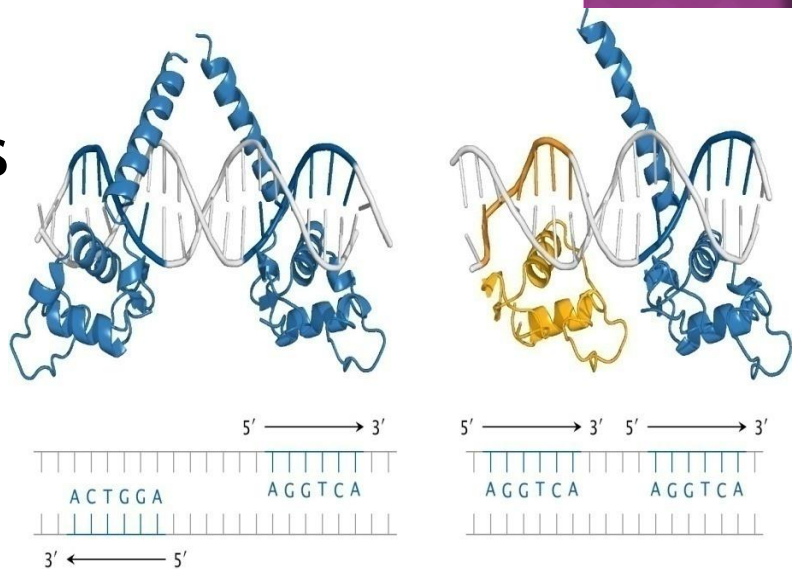
THYROID STIMULATING HORMONE

Dr. Kalsoom Tariq

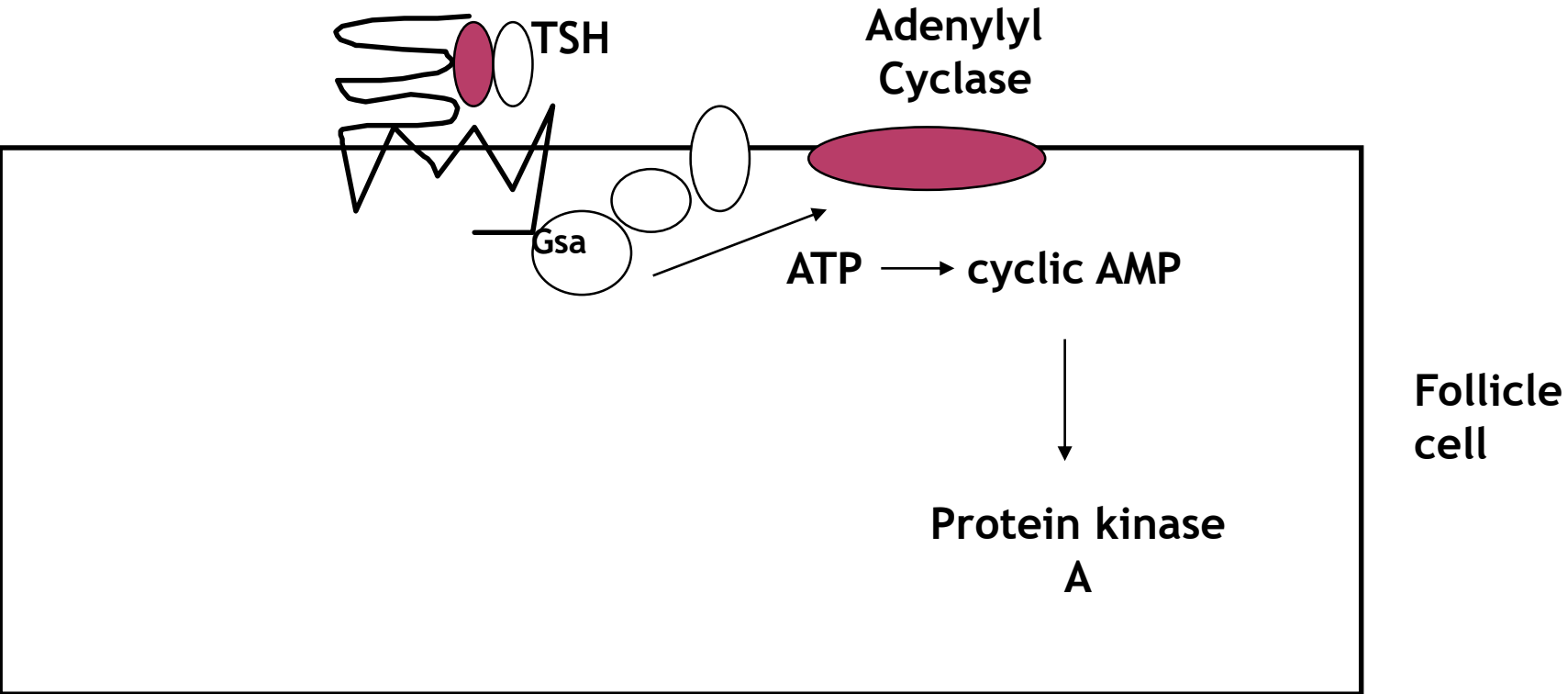
THYROTROPIC HORMONE

- Produced by basophil cells of anterior pituitary, **glycoprotein** in nature.
- Molecular wt 30,000 ,carbohydrate content is 21%.
- Compose of two subunits ,alpha and beta.
- Alpha chain is common in TSH,LH,FSH .
- beta sub units are different and confers hormonal specificity.
- Alpha subunit has 92 amino acids
- Beta has 112 amino acids.
- Have several di sulphide bridges,
- α has 5& β has 6 S-S bridges.



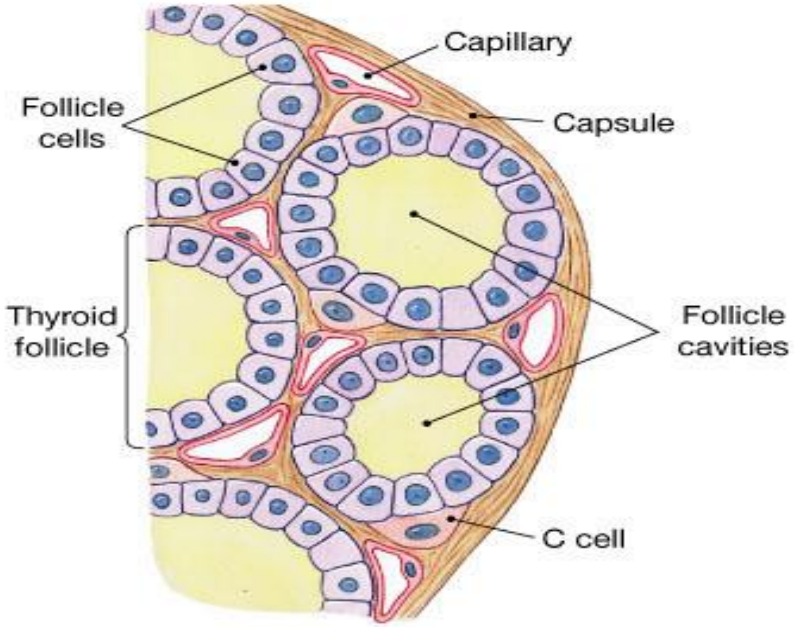
Mechanism of Action of TSH

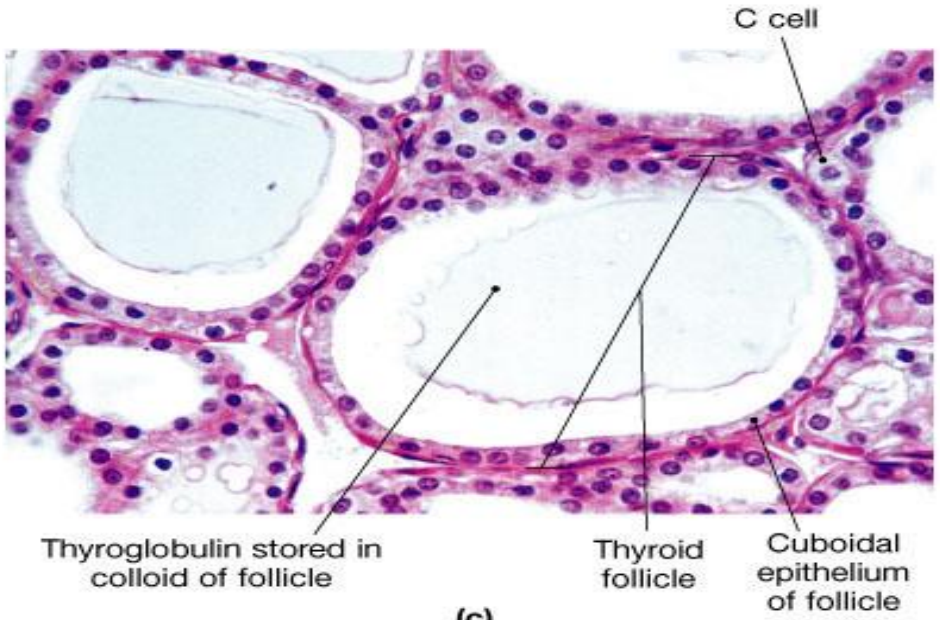
- Receptor binding site on beta subunit of TSH bind to glycoprotein receptors on thyroid cell membrane
- The complex then activates adenylate cyclase which catalyzes formation of c- AMP ,acts as 2nd messenger for most TSH actions.



