HSP).

The Steroid-receptor complex binds to DNA through its Hormone Regulatory Element domain. This initiates the lecture of one gene and the sythesis of a specific mRNA.

The specific mRNA migrates to the ribosomes where it initiates the sythesis of a specific protein.

The specific protein initiates the biological response.

## MEMBRANE RECEPTOR COUPLED TO ADENYLATE CYCLASE



**HORMONE RECEPTOR**

The hormone binds to the acceptor site and favors binding of GTP to N protein

**TRANSDUCER**

GTP-NProt complex activates adenylate cyclase (AC).

**INACTIVE ENZYME**

Activated AC migrates to the membrane surface towards the inner side of the cell.

**ACTIVE ENZYME**

Activated AC transforms ATP into cAMP.

**2<sup>nd</sup> MESSANGER**

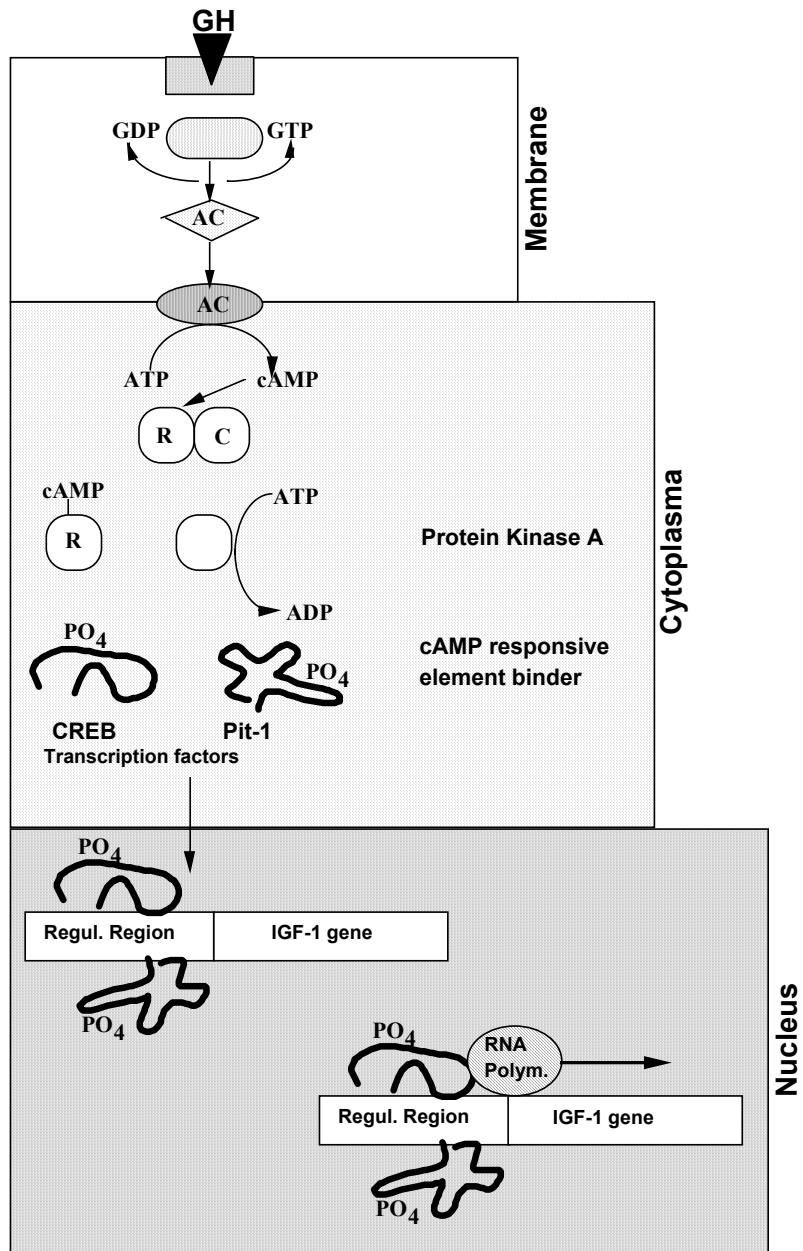
cAMP activates Protein kinase C by binding to its Regulatory unit (R). The Catalytic unit (C) is liberated.

**PROTEIN KINASE C**

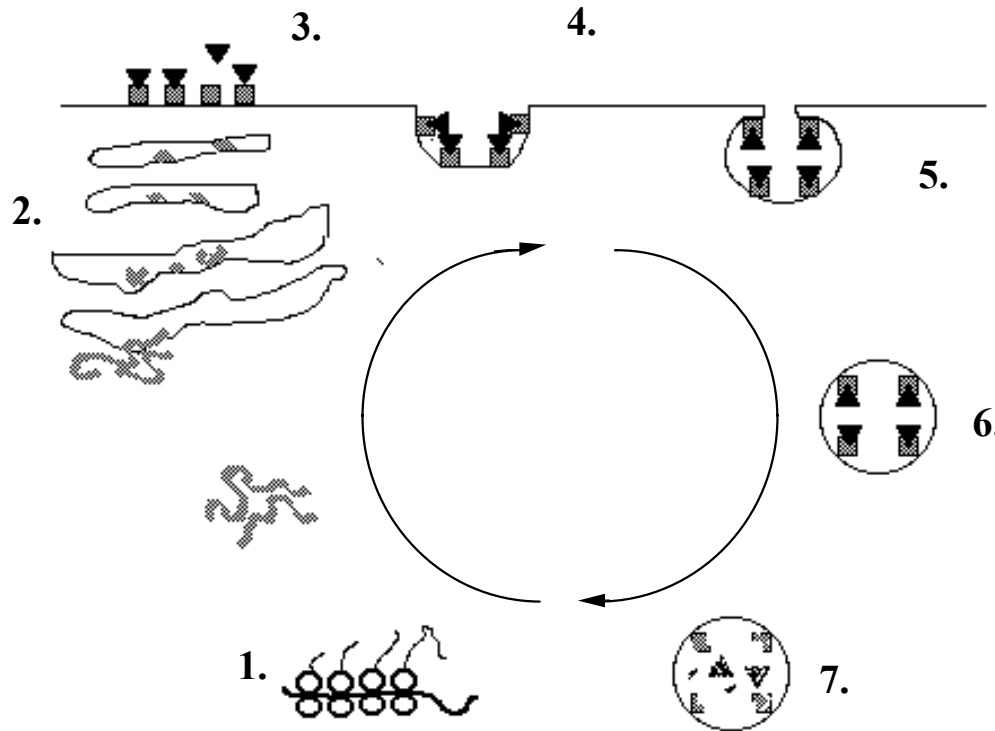
The catalytic unit phosphorylates proteins or enzymes which become active.

