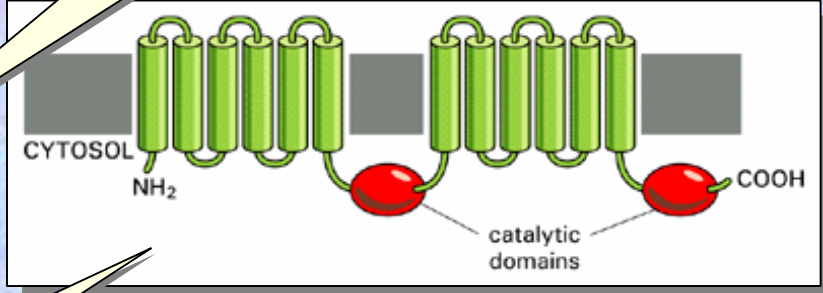


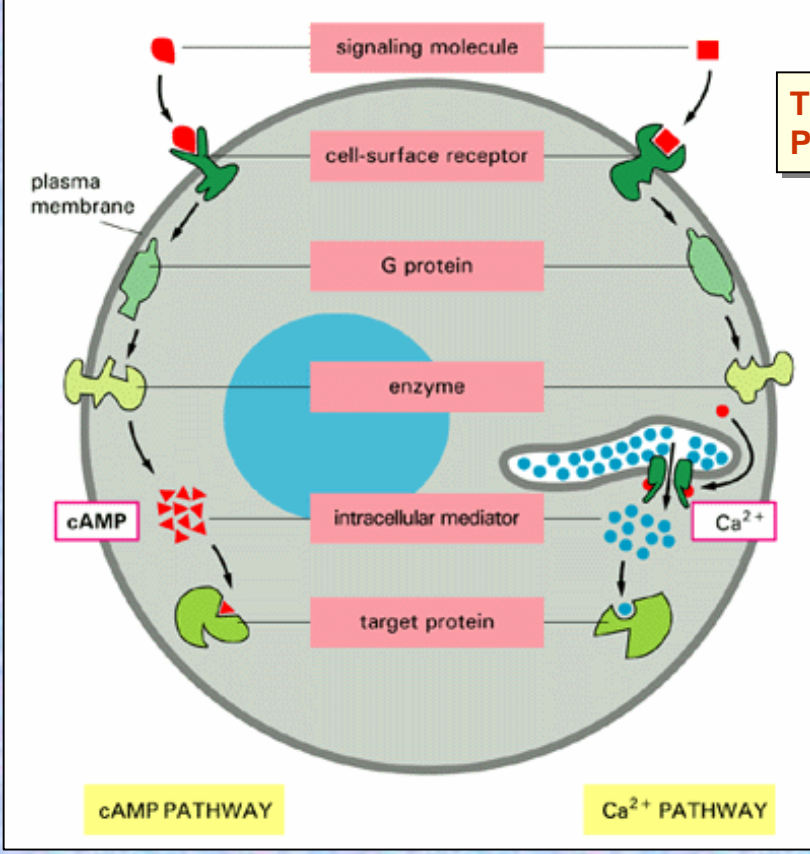
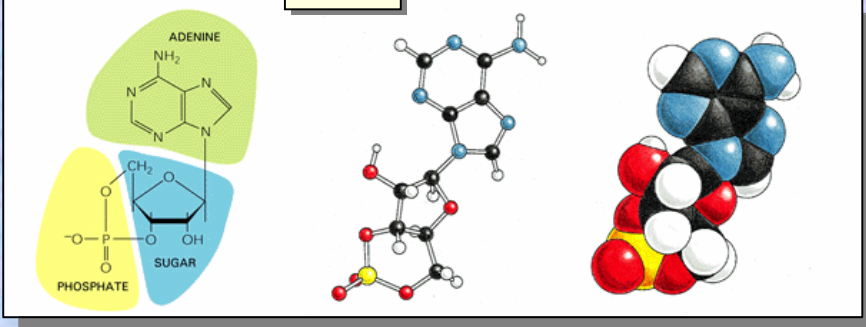
receptor contains 7 transmembrane alpha-helical segments & intracellular and extracellular domains