METABOLIC ACTIONS

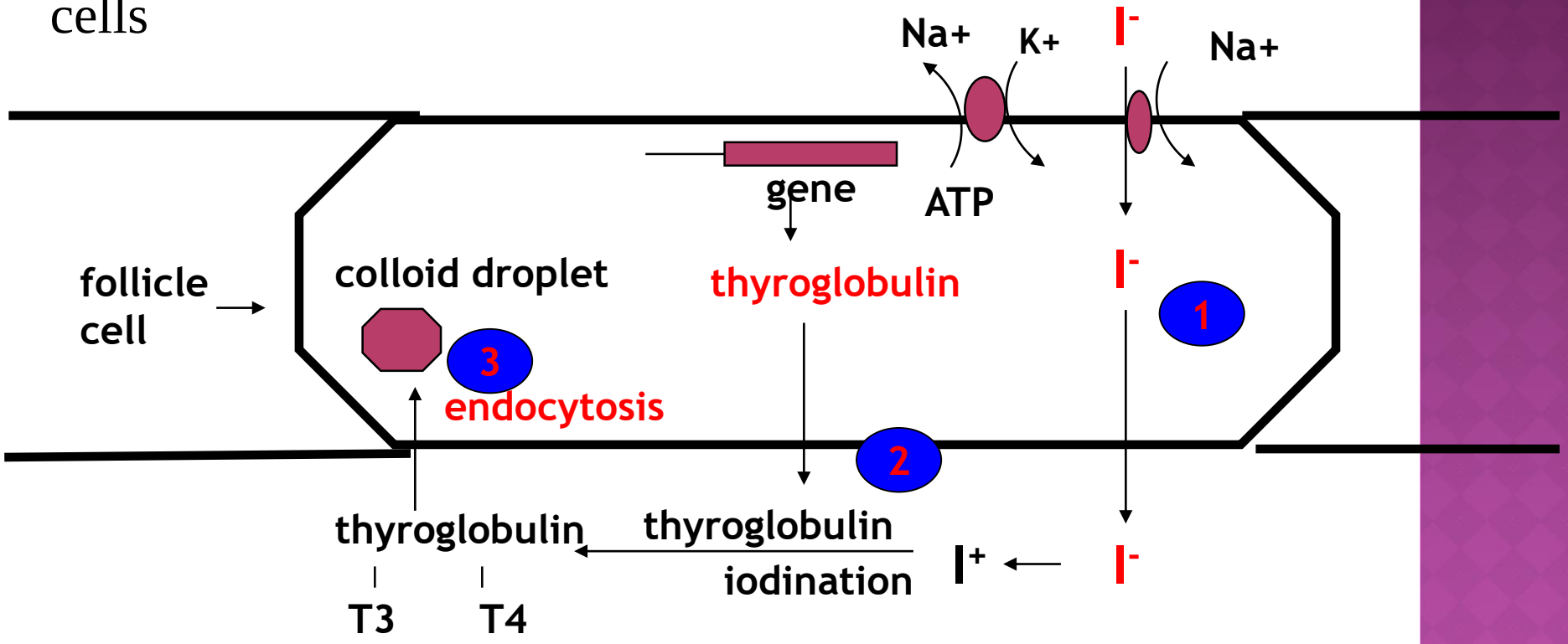
- Increase release of stored thyroid hormone.
- Increase DNA content, RNA and translation of proteins, cell size.
- Stimulates glycolysis ,TCA cycle, HMP and phospholipid synthesis.
- Activates adipose tissue lipase to enhance lipolysis.





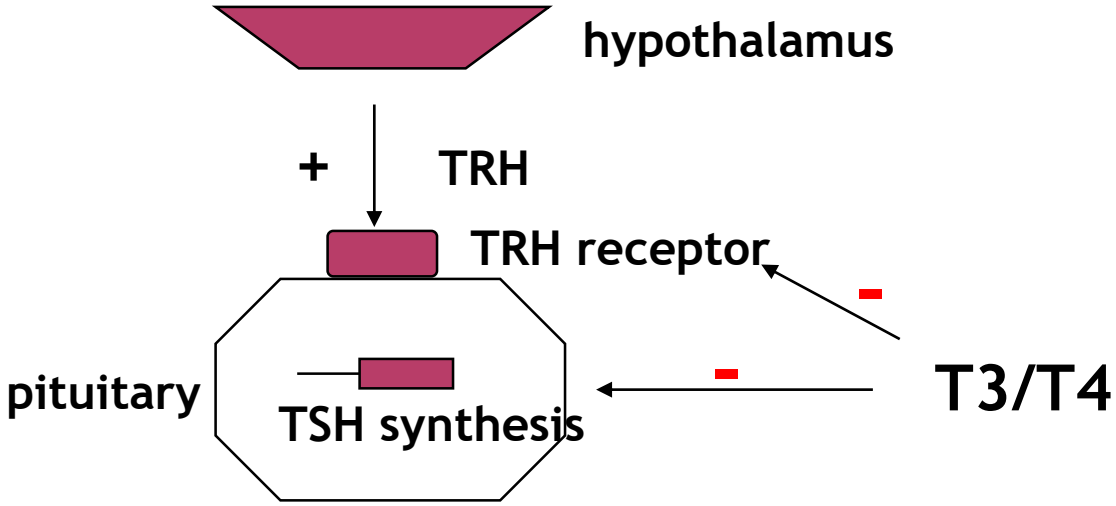
Action of TSH on the Thyroid

- TSH stimulates the synthesis of thyroid hormone at all stages ,such as
  - increase iodide transport into follicular cells
  - increases production and iodination of thyroglobulin
  - increases endocytosis of colloid from lumen into follicular cells

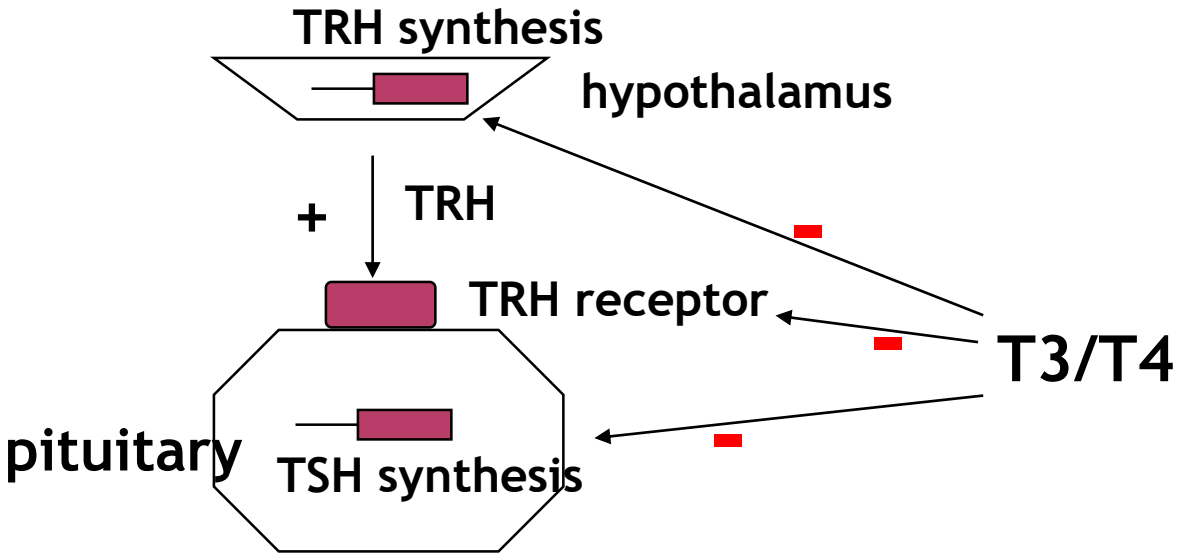


Regulation of TSH Release from the Anterior Pituitary

- TSH release is influenced by hypothalamic TRH (thyrotropin releasing hormone), and by thyroid hormones themselves.



Negative Feedback Actions of Thyroid Hormones on TSH Synthesis & Release



Thyroid hormones exert negative feedback on TSH release at the level of the anterior pituitary.

