

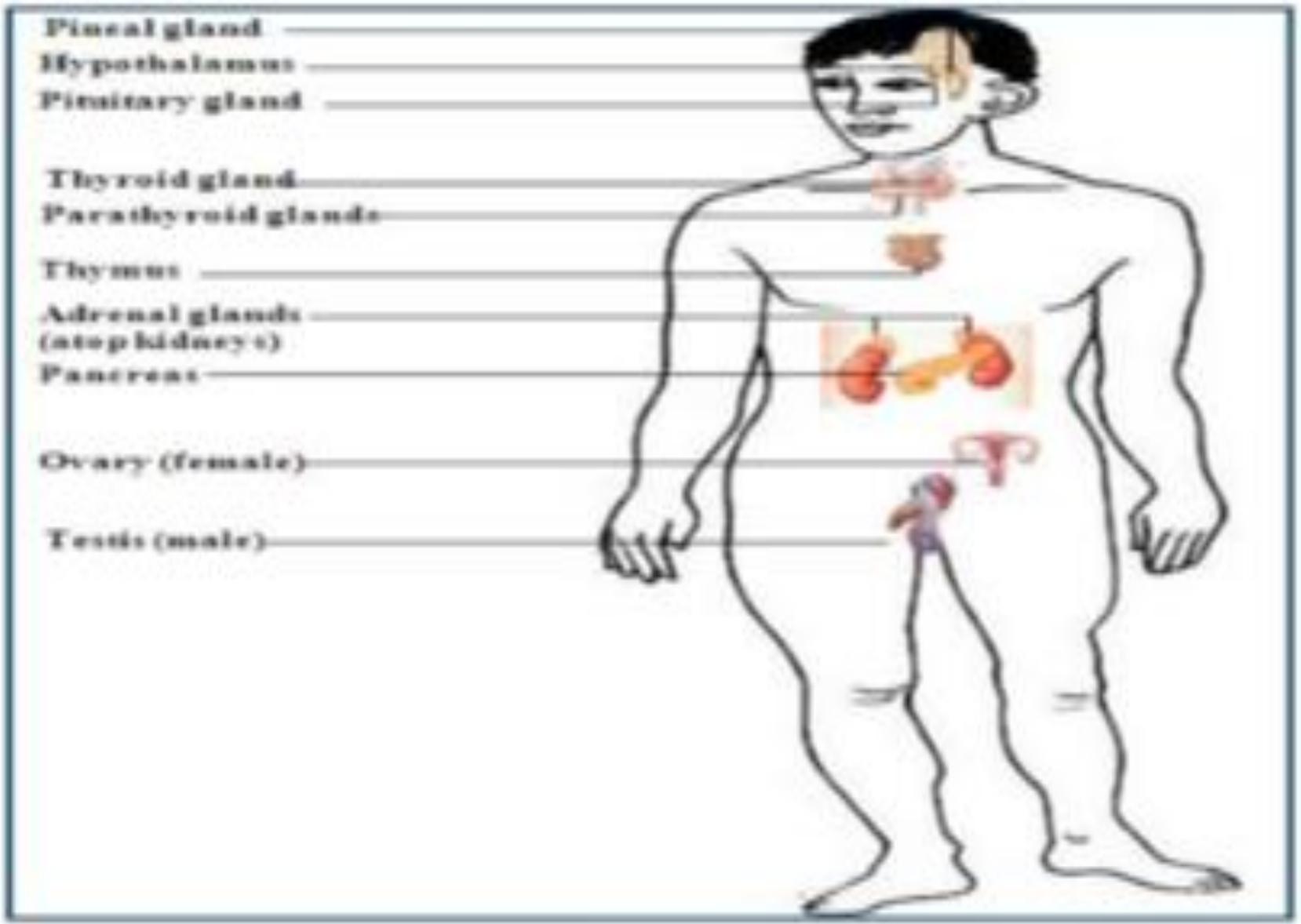
HORMONES

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- ❑ communication system to coordinate its biological functions
- ❑ This is achieved by **two** distinctly organized **functional systems**:
 - ❖ The **nervous system** coordinates the body functions through the **transmission of electrochemical impulses**
 - ❖ The **endocrine system** acts through a wide range of **chemical messengers** known as **hormones**
- ❑ Hormones are **chemical messengers** of the body having **diverse structures and functions**