ADENYL CYCLASE



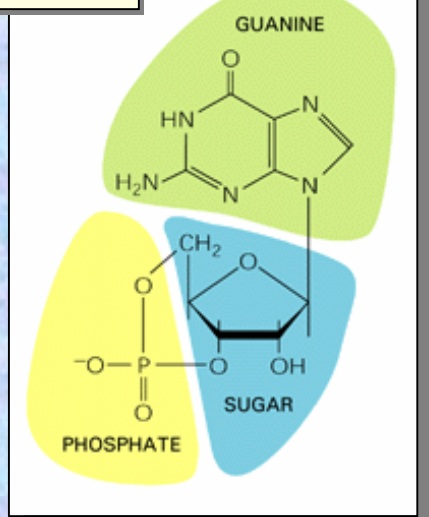
Enzyme contains about 1100 amino acids, two clusters of six transmembrane segments separating two similar cytoplasmic catalytic domains. There are at least six types of this form of adenylyl cyclase in mammals (types I-VI).

cAMP

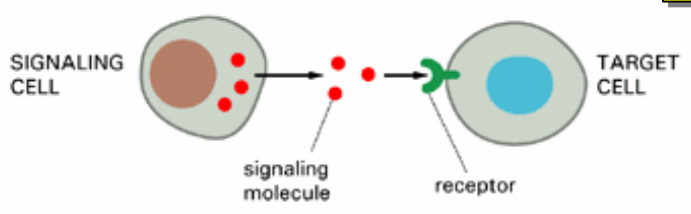


TWO PRINCIPAL SIGNALLING PATHWAYS

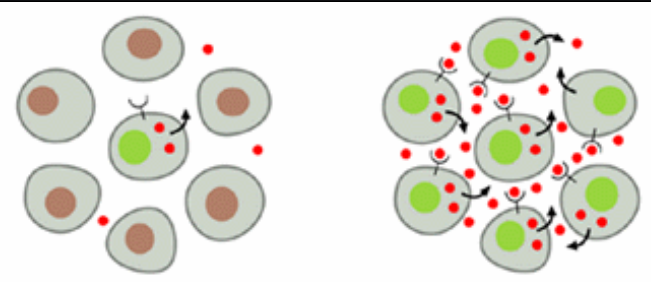
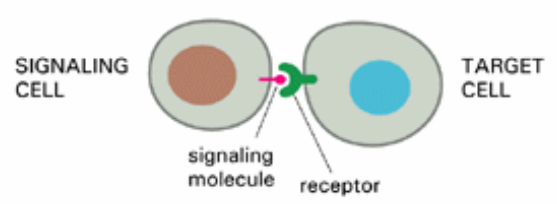
cGMP