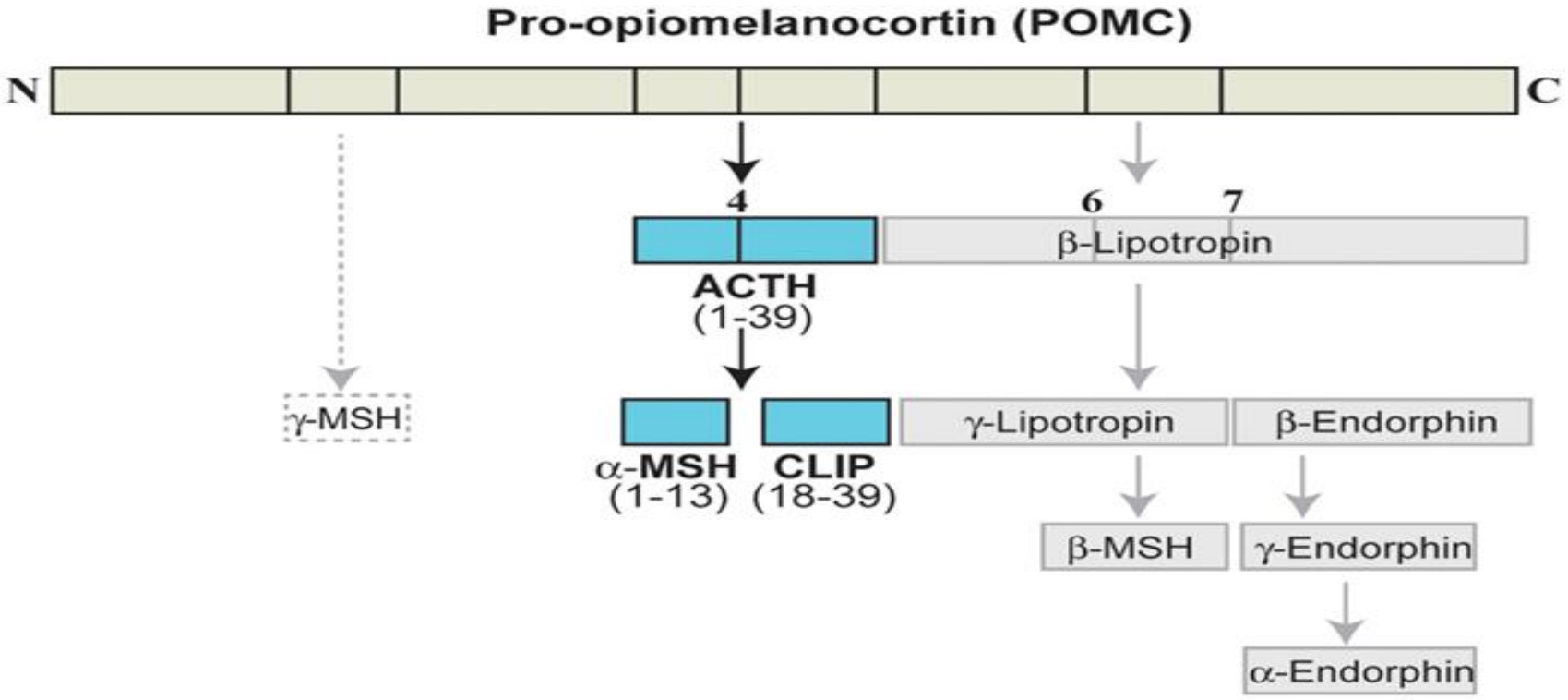
- inhibition of TSH synthesis
- decrease in pituitary receptors for TRH

ADRENO CORTICOTROPIC HORMONE

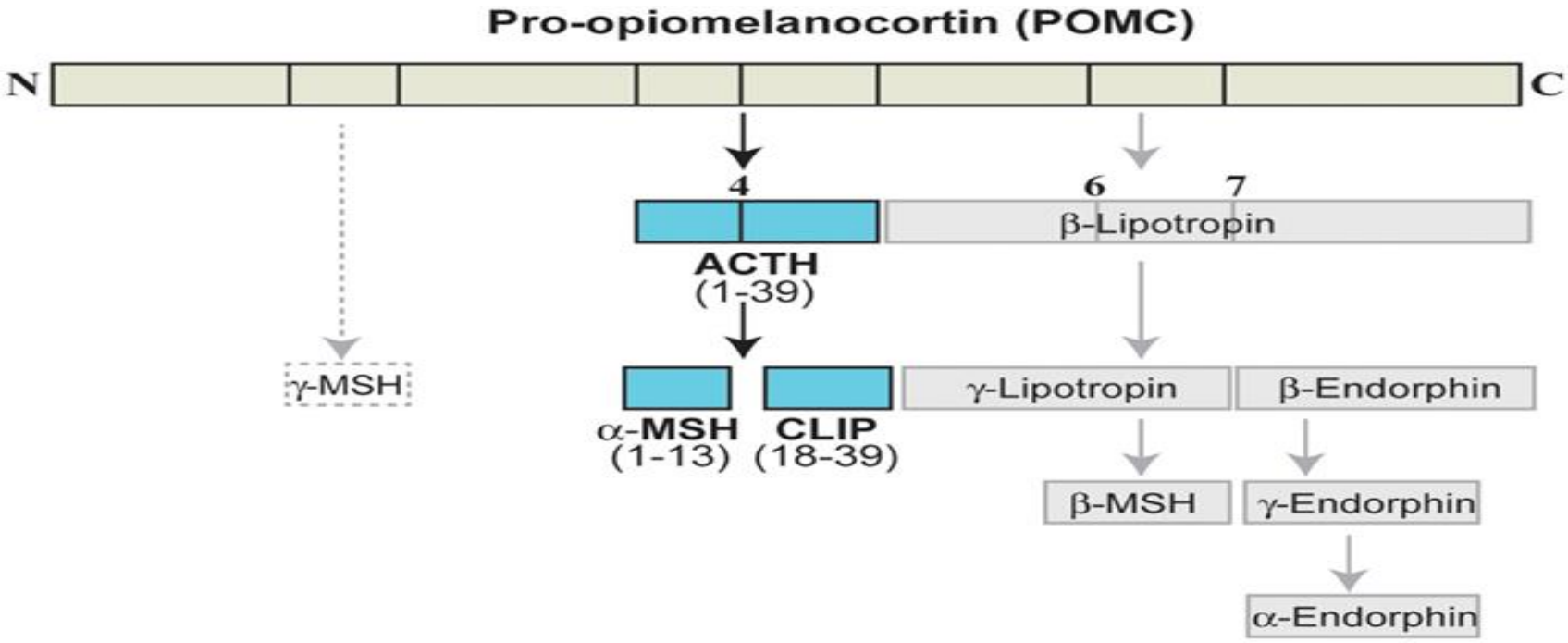
Dr. Kalsoom Tariq

PRO-OPIOMELANOCORTIN (POMC) PEPTIDE FAMILY

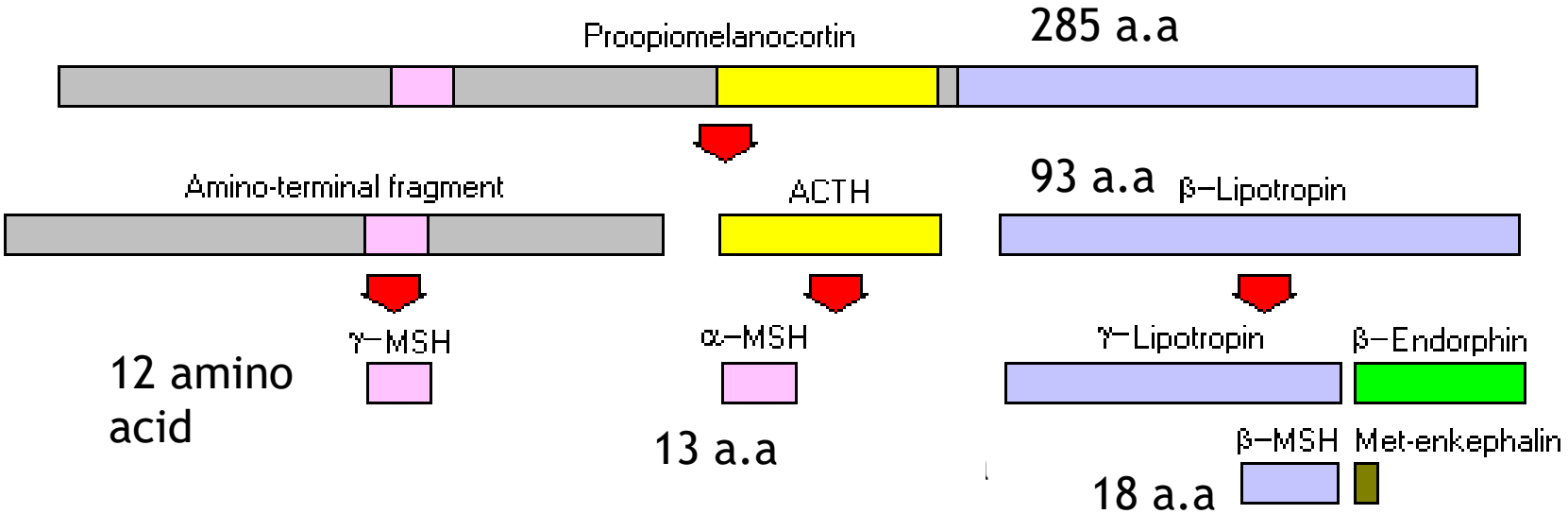
- This family consist of
- Adrenocorticotropic hormone(ACTH)
- Lipotropin (LPH)
- Melanocyte stimulating hormone(MSH)



- The name Pro-opiomelano cortin is derived since it is a prohormone to opiods, melanoyte-stimulating hormone and corticotropin.
- Endorphin and encephalin are natural analgesics.

