SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES

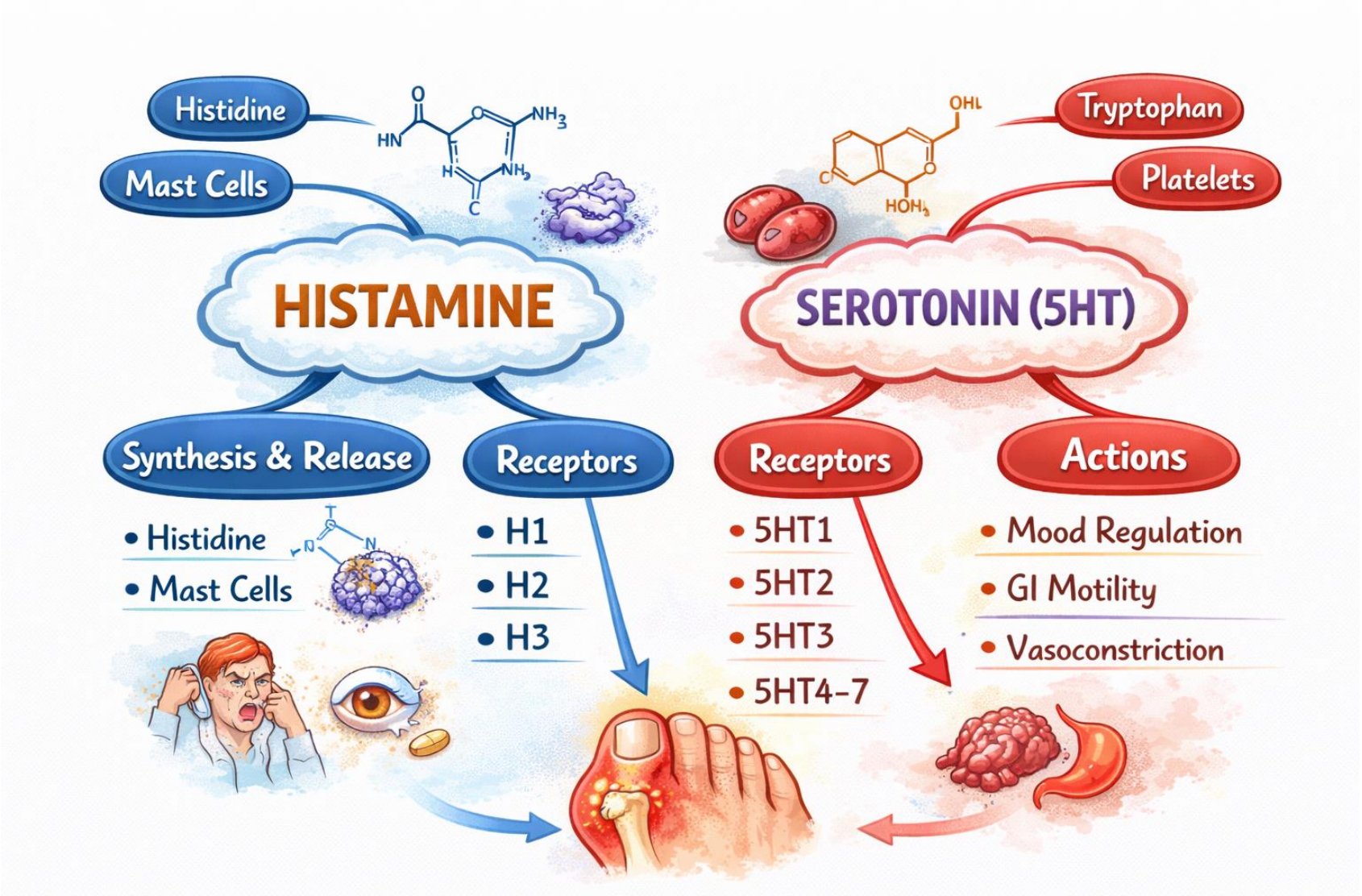
Affiliated To The Tamil Nadu Dr. MGR Medical University, Chennai
Approved by Pharmacy Council of India, New Delhi