SIGNALING BY SECRETED MOLECULES



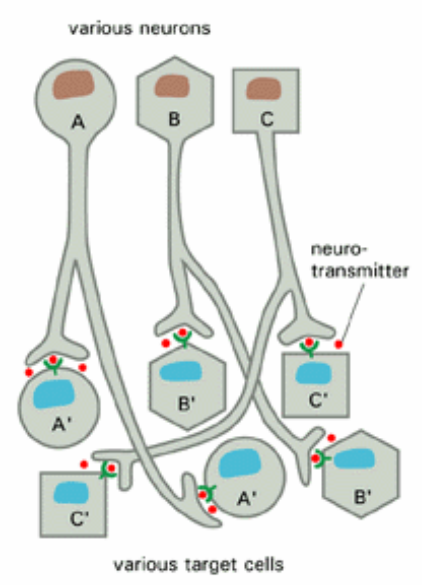
SIGNALING BY PLASMA-MEMBRANE-BOUND MOLECULES



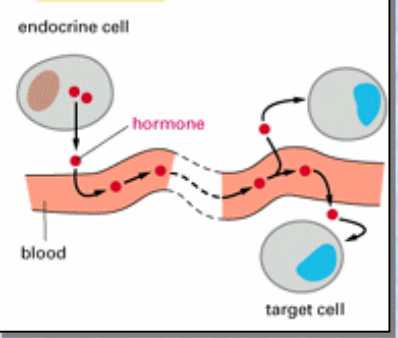
A SINGLE SIGNALING CELL RECEIVES WEAK AUTOCRINE SIGNAL

IN A GROUP OF IDENTICAL SIGNALING CELLS, EACH CELL RECEIVES A STRONG AUTOCRINE SIGNAL

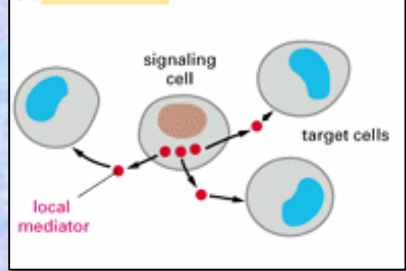
(B) SYNAPTIC SIGNALING



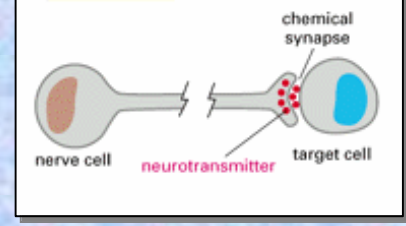
(C) ENDOCRINE



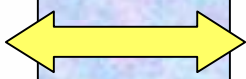
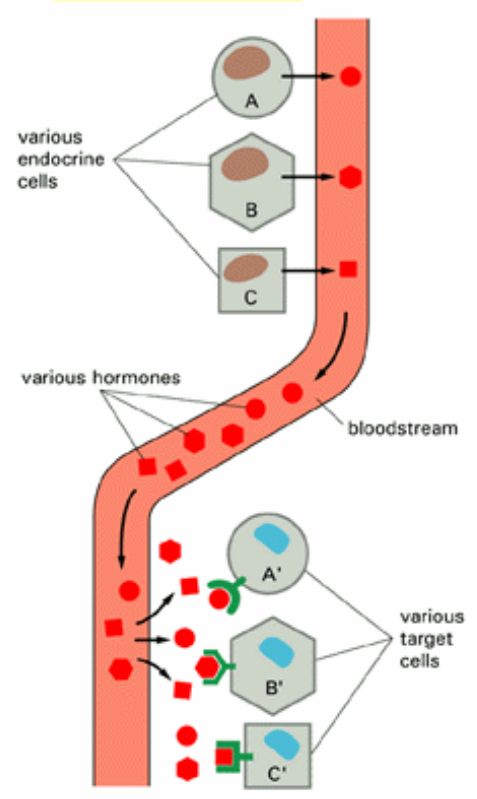
(A) PARACRINE



(B) SYNAPTIC



(A) ENDOCRINE SIGNALING



RECEPTORS

Cell surface receptors

Intracellular receptors

without enzymatic activity

- Ion channel linked
- GPCR

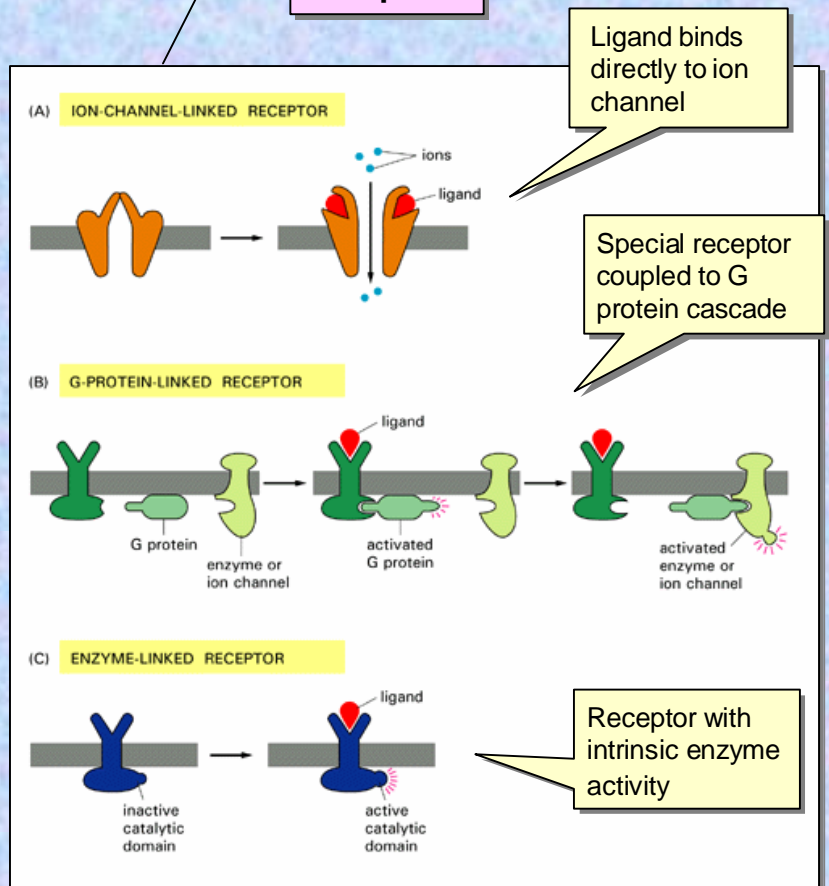
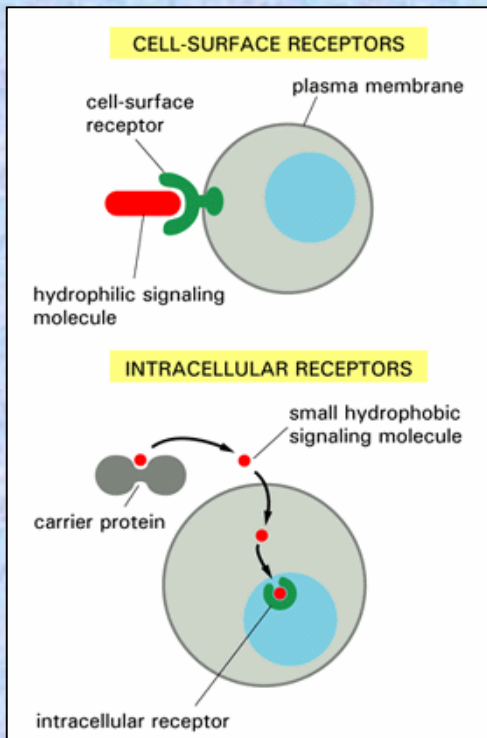
with enzymatic activity

