HISTAMINE RECEPTORS

- Histamine
- Histamine receptors(H1, H2, H3 & H4)
- Signal Transduction of the Histamine Receptors

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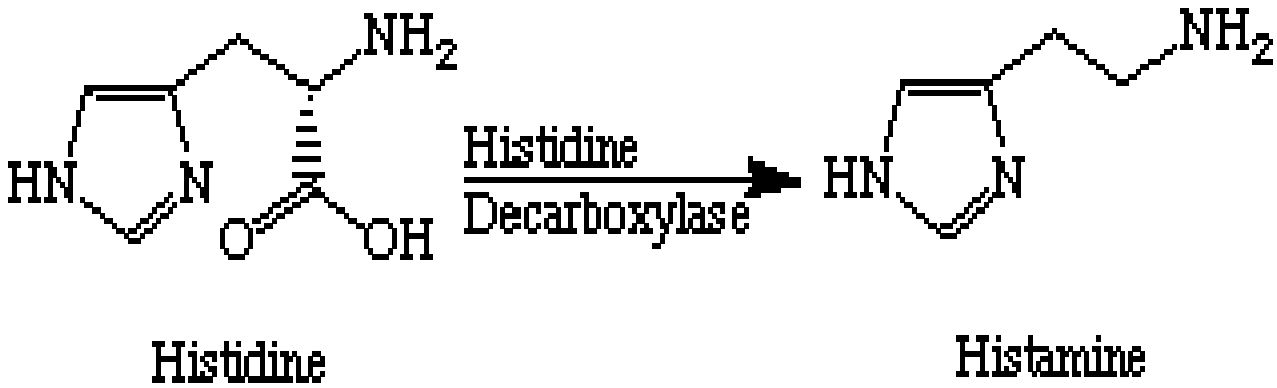
Histidine

Histamine

Histamine is one of the aminergic neurotransmitters, playing an important role in the regulation of several physiological processes

Histamine is formed from the amino acid histidine by histidine decarboxylase



In the mammalian brain histamine is synthesized in a restricted population of neurons located in the tuberomammillary nucleus of the posterior hypothalamus.

In peripheral tissues histamine is stored in mast cells, basophils, enterochromaffin cells. Mast cell histamine plays an important role in the pathogenesis of various allergic conditions

SUBTYPES OF HISTAMINE RECEPTORS

Histamine-mediated effects are mediated through four pharmacologically distinct subtypes of receptors, the H1R, H2R , H3R and H4R receptors, which are all members of the G-protein coupled receptor (GPCR) family. Histamine receptors display 7 domains, an extracellular N-terminus, and a cytoplasmic C-terminus of variable length.

H1 RECEPTORS:

- H1R is distributed in the brain, most smooth muscle cells, endothelial cells, adrenal medulla, and heart.
- It plays roles in smooth muscle contraction, stimulation of nitric oxide formation, endothelial cell contraction, and increasing vascular permeability.

- H1 receptor preferentially couples to the Gq/11 family of G-proteins and causes mobilization of intracellular Ca 2+ in a pertussis toxin-insensitive fashion.
- H1 antagonists; mepyramine, triprolidine, cetirizine, astemizole or loratadine, are used to treat allergic conditions.

H_2 RECEPTORS:

- Receptors located exclusively in the GI tract
- Activation of H_2 receptor causes increased production of gastric acid
- It causes cAMP accumulation in the gastric cells, cardiac tissues, smooth muscle cells and immune cells.

- H2R agonists have been proven to be effective for acid peptic disorders of the GI tract.
- H2 antagonists; Cimetidine, Ranitidine, Tiotidine.