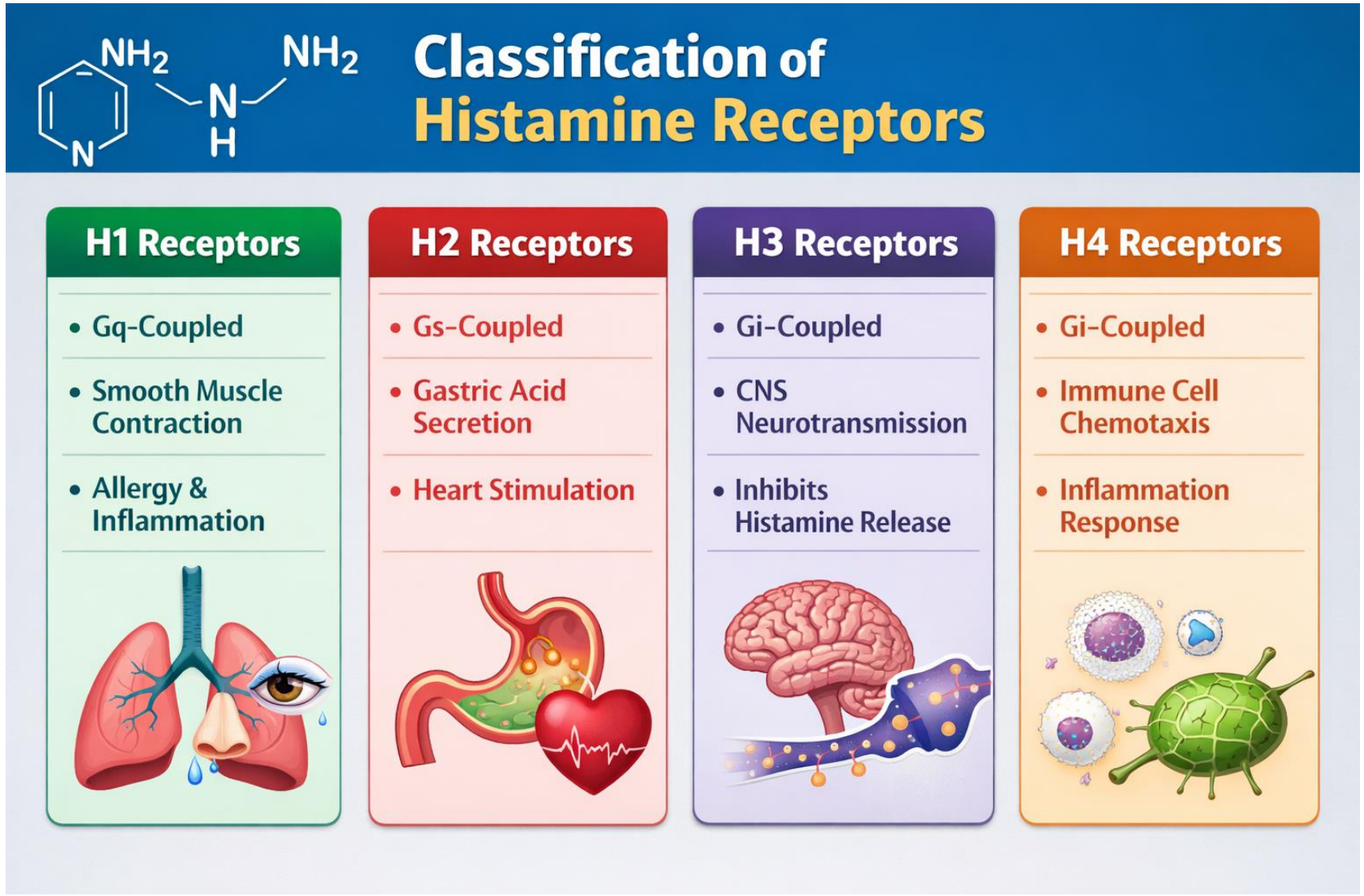
Coimbatore-641035

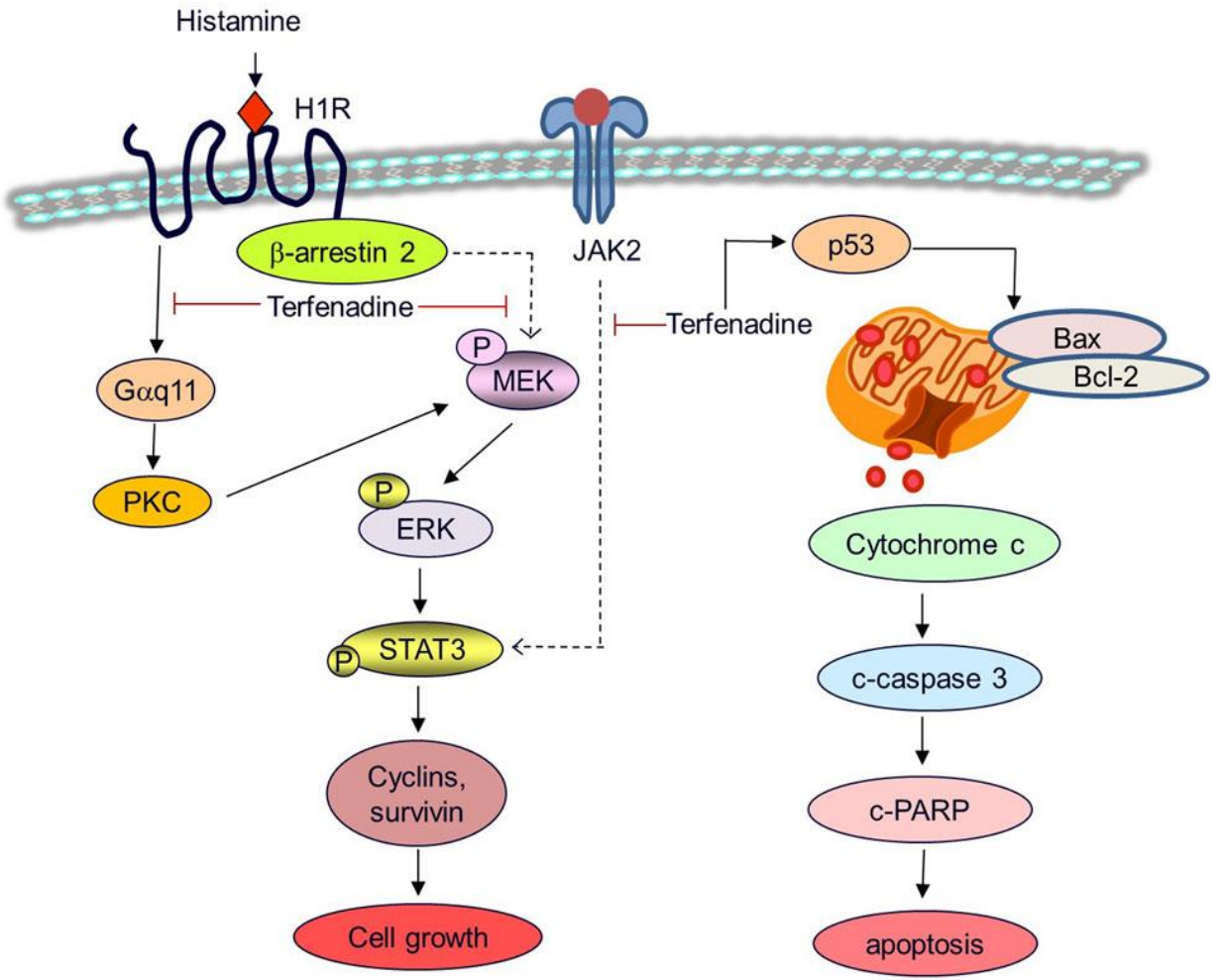
TOPIC :HISTAMINE , 5 HT AND THEIR ANTAGONISTS