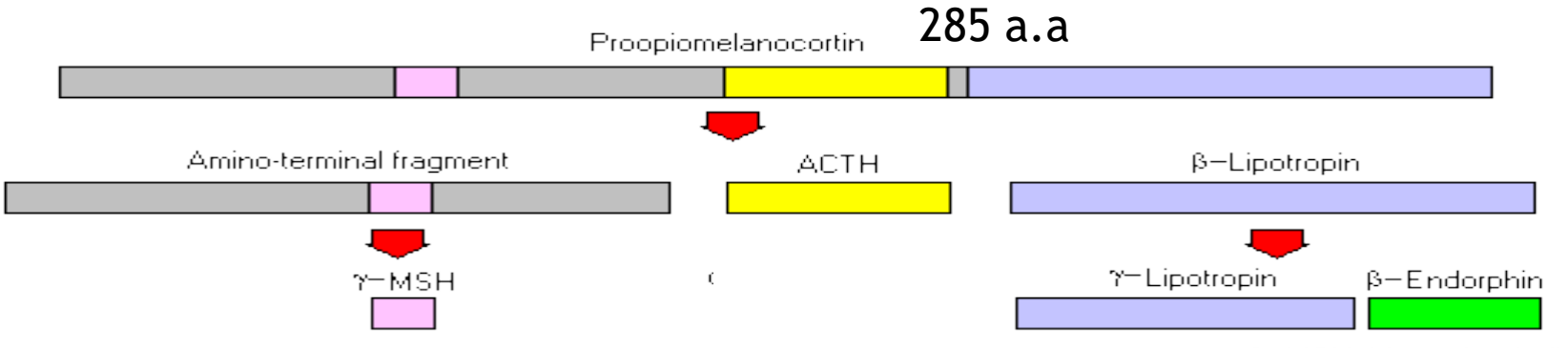


ACTH is synthesized as a part of precursor peptide of mol.wt of 31500 with 285 amino acid, known as pro- opiomelanocortin(POMC).
Other products are alpha,beta lipotrophin(93a.a),beta MSH(18a.a), r-MSH(12a.a).
Beta endorphin,encephalin(natural analgesics).



ADRENOCORTICOTROPIC HORMONE

- Peptide with 39 amino acids arranged in a single chain, molecular weight 4500.
- Two forms have been isolated.
- Alpha corticotropin ,beta corticotropin.
- Biological activity resides in the first 23 amino acids from N- terminal end.
- Species specific variation occur in remaining residues.



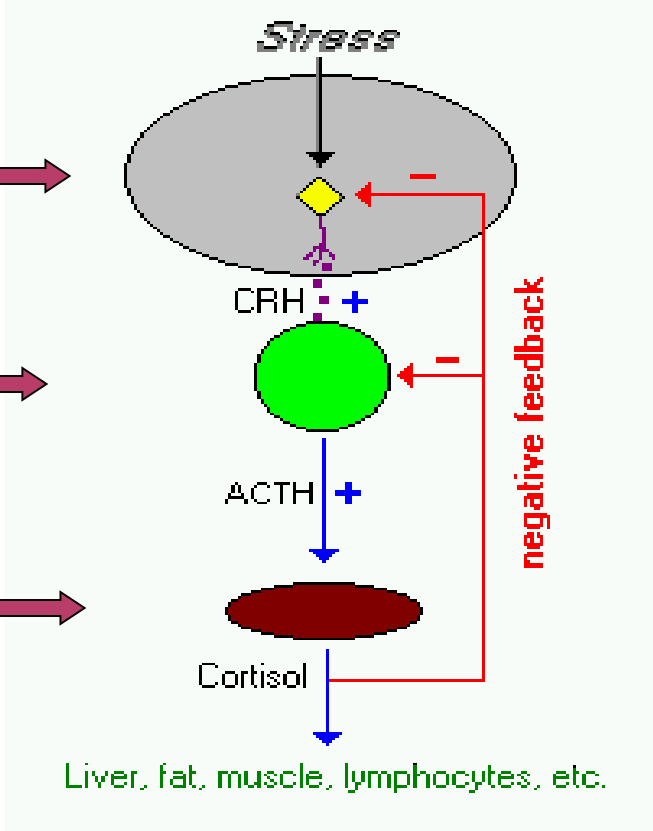
MECHANISM OF ACTION OF ACTH

- Stimulates adrenal steroidogenesis by binding to receptors in the adrenocortical membrane and subsequent activation of adenylate cyclase.
- This activation is calcium dependant.
- This result in ↑ DNA content and RNA is transcribed.
- Proliferation of fasciculata cells and growth of adrenal cortex.

THE HYPOTHALAMIC-PITUITARY-ADRENAL CORTEX AXIS

Control of ACTH secretion is under the influence of Hypothalamic CRH, secretion of which in turn is determined by blood cortisol acting by negative feedback.

- Hypothalamus
- pituitary
- adrenal cortex



METABOLIC ROLE OF ACTH

- ↑ transfer of cholesterol from plasma lipoprotein into fasciculata cells.
- Promotes binding of cholesterol to mitochondrial cytochrome P450 required for hydroxylation of cholesterol.
- Activate rate limiting enzyme for conversion of cholesterol to pregnenolone.
- Activate dehydrogenases of HMP shunt to ↑ concentration of NADPH for hydroxylation.

METABOLIC ROLE OF ACTH

- Activate adenylate cyclase of adipose tissue, increase intracellular c-AMP which activates hormone sensitive lipase---lipolysis to increase free fatty acids.
- ↓ Blood glucose due to release of insulin.
- ↑ glucose tolerance.
- Liberation of histamine.
- Pigmentation of skin, due to homology between MSH & ACTH.
- Overproduction causes Cushing's syndrome.

GONADOTROPINS

Dr. Kalsoom Tariq

GONADOTROPINS

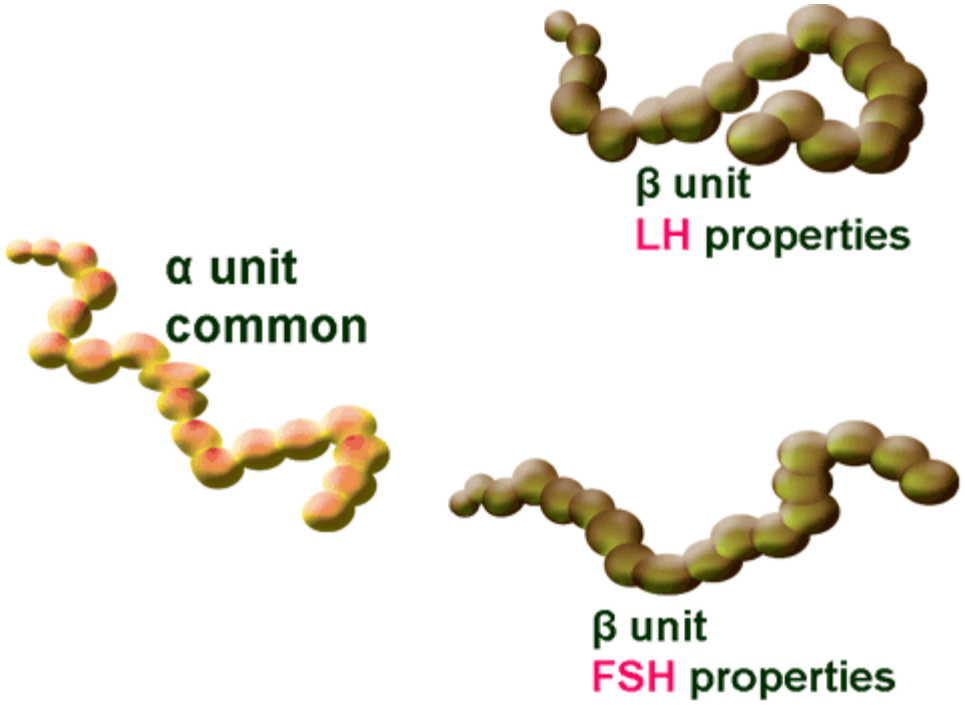
- Influence the maturation and functions of testes and ovaries.

Two types

- FSH (follicle stimulating hormone)
- LH (luteinizing hormone)

GONADOTROPINS

1. These are tropic hormones
2. Both consists of alpha and beta peptides chains linked noncovalently.
3. Both are glycoproteins



SOURCE OF SECRETION

Both are secreted by Gonadotroph cells of Anterior Pituitary gland.

Its secretion is controlled by Gonadotropin-releasing hormone(GnRH) from Hypothalamus through Hypothalamic-hypophysial portal vessels.

CHEMISTRY

Both are glycoprotein with sialic acid, hexose and hexosamine as carbohydrate moiety(16%) and two amino acid chains.