- Guanyl cyclase
- Tyr- kinase
- Ser/Thr - kinase
- Ser/Thr - phosphatase

- cytoplasmatic receptors
- nuclear receptors

Cell surface receptors

Binding of secreted signals to receptors



Some Hormone-induced Cellular Responses Mediated by Cyclic AMP

Hormone	Target Tissue	Major Response
Thyroid-stimulating hormone (TSH)	Thyroid gland	thyroid hormone synthesis and secretion
Adrenocorticotrophic hormone (ACTH)	Adrenal cortex	cortisol secretion
Luteinizing hormone (LH)	Ovary	progesterone secretion
Adrenaline	Muscle	glycogen breakdown
Noradrenalin, Adrenaline	Heart	increase in heart rate and force of contraction
Parathormone	Bone	bone resorption
Glucagon	Liver	glycogen breakdown
Vasopressin	Kidney	water resorption
Adrenaline, ACTH, glucagon, TSH	Fat	triglyceride breakdown

Some Cellular Responses Mediated by G-Protein-linked Receptors Coupled to the Inositol-Phospholipid Signaling Pathway

Signaling Molecule	Target Tissue	Major Response
Vasopressin	Liver	glycogen breakdown
Acetylcholine	Pancreas	amylase secretion
Acetylcholine	Smooth muscle	contraction
Antigen	Mast cells	histamine secretion
Thrombin	Blood platelets	thrombin

Endocrine disorders associated with mutation of serpentine receptors

Mutated protein	Disorder	Type of mutation
Gain of function		
LH receptors	Familiar male precocious puberty	Autosomal dominant
TSH receptor	Non-autoimmune hereditary hyperthyroidism	Autosomal dominant
PTH receptor	Hyperfunctioning thyroid adenoma	Somatic
	Jansen metaphysal chondrodysplasia	Autosomal dominant
Calcium receptor	Hypoparathyroidism	Autosomal dominant
Loss of function		
LH receptor	Male pseudohermafroditism	Autosomal recessive
FSH receptor	Hypergonadotrophic ovarian dysgenesis	Autosomal recessive
GHRH	Laron dwarfism	Autosomal recessive
TSH receptor	Congenital hypothyroidism	Autosomal recessive
TRH receptor	Congenital hypothyroidism	Autosomal recessive
ACTH	Familial ACTH resistance	Autosomal recessive
Vasopressin	Nephrogenic diabetes insipidus	X-linked
Calcium receptor	Familial hypocalciuric hypercalcaemia	Autosomal dominant
	