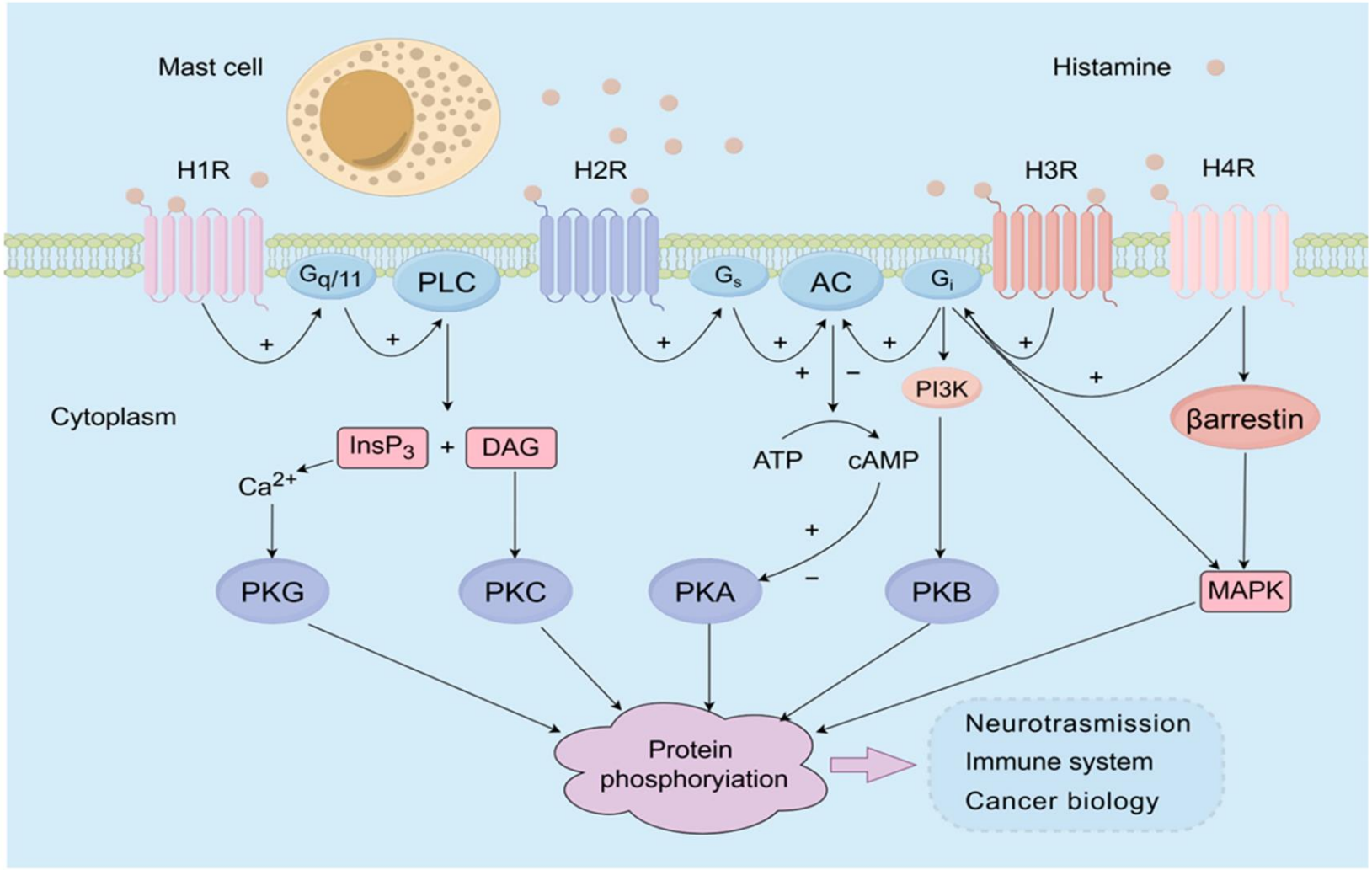
COURSE:PHARMACOLOGY II

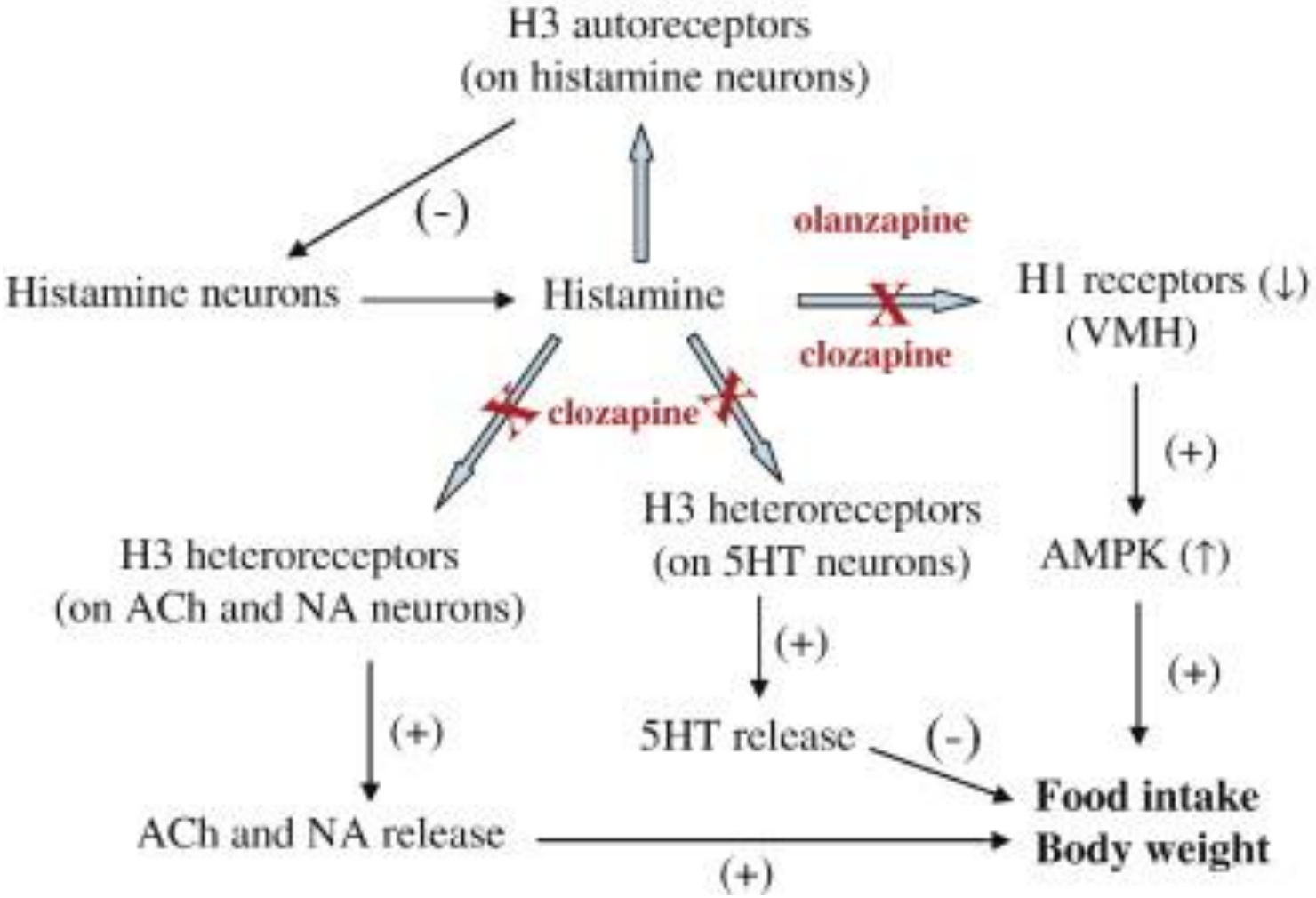
MIND MAP:

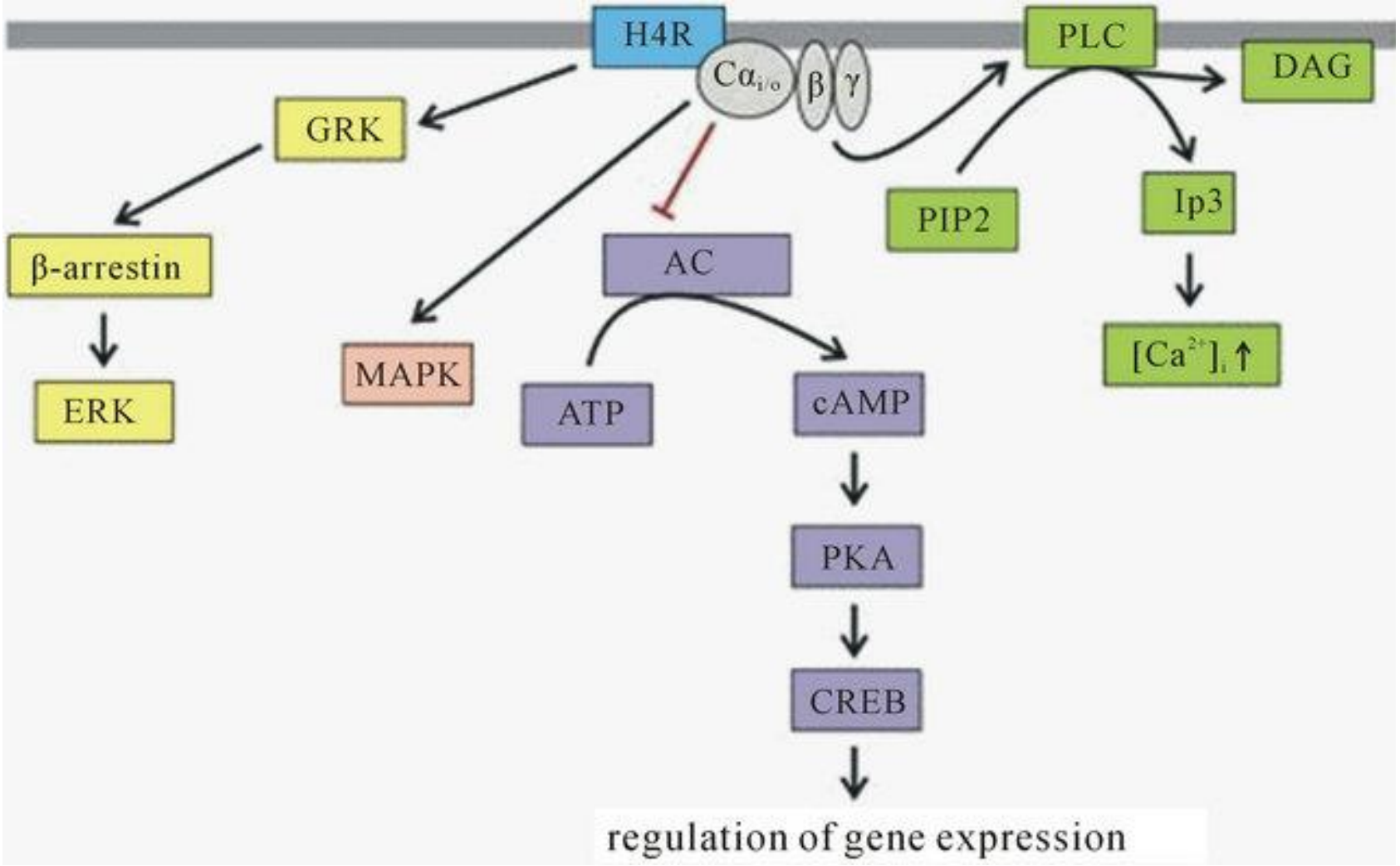

Histidine
Mast Cells
HISTAMINE
Synthesis & Release
Receptors
• Histidine
• Mast Cells
• H1
• H2
• H3
Tryptophan
Platelets
SEROTONIN (5HT)
Receptors
Actions
• 5HT1
• 5HT2
• 5HT3
• 5HT4-7
• Mood Regulation
• GI Motility
• Vasoconstriction