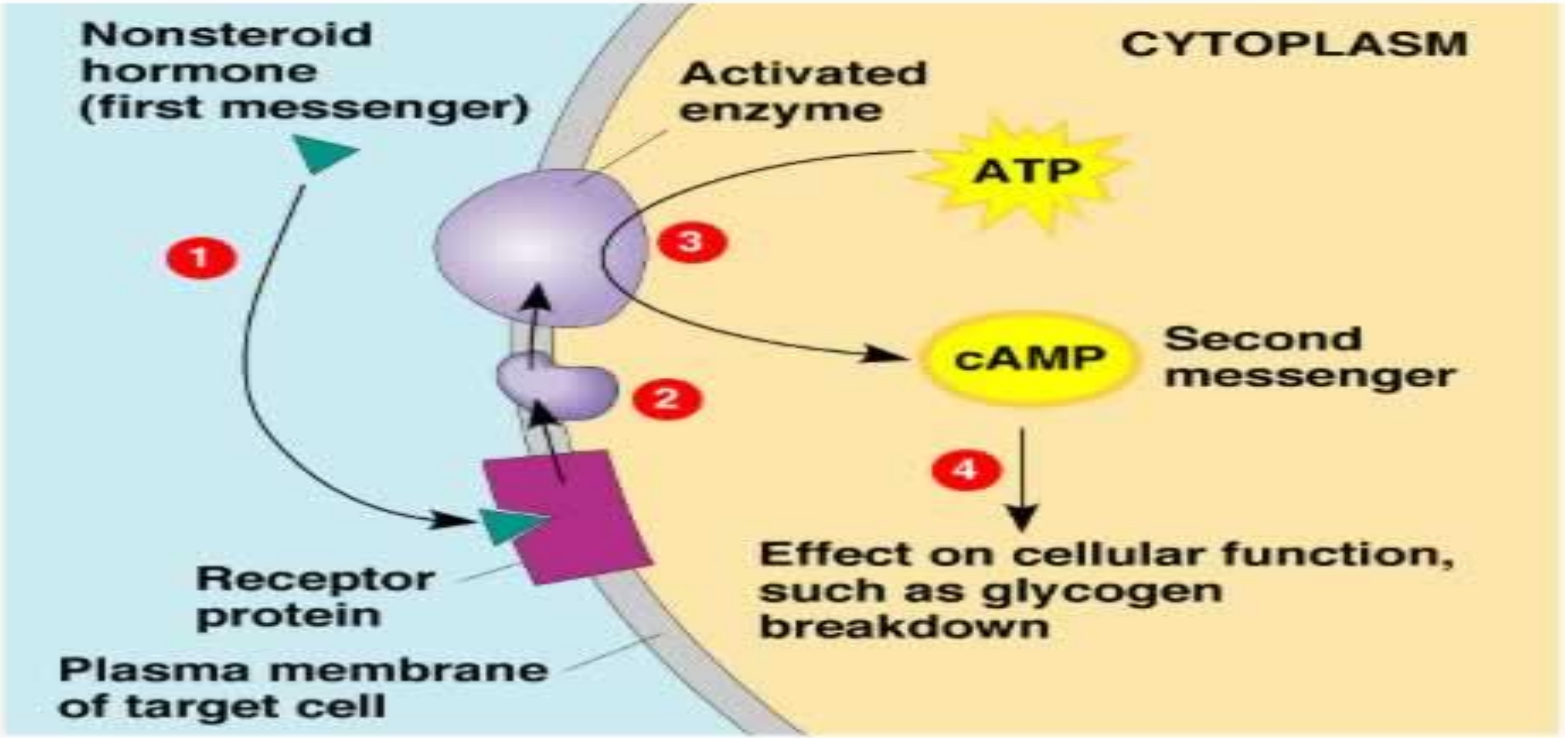
Molecular weight of FSH is 25000

LH is 40000

α is identical for TSH,LH & FSH of the same species and beta chain of FSH and LH have 118 and 112 amino acids residues.

MECHANISM OF ACTION

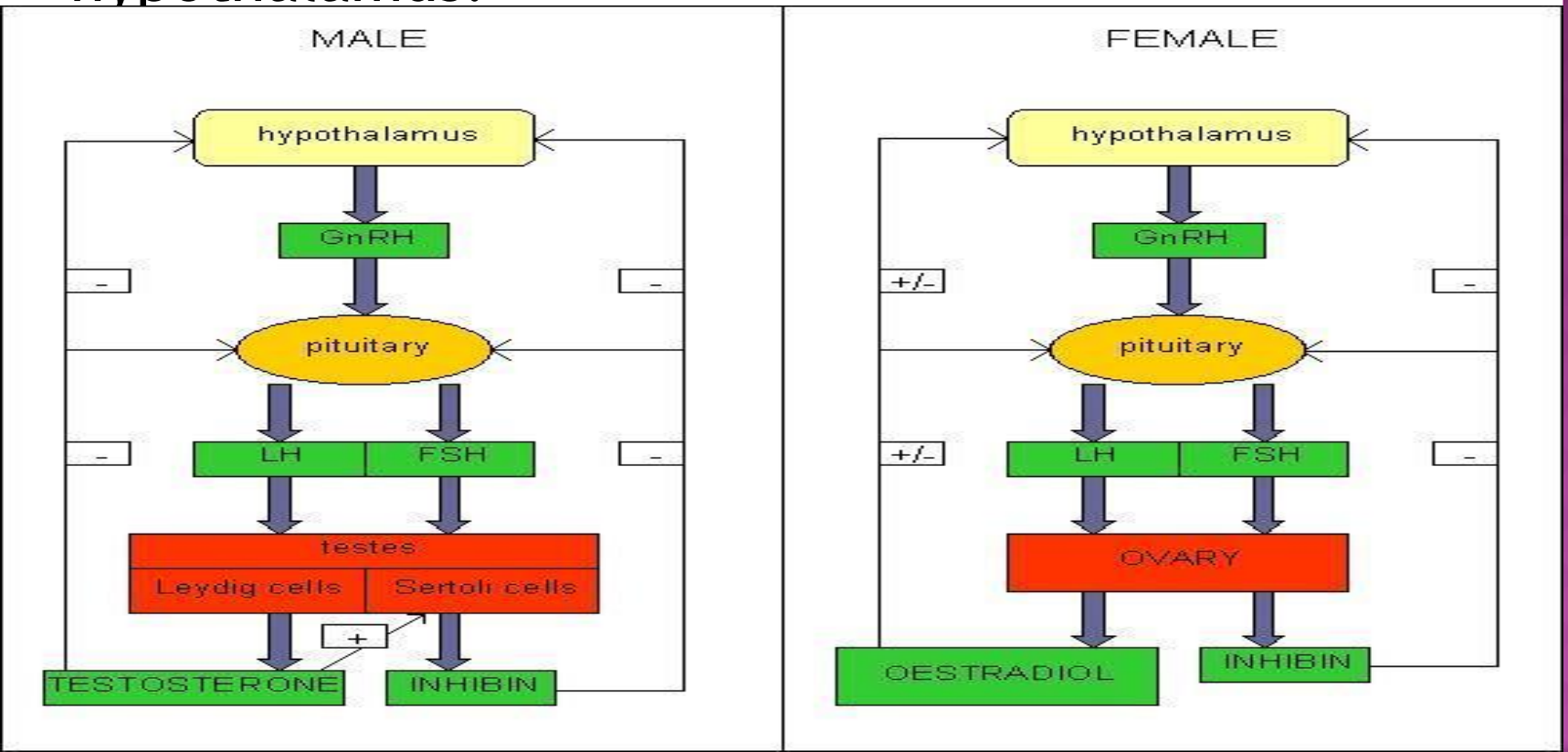
Both activates membrane receptors, which in turns activates second messenger system inside the cell for various cell functions.



REGULATION OF SECRETION NEGATIVE FEEDBACK EFFECT

Estrogen assisted by progesterone has an inhibitory effect on the production of FSH and LH.

This feedback effects mainly operate directly on anterior pituitary but also to lesser extent on hypothalamus.