- ❑ act **either directly** or **through messengers** to coordinate and perform biological functions → growth, reproduction and **digestion** etc
- ❑ defined as **organic substances, produced in small amounts by specific tissues** (endocrine glands), secreted into blood stream to **control metabolic and biological activities** in target cells
- ❑ regarded as **chemical messengers** involved in **transmission of information from one tissue to another and from cell to cell**

Location of endocrine glands



Classification of Hormones

❑ Based on **chemical nature** hormones can be categorized into **three groups**:

1. Protein or peptide hormones e.g. insulin, glucagon, antidiuretic hormone, oxytocin.

2. Steroid hormones e.g. glucocorticoids, mineralocorticoids, sex hormones.

3. Amino acid derivatives e.g. epinephrine, norepinephrine, thyroxine (T4), triiodothyronine (T3)

❑ Based on **mechanism of action** hormones are classified into **two broad groups (I and II)**:

❖ based on **location of the receptors** to which they bind

❖ the **signals used** to mediate their action

Group I hormones:

- ❑ bind to **intracellular receptors** to form **receptor-hormone complexes** (**intracellular messengers**) through which their **biochemical functions are mediated**.
- ❑ **lipophilic** in nature and are mostly **derivatives of cholesterol** (**exception – T3 and T4**). e.g. estrogens, androgens, glucocorticoids, calcitriol.

Group II hormones:

- ❑ bind to **cell surface** (plasma membrane) **receptors** and **stimulate the release of** certain molecules, namely **second messengers** which, in turn, perform the biochemical functions.
- ❑ **hormones themselves are the first messengers**

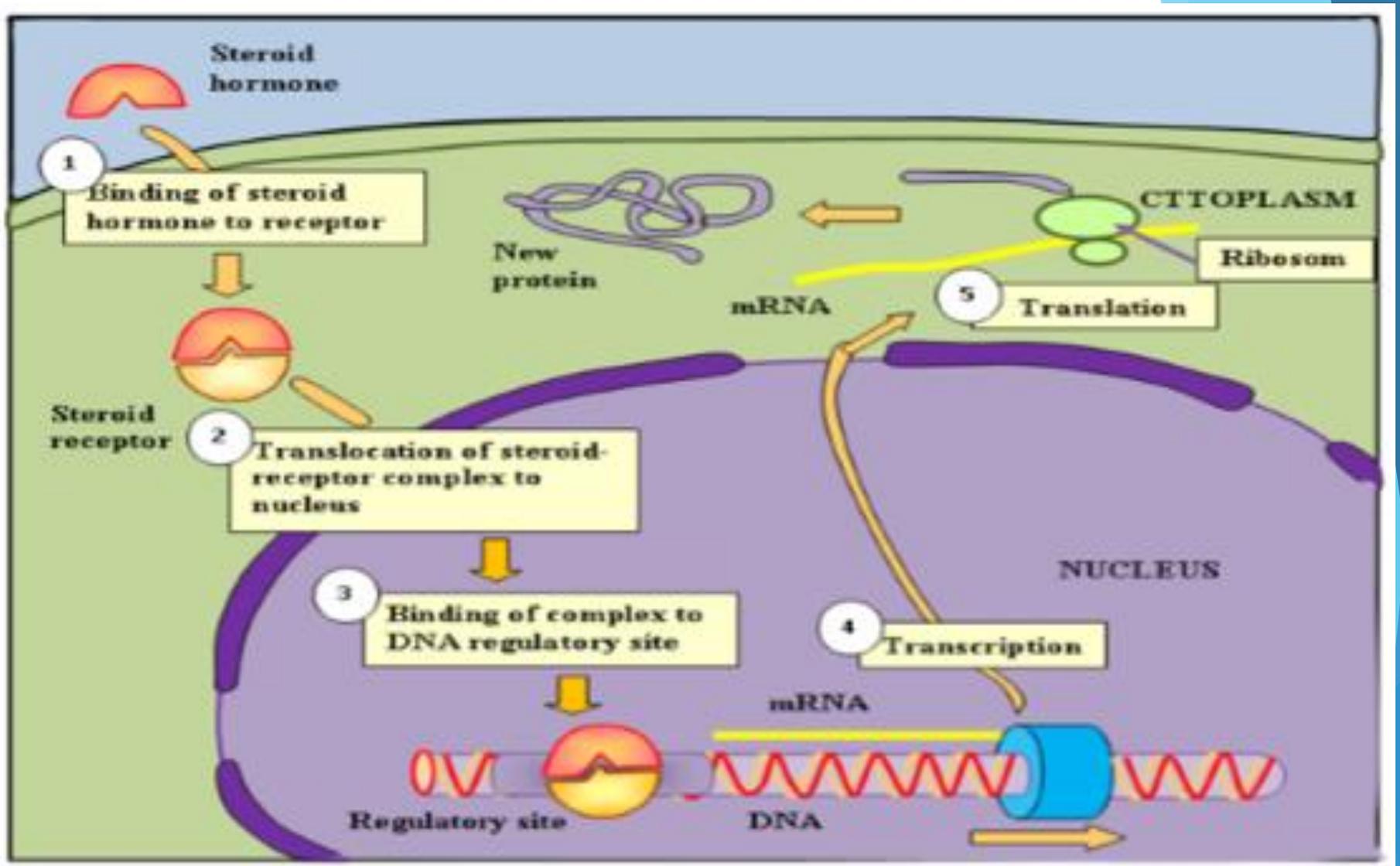
□ Group II hormones are **subdivided** into **three categories** based on **chemical nature of second messengers**:

- ❖ The second messenger is **cAMP** e.g. **ACTH, FSH, LH, PTH, glucagon, calcitonin.**
- ❖ The second messenger is **phosphatidylinositol / calcium** e.g. **TRH, GnRH, gastrin, CCK.**
- ❖ The second messenger is **unknown** e.g. **growth hormone, insulin, oxytocin, prolactin.**

Mechanism of action

Group I hormones

- ❑ **lipophilic** in nature and can **easily pass across plasma membrane**
- ❑ act through **intracellular receptors** located either in cytosol or nucleus
- ❑ hormone-receptor complex binds to specific regions on **DNA** called hormone responsive element (HRE) and causes increased expression of specific genes
- ❑ It is believed that interaction of hormone receptor complex with HRE **promotes initiation** and, to a lesser extent, elongation and termination of RNA synthesis (**transcription**)
- ❑ ultimate outcome is **production of specific proteins** (**translation**) in response to hormonal action



Mechanism of action of intracellular receptor hormones

Group II hormones

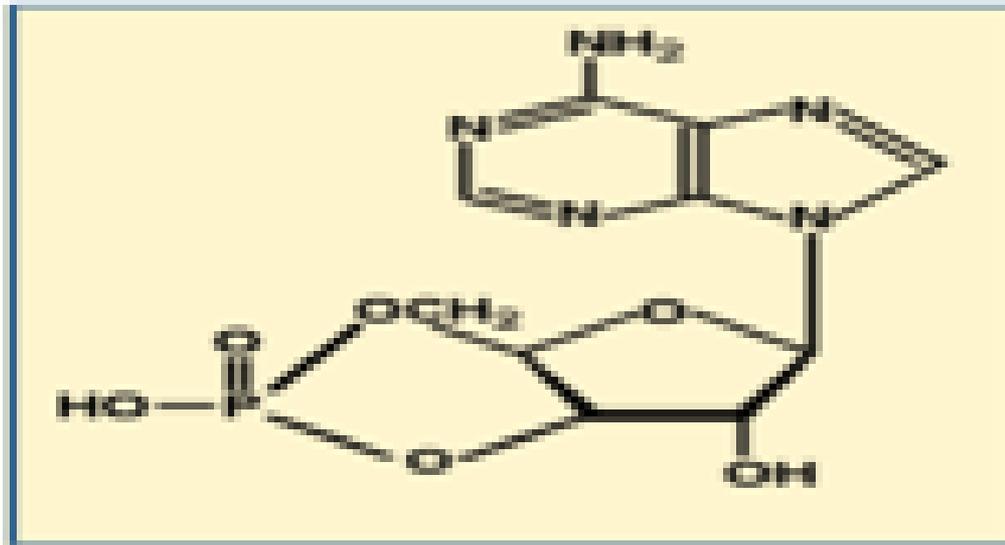
H – cAMP – PKA --- C – Phospho pr. – Biochemical response

- ❑ considered as **first messengers**
- ❑ exert their **action through mediatory molecules** → called **second messengers**
- ❑ **Cyclic AMP (cAMP)** is a ubiquitous nucleotide
- ❑ consists of **adenine, ribose and a phosphate**
- ❑ **cAMP** acts as a **second messenger** for a majority of **polypeptide hormones**
- ❑ membrane-bound enzyme **adenylate cyclase** converts ATP to cyclic AMP
- ❑ cAMP is hydrolysed by **phosphodiesterase**
- ❑ • **Adenylate cyclase system**
- ❑ A series of events occur **at the membrane level** that influence the activity of adenylate cyclase leading to **synthesis of cAMP**
- ❑ This process is **mediated by G-proteins**, so designed due to their ability to bind to guanine nucleotides.
 - **Action of cAMP** – a general view

- ❑ Once produced → cAMP performs its role as a **second messenger** in eliciting biochemical responses
- ❑ **cAMP activates protein kinase A (PKA)**
- ❑ This enzyme is a **heterotetramer** consisting of **2 regulatory subunits (R)** and **2 catalytic subunits (C)**
- ❑ **cAMP binds** to inactive protein kinase and causes **dissociation** of R and C subunits
- ❑ $4\text{cAMP} + \text{R}_2\text{C}_2 \rightarrow \text{R}_2(4\text{cAMP}) + 2\text{C}$
- ❑ (inactive) (inactive) (active)
- ❑ **active subunit (C) catalyses phosphorylation of proteins** (transfer of phosphate group to serine and threonine residues)
- ❑ It is the phosphoprotein that ultimately causes the **biochemical response**

❑ **cAMP does not act on all protein kinases.**

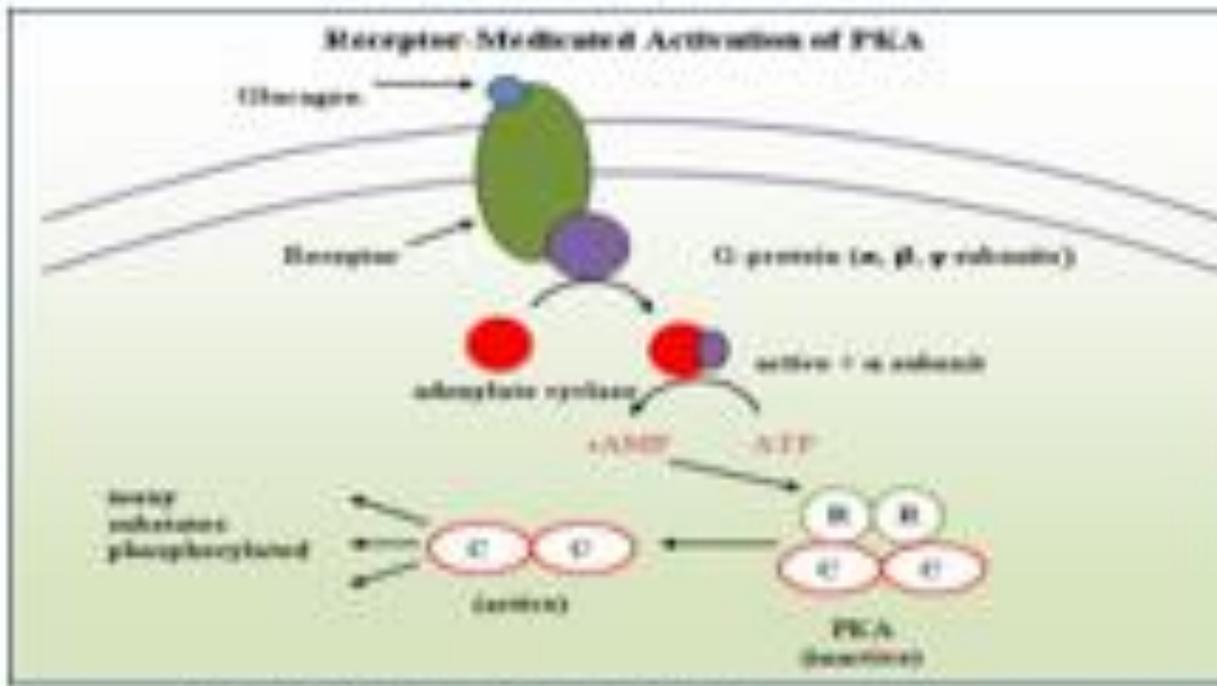
❑ For instance, on protein kinase C (the second messenger is diacylglycerol).



cAMP – The second messenger

Dephosphorylation of proteins:

- ❖ A group of enzymes called **protein phosphatases** hydrolyse and remove the phosphate group added to proteins



| Mechanism of action of cell surface receptor hormones

Principal human hormones – classification (by mechanism of action), origin and major functions

<i>Hormone (s)</i>	<i>Origin</i>	<i>Major Function (s)</i>
Group I. HORMONES THAT BIND TO INTRACELLULAR RECEPTORS		
Estrogens	Ovaries and adrenal cortex	Female sexual characteristics, menstrual cycle
Progestins	Ovaries and placenta	Involved in menstrual cycle and maintenance of pregnancy.
Androgens	Testes and adrenal cortex	Male sexual characteristics, spermatogenesis.
Glucocorticoids	Adrenal cortex	Affect metabolism, suppress immune system.
Mineralocorticoids	Adrenal cortex	Maintenance salt or water balance.
Calcitriol (1,25-DHCC)	Kidney (final form)	Promotes absorption of Ca^{2+} from intestine, kidney and bone.
Thyroid hormones (T_3 , T_4)	Thyroid	Promote general metabolic rate.

Principal human hormones – classification (by mechanism of action), origin and major functions

<i>Hormone (s)</i>	<i>Origin</i>	<i>Major Function (s)</i>
Group II. HORMONES THAT BIND TO CELL SURFACE RECEPTORS		
A. The second messenger is cAMP		
Adrenocorticotropic hormone (ACTH)	Anterior pituitary	Stimulates the release of adrenocorticosteroids.
Follicle stimulating hormone (FSH)	Anterior pituitary	In females, stimulates ovulation and estrogen synthesis. In males, promotes spermatogenesis
Luteinizing hormone (LH)	Anterior pituitary	Stimulates synthesis of estrogens and progesterone and causes ovulation. Promotes androgen synthesis by testes.
Chorionic gonadotropin (hCG)	Anterior pituitary	Stimulates progesterone release from placenta.
Thyroid stimulating hormone (TSH)	Anterior pituitary	Promotes the release of thyroid hormones (T_3 , T_4).
β -Endorphins and enkephalins	Anterior pituitary	Natural endogenous analgesics (pain relievers).
Antidiuretic hormone (ADH)	Posterior pituitary (stored)	Promotes water reabsorption by kidneys.
Glucagon	Pancreas	Increases blood glucose level, stimulates glycogenolysis & lipolysis
Parathyroid hormone (PTH)	Parathyroid	Increases serum calcium, promotes Ca^{2+} release from bone.
Calcitonin	Thyroid	Lowers serum calcium. Decreases Ca^{2+} uptake by bone and kidney.
Epinephrine	Adrenal medulla	Increases heart rate and blood pressure. Promotes glycogenolysis in liver and muscle and lipolysis in adipose tissue.
Norepinephrine	Adrenal medulla	Stimulates lipolysis in adipose tissue.

Principal human hormones – classification (by mechanism of action), origin and major functions

<i>Hormone (s)</i>	<i>Origin</i>	<i>Major Function (s)</i>
B. The second messenger is phosphatidylinositol/calcium		
Thyrotrophin-releasing hormone (TRH)	Hypothalamus	Promotes TSH release.
Gonadotrophin-releasing hormone (TRH)	Hypothalamus	Stimulates release of FSH and LH.
Gastrin	Stomach	Stimulates gastric HCl and pepsinogen secretion.
Cholecystokinin (CCK)	Intestine	Stimulates gall bladder and secretion of pancreatic enzymes.

Principal human hormones – classification (by mechanism of action), origin and major functions

<i>Hormone (s)</i>	<i>Origin</i>	<i>Major Function (s)</i>
C. The second messenger is unknown/unsettled		
Growth hormone (GH)	Anterior pituitary	Promotes growth of the body (bones and organs).
Prolactin (PRL)	Anterior pituitary	Growth of mammary glands and lactation.
Oxytocin	Posterior pituitary (stored)	Stimulates uterine contraction and milk ejection.
Insulin	Pancreas	Hypoglycemic effect, promotes protein synthesis and lipogenesis.
Somatomedins (insulin-like growth factors, IGF-1, IGF-II)	Liver	Stimulates growth of cartilage.

Thank you!