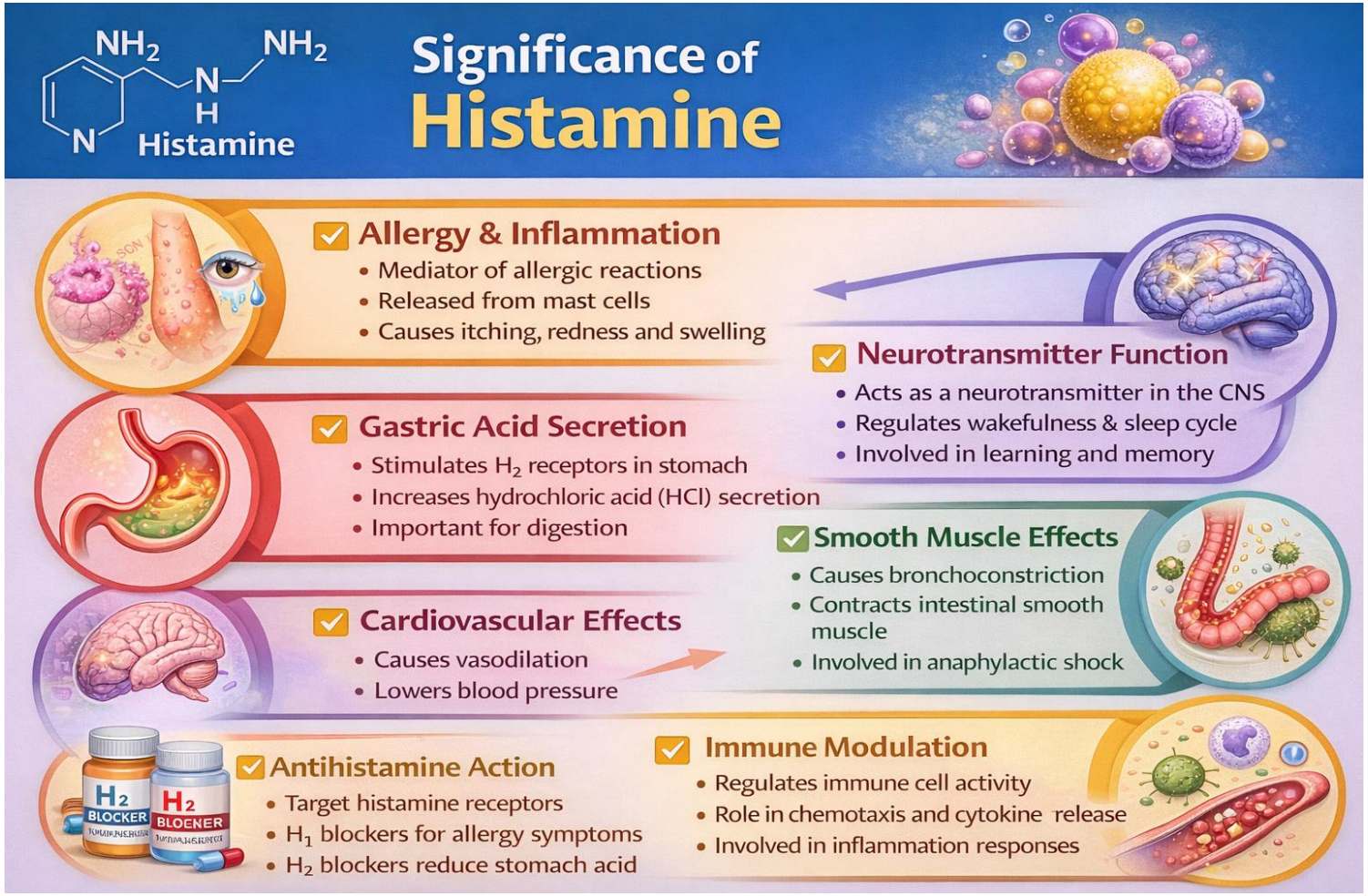

Classification of
Histamine Receptors
H1 Receptors
• Gq-Coupled
• Smooth Muscle Contraction
• Allergy & Inflammation
H2 Receptors
• Gs-Coupled
• Gastric Acid Secretion
• Heart Stimulation
H3 Receptors
• Gi-Coupled
• CNS Neurotransmission
• Inhibits Histamine Release
H4 Receptors
• Gi-Coupled
• Immune Cell Chemotaxis
• Inflammation Response

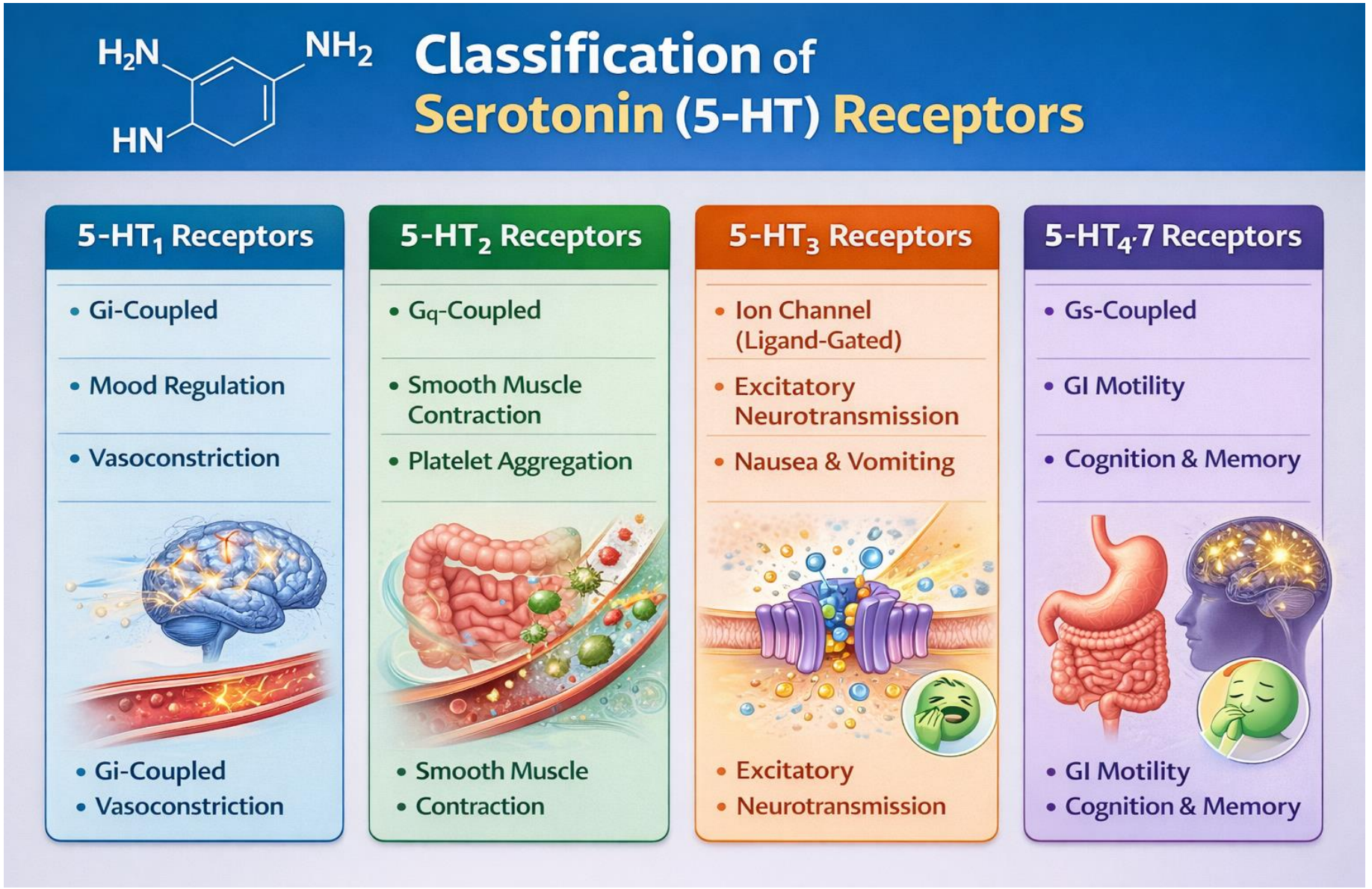

Histamine
H1R
β-arrestin 2
JAK2
p53
Terfenadine
Terfenadine
P
MEK
Gαq11
Bax
Bcl-2
PKC
P
ERK
Cytochrome c
P
STAT3
c-caspase 3
Cyclins,
survivin
c-PARP
Cell growth
apoptosis


Mast cell
Histamine
H1R
H2R
H3R
H4R
Gq/11
PLC
Gs
AC
Gi
PI3K
βarrestin
Cytoplasm
InsP3
DAG
Ca2+
ATP
cAMP
PKG
PKC
PKA
PKB
MAPK
Protein phosphoryiation
Neurotrasmission
Immune system
Cancer biology