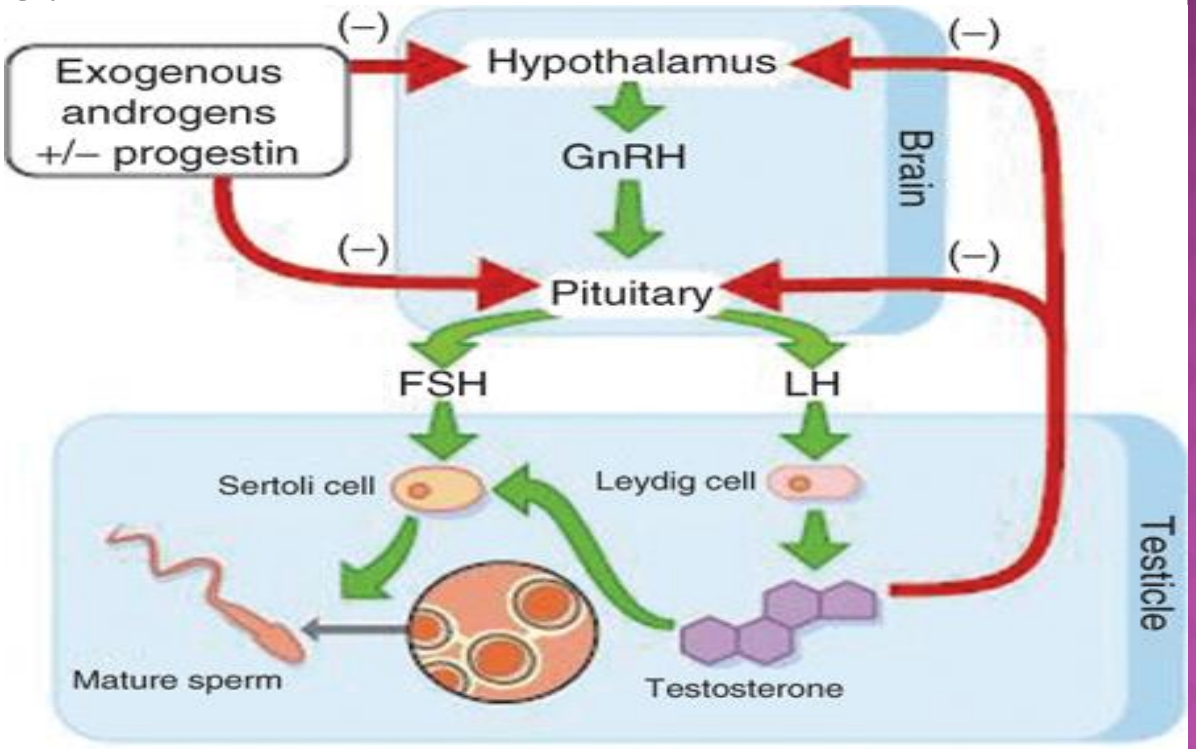


METABOLIC ROLE OF FSH IN MALES

- It stimulates the growth of seminal tubules and testis.
- In the absence of FSH , atrophy of testes will occur.
- In males it acts on sertoli cells ,causes spermatogenesis.
- In the absence of FSH spermatogenesis cannot proceed, however, it cannot cause complete formation of spermatozoa, testosterone is required for the final maturation .

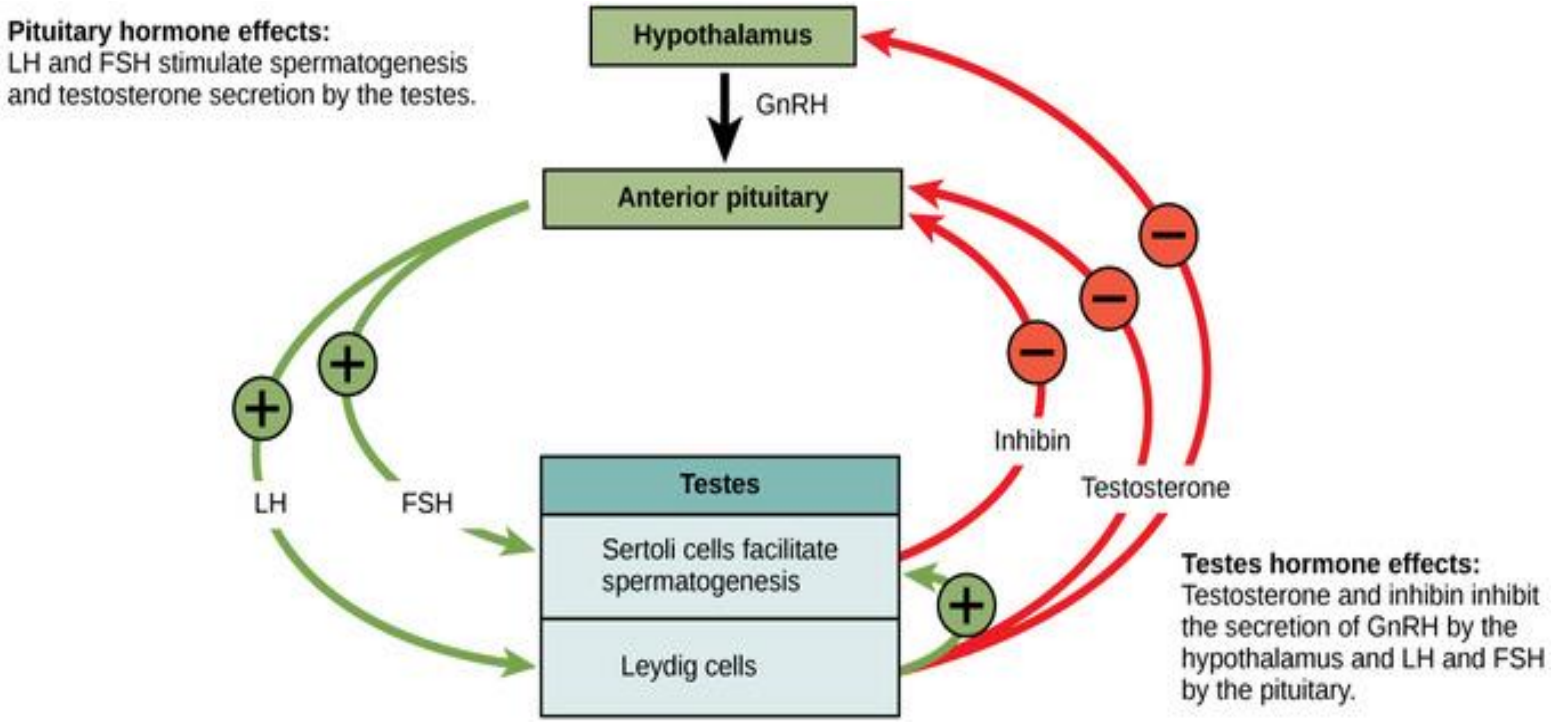
ROLE OF FSH IN SPERMATOGENESIS

- It stimulates the conversion of primary spermatocyte into secondary spermatocyte
- It initiates proliferation of process of spermatogenesis and but its completion requires testosterone.



METABOLIC ROLE OF LH IN MALES

It causes secretion of testosterone from leydig cells which potentiates the stimulant effect of FSH on maturation of spermatids to sperms.

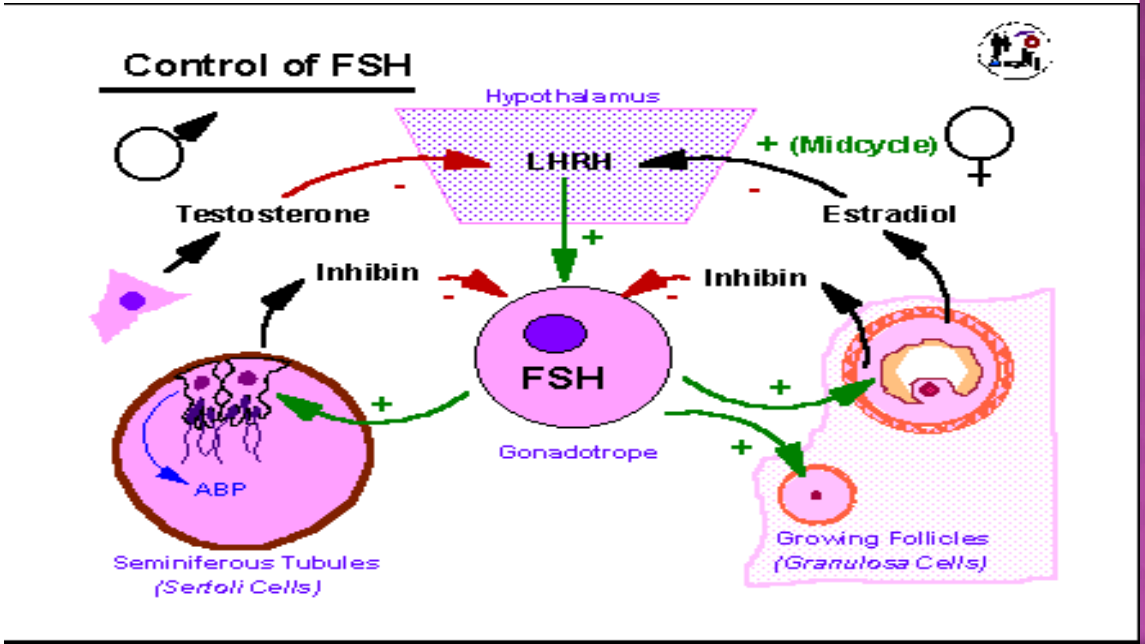


REGULATION OF TESTOSTERONE SECRETION BY LH

- Testosterone is produced by interstitial cells of Leydig only when testes are stimulated by LH.
- The quantity of testosterone secreted is proportional to the amount of LH available.
- Thus LH stimulates the development and functional activity of leydig cell and consequently testicular androgen.