The phosphorylated proteins or enzymes become activated and start the biological effect.

**BIOLOGICAL EFFECT**

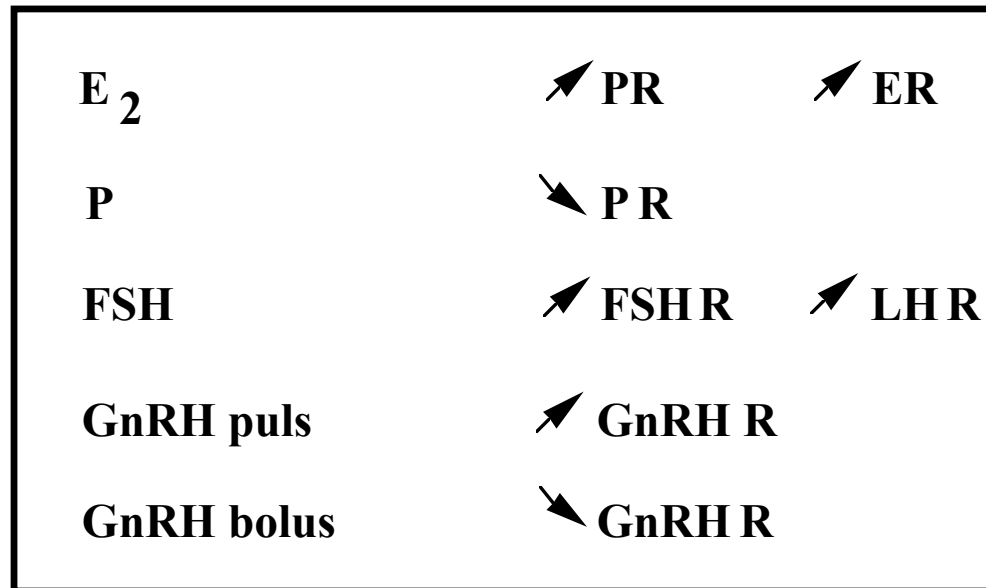


# THE RECEPTOR CYCLE

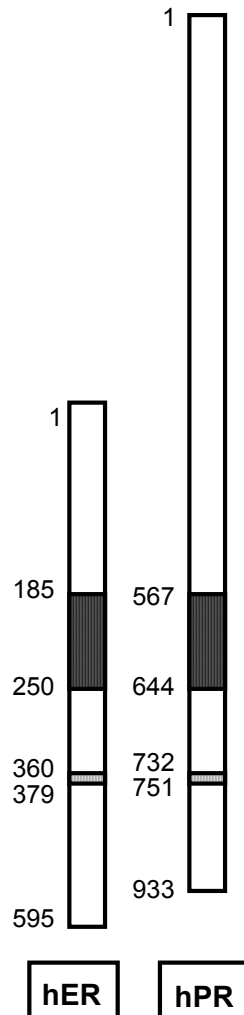


1. Synthesis of receptor proteins in the ribosomes
2. Processing of receptor proteins in the endoplasmic reticulum and transport of receptors through the Golgi to the plasma membrane.
3. Binding of the hormone to the membrane receptor.
4. Start of internalization through the formation of Coated Pits .
5. Invagination of plasma membrane portion rich in saturated receptors.
6. Formation of Coated Vesicles
7. Degradation of receptors and hormones and liberation of amino acids ready to be reused for protein synthesis.

# REGULATION OF RECEPTORS



# STEROID RECEPTOR STRUCTURE



Androgens, Progestogens, Oestrogens, Glucocorticoid, vitamin D and Tyroxine receptors have a similar structure. They are all cytosoluble dimers.

■ They have a 60-80 % homologous DNA binding domain (Zinc finger) also called Hormone Responsive Element (HRE). This domain contains 8 cysteines and positively charged amino acids

■ They have a less homologous hormone binding domain (250 aa) in the C terminal region which contains hydrophobic amino acids.

hER

hPR

hER 2x68 kDa hPR 2x110 kDa

Hormones are produced by Endocrine Glands and secreted into the circulation. They thus come into contact with all cells of the body. Only TARGET CELLS respond to the hormone. These cells have specific RECEPTORS for the hormone.

**WHAT IS THE DISTRIBUTION OF RADIOACTIVE OESTRADIOL WHEN INJECTED IN A RAT ?**