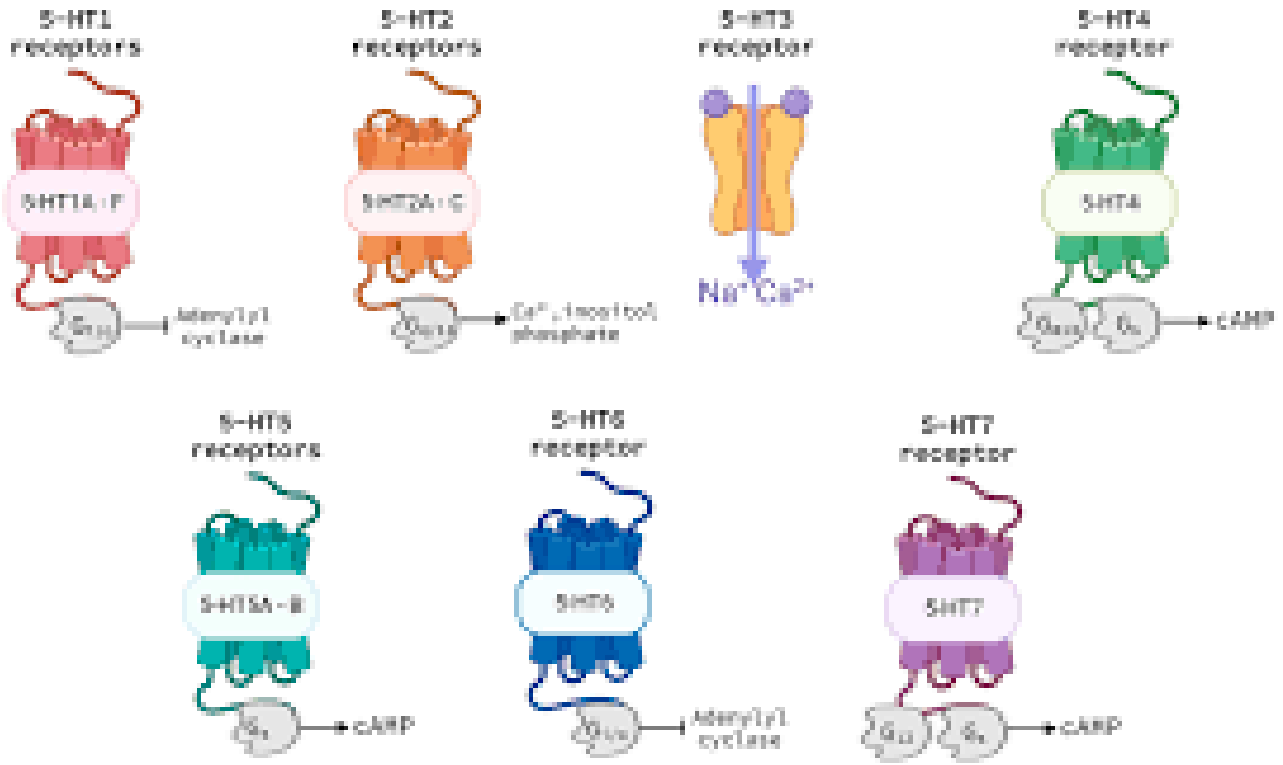

H3 autoreceptors
(on histamine neurons)
(-)
Histamine neurons
Histamine
olanzapine
clozapine
H1 receptors (↓)
(VMH)
clozapine
(+)
H3 heteroreceptors
(on 5HT neurons)
H3 heteroreceptors
(on ACh and NA neurons)
AMPK (↑)
(+)
(+)
5HT release
(-)
(+)
Food intake
Body weight
ACh and NA release
(+)


H4R
Cα$_{i/o}$
β
γ
PLC
DAG
GRK
β-arrestin
ERK
MAPK
AC
ATP
cAMP
PKA
CREB
PIP2
Ip3
[Ca^{2+}]$_i$↑
regulation of gene expression

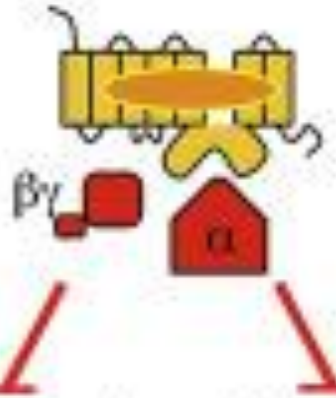

Histamine
Significance of
Histamine
Allergy & Inflammation
Mediator of allergic reactions
Released from mast cells
Causes itching, redness and swelling
Neurotransmitter Function
Acts as a neurotransmitter in the CNS
Regulates wakefulness & sleep cycle
Involved in learning and memory
Gastric Acid Secretion
Stimulates H2 receptors in stomach
Increases hydrochloric acid (HCl) secretion
Important for digestion
Smooth Muscle Effects
Causes bronchoconstriction
Contracts intestinal smooth muscle
Involved in anaphylactic shock
Cardiovascular Effects
Causes vasodilation
Lowers blood pressure
H2 BLOCKER
H2 BLOCKER
Antihistamine Action
Target histamine receptors
H1 blockers for allergy symptoms
H2 blockers reduce stomach acid
Immune Modulation
Regulates immune cell activity
Role in chemotaxis and cytokine release
Involved in inflammation responses


H_2N
NH_2
HN
Classification of Serotonin (5-HT) Receptors
5-HT_1 Receptors
• Gi-Coupled
• Mood Regulation
• Vasoconstriction
• Gi-Coupled
• Vasoconstriction
5-HT_2 Receptors
• G_q-Coupled
• Smooth Muscle Contraction
• Platelet Aggregation
• Smooth Muscle
• Contraction
5-HT_3 Receptors
• Ion Channel (Ligand-Gated)
• Excitatory Neurotransmission
• Nausea & Vomiting
• Excitatory
• Neurotransmission
5-HT_4·7 Receptors
• Gs-Coupled
• GI Motility
• Cognition & Memory
• GI Motility
• Cognition & Memory