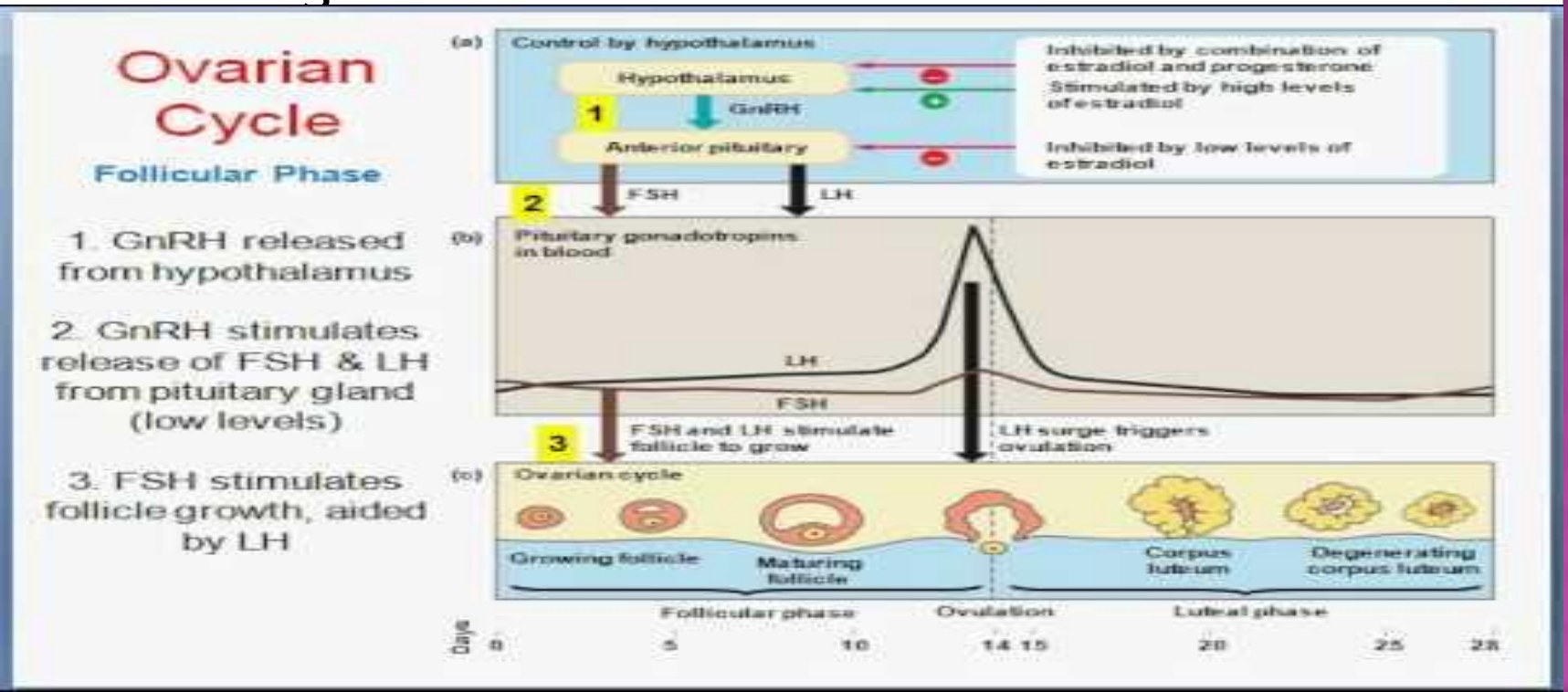
METABOLIC ROLE OF FSH IN FEMALES

1) It promotes follicular growth(follicular maturation)
2) Prepares Graafian follicle for the action of LH
3) Enhances the release of estrogen induced by LH



METABOLIC ROLE OF LH IN FEMALES

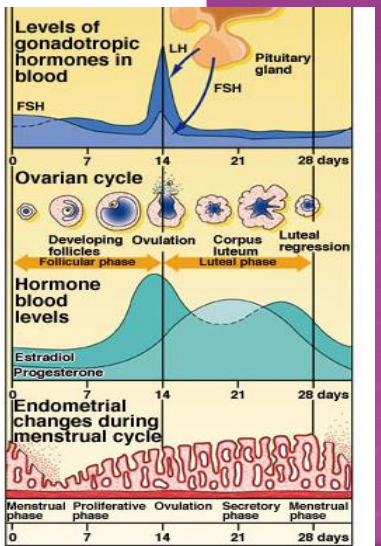
- Necessary for final follicular growth and maturation
- Stimulates secretion of estrogen by theca and granulosa cells.



OVULATORY SURGE FOR LH

- LH acts synergistically with FSH to cause swelling of follicle shortly before ovulation.
- Large amount of LH called **OVULATORY SURGE** is secreted by pituitary during day immediately preceding ovulation.
- In female it acts on theca cell of ovary and cause ovulation and sustain corpus luteum.

Human Menstrual Cycle



DEFICIENCY OF GONADOTROPINS

A. In preadolescent children results in retarded sexual maturation.

B. In adults results in loss of libido, impotence, loss of muscular mass and decreased facial hair in men, amenorrhea and vaginal atrophy in women.

PROLACTIN

STRUCTURE OF PROLACTIN

- Also known as Leuteotropic hormone.
- Similar to GH
- Consist of single peptide chain having 199 amino acids, three intra chain disulfide bonds.
- slightly longer than GH, has Mol.wt 23000.
- Secreted by lactotroph ,alpha cells of anterior pituitary .

MECHANISM OF ACTION OF PROLACTIN AND REGULATION.

- Receptors for prolactin are similar in structure as for GH.
- PRL secretion is under dominant negative control of dopamine .
- Conc. increases 10 fold during pregnancy, remain elevated during lactation ,stimulated by suckling .
- L-methyl dopa↓ its secretion.
- Dopamine agonist and bromocriptin↓ secretion.

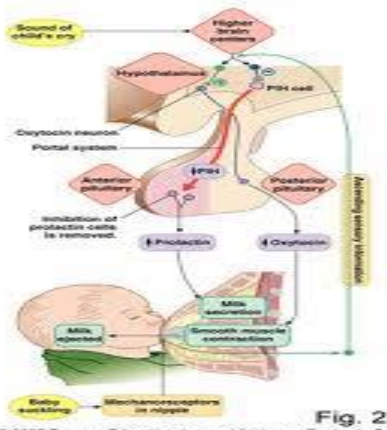


Fig. 26-23

EFFECTS OF PROLACTIN

- Stimulate mammary gland's growth and secretion of milk .
- Stimulates mRNA synthesis, leads to enlargement of breast.**(mammotropic action).**
- Synthesis of milk proteins such as lactalbumin, and casein **(lactogenic action).**
- Estrogen ,thyroid hormones, glucocorticoid, increase the number of prolactin receptors on the mammary cell membrane.
- Progesterone has opposite effects.

HYPERPROLACTANEMIA

- Excessive secretion of prolactin due to **micro adenoma** of the prolactin secreting cells.

CAUSES OF HYPERPROLACTENEMIA

- Physiological factors
- Pain
- Nipple stimulation
- Pregnancy
- Exercise
- Sleep

Drugs

Dopamine- antagonist

Dopamine-depleting agent.

Narcotics

pathological factors

Hypothalamus

Pituitary

Thyroid

- Idiopathic hyperprolactenemia

MANIFESTATION OF HYPERPROLACTENEMIA

In females

- 15%---20% of cases involving secondary amenorrhea or oligomenorrhea .
- 30% of cases involving galactorrhoea or infertility.
- 75% of cases involving both amenorrhea and galactorrhoea.
- Osteoporosis, Hirsutisim .

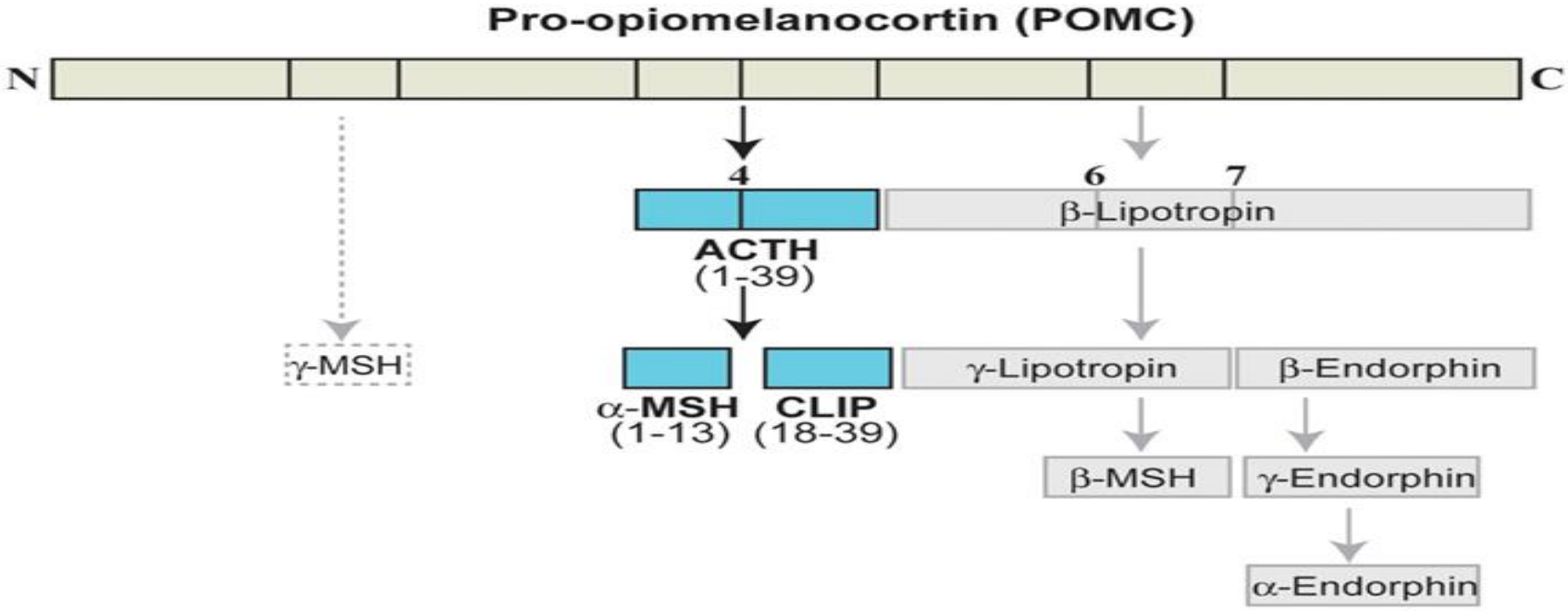
In males

- Impotence
- Oligo spermia
- Gynecomastia
- Visual fields defects in both sexes.