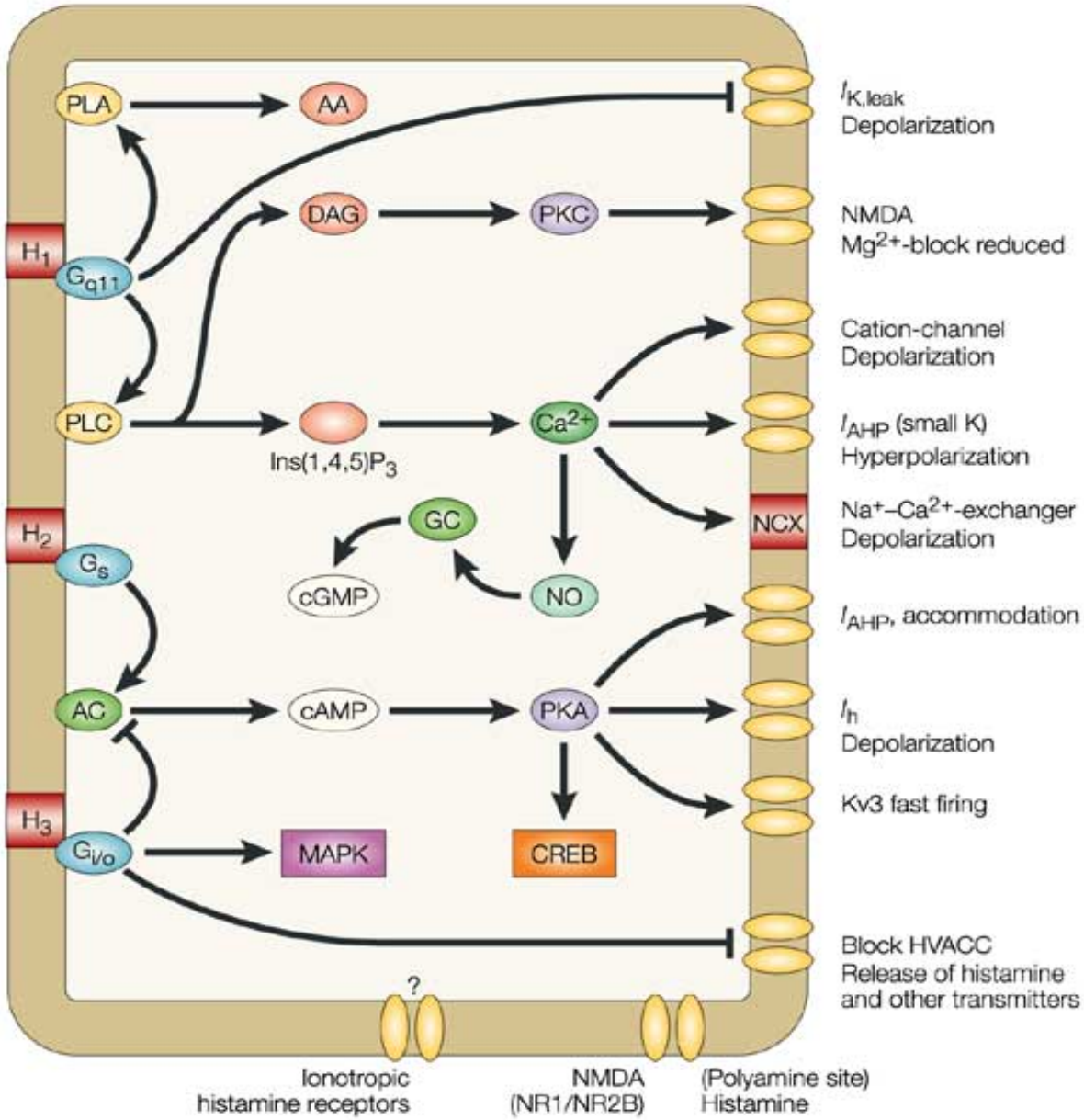
H3 RECEPTORS:

- H3 receptor has been shown to be a presynaptic heteroreceptor in nonhistamine-containing neurons in both the central and peripheral nervous systems.
- H3R is primarily expressed in the brain.

- Several studies using H3 selective agonists revealed that H3 receptor couples to pertussis toxin-sensitive Gi/o protein.
- H3 antagonists; Thioperamide, Clobenprıpit, Idopenpropit.

H4 RECEPTORS:

- It is most closely related to H3R. Unlike H3R, H4R has a distinct tissue distribution and it is localized in the peripheral blood leukocytes, spleen, thymus and colon.



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Signal Transduction of the Histamine Receptors

Histamine induces production of inositol phosphates in several tissues including brain, airway, intestinal and vascular smooth muscle.

- The histamine H2 receptor is coupled to the adenylate cyclase system in a variety of tissues e.g. brain, stomach, heart, gastric mucosa, lung. Moreover, cell lines transfected with the cloned H2 receptor genes showed an H2 receptormediated increase of cAMP. New signal transduction pathways are both regulated via unknown, cAMP-independent pathways.

THANK YOU!!

Any Questions?
Thoughts?
Suggestions?