Serotonin 5-HT receptor classes and subtypes



5-HT1A autoreceptor

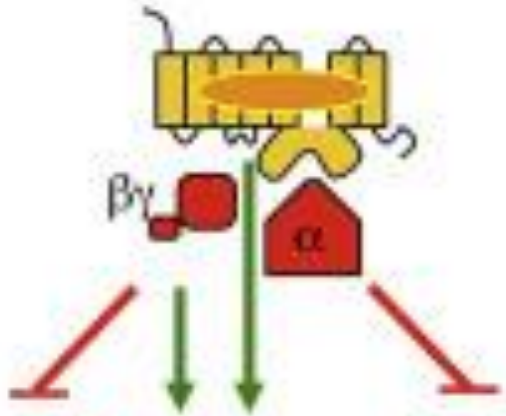


Ion channels PLC — Adenylyl Cyclase

↓ 5-HT neuronal activity

Anxiety, depression behavior
Resistance to SSRI

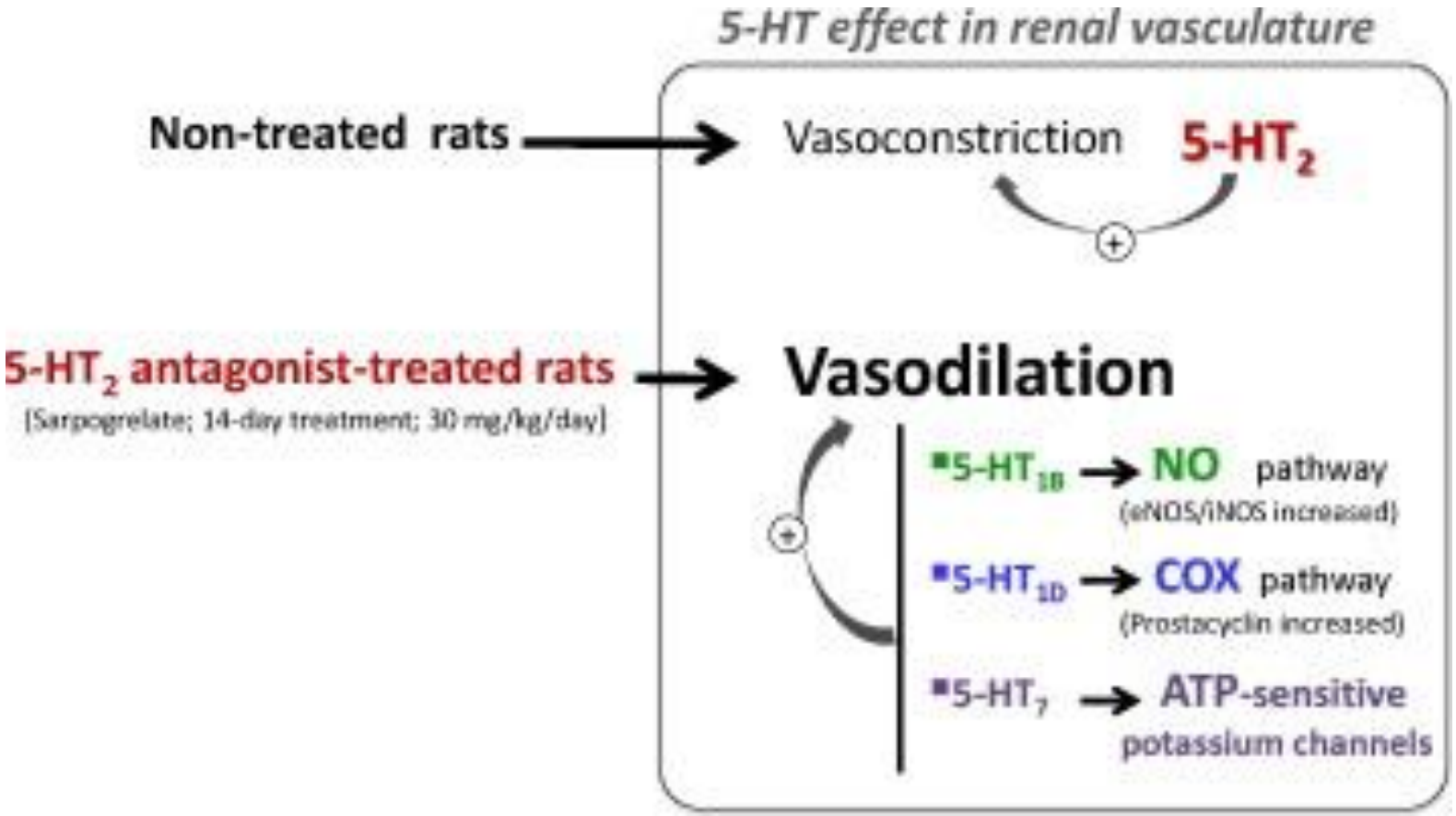
5-HT1A heteroreceptor

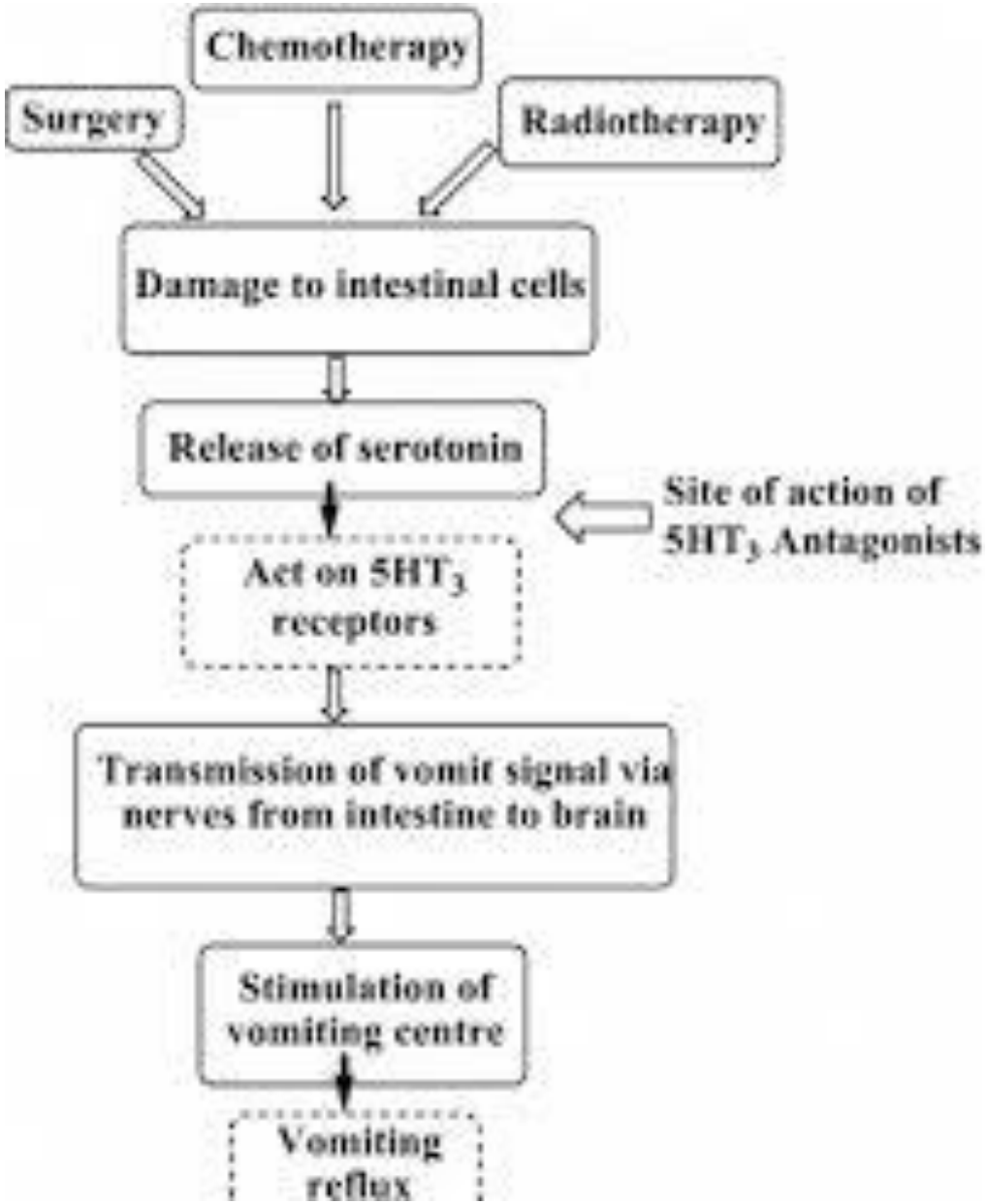


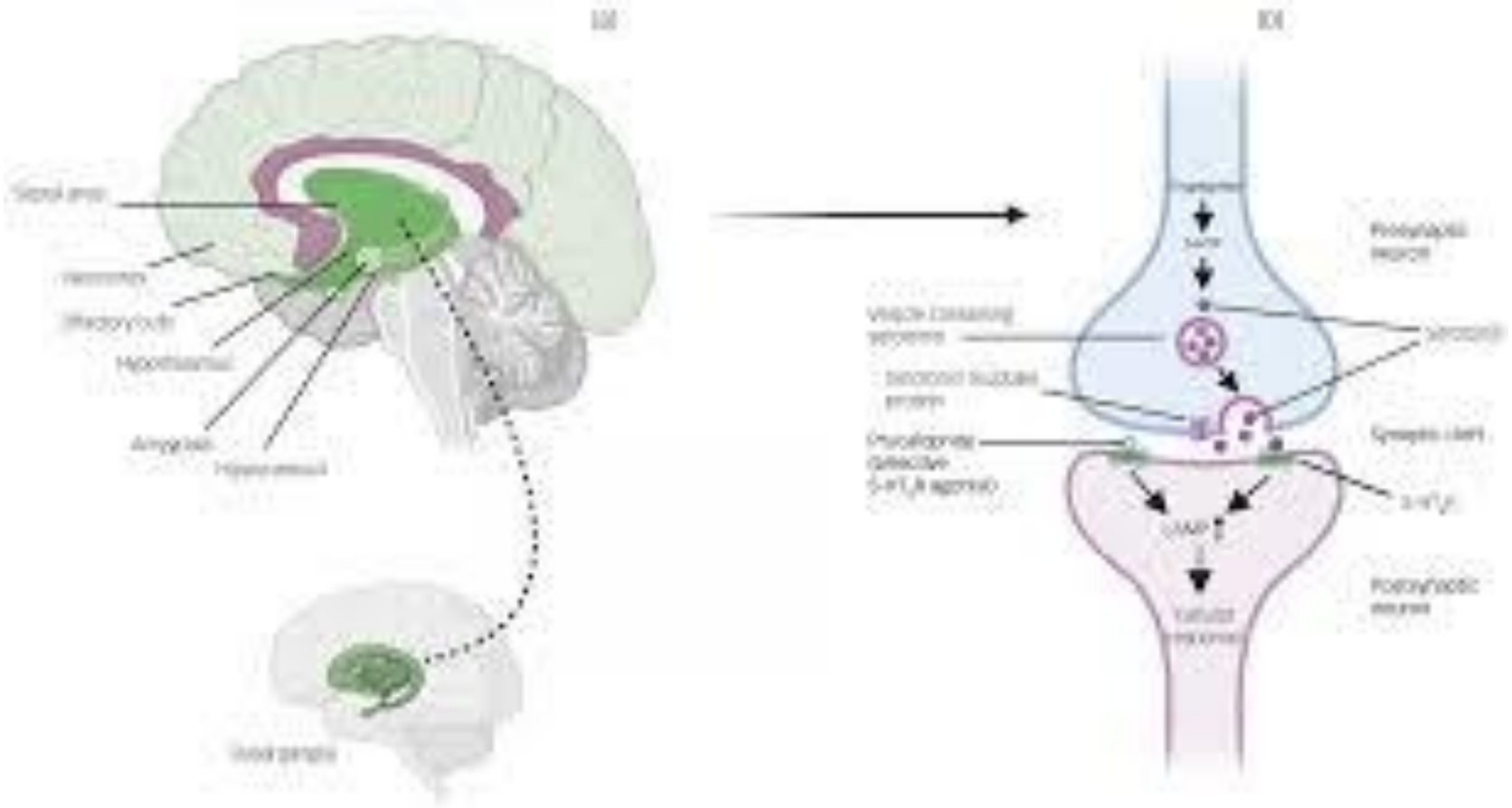
Ion channels — ACII PLC — ERK1/2 GSK3β — AC

↓ CAMKII, NMDA/AMPA

Synaptic plasticity
SSRI-response


5-HT effect in renal vasculature
Non-treated rats
Vasoconstriction
5-HT2
5-HT2 antagonist-treated rats
[Sarpogrelate; 14-day treatment; 30 mg/kg/day]
Vasodilation
5-HT1B → NO pathway
(eNOS/iNOS increased)
5-HT1D → COX pathway
(Prostacyclin increased)
5-HT7 → ATP-sensitive potassium channels


Chemotherapy
Surgery
Radiotherapy
Damage to intestinal cells
Release of serotonin
Site of action of 5HT3 Antagonists
Act on 5HT3 receptors
Transmission of vomit signal via nerves from intestine to brain
Stimulation of vomiting centre
Vomiting reflex



MULTIPLE CHOICE QUESTIONS :

1.Histamine is synthesized from which amino acid?

A. Tyrosine
B. Tryptophan
C. Histidine
D. Phenylalanine

2.Which histamine receptor acts as a presynaptic autoreceptor in the CNS?

A. H1
B. H2
C. H3
D. H4

3.The rate-limiting enzyme in serotonin synthesis is:

A. DOPA decarboxylase
B. Monoamine oxidase
C. Tryptophan hydroxylase
D. Tyrosine hydroxylase

4.Which drug is a 5-HT3 receptor antagonist used as an antiemetic?

A. Metoclopramide
B. Ondansetron
C. Sumatriptan
D. Fluoxetine

5.Which mediator increases capillary permeability most prominently?

A. Serotonin
B. Histamine
C. Dopamine
D. Noradrenaline

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THANK YOU !