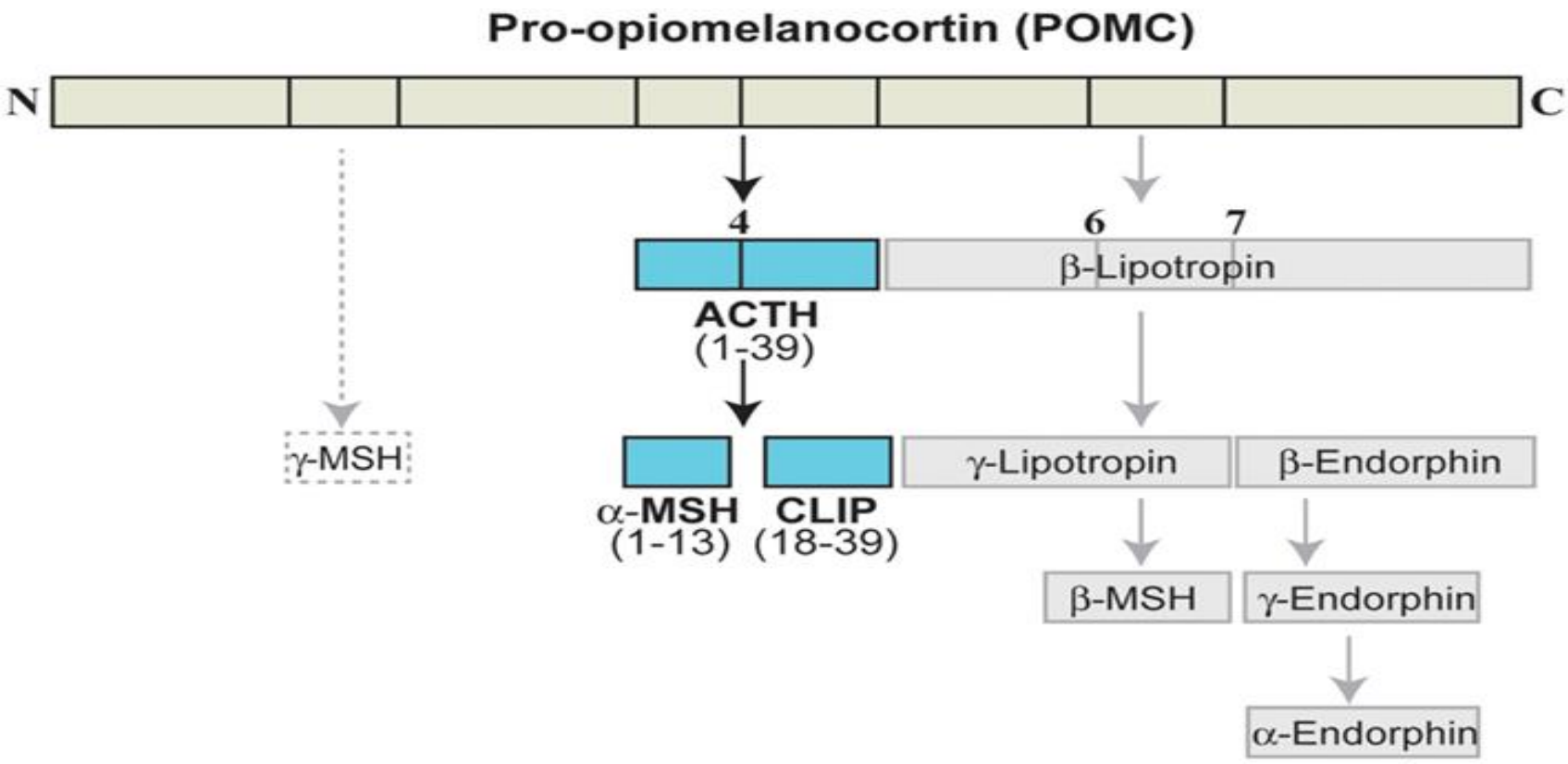
MELANOCYTE STIMULATING HORMONE

MELANOCYTE STIMULATING HORMONE

- Three types
- Alpha, beta, gamma .
- All are present in precursor POMC.
- Gamma is important in humans,
- Its activity is contained in the molecule of gamma LPH or beta LPH.

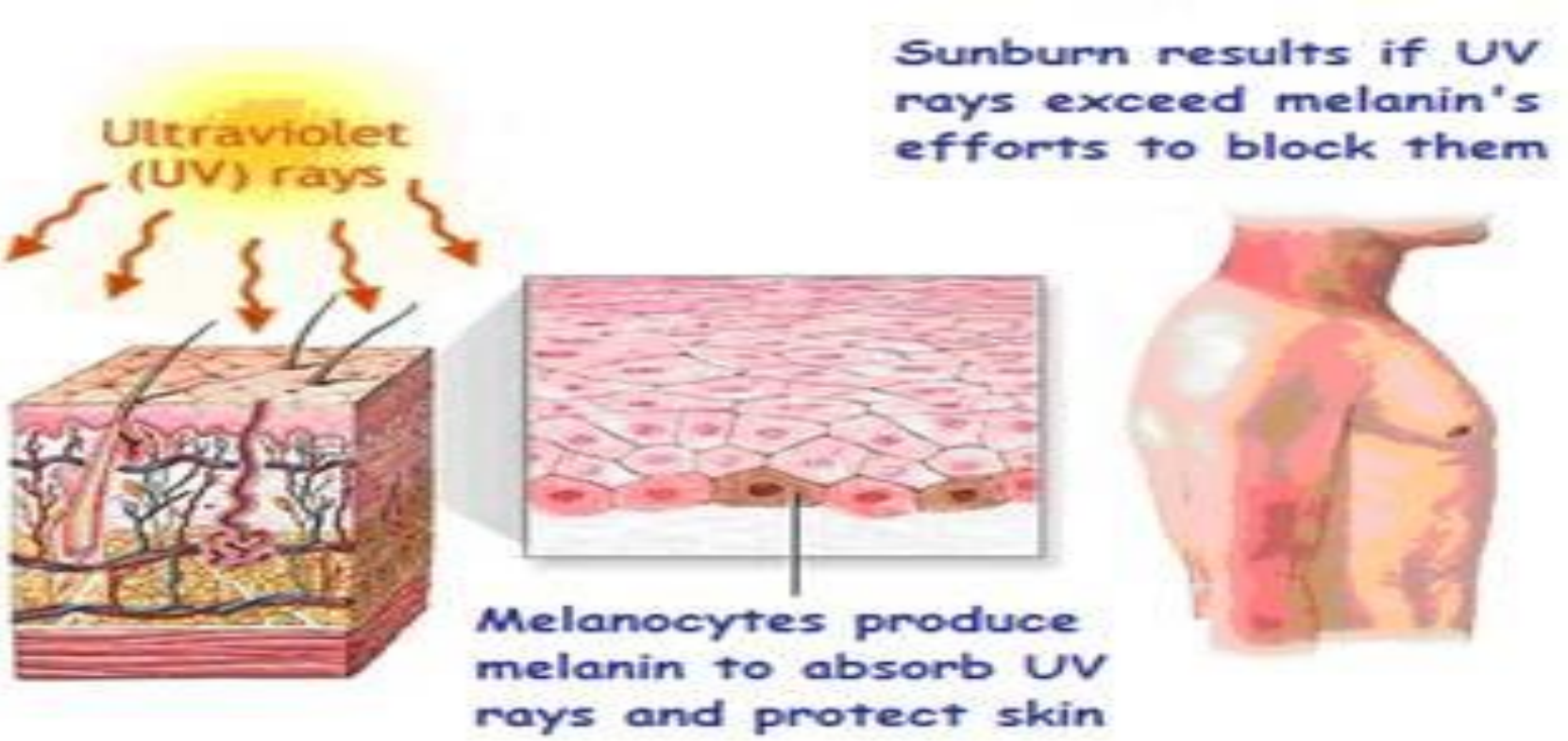


ACTH give rise to ----alpha MSH
Beta LPH produce----gamma-LPH ,beta MSH, beta –Endorphin.
N -terminal peptide form gamma- MSH.



FUNCTIONS

- Promotes the synthesis of skin pigment melanin and disperse melanin granules that lead to darkening of skin.



THANK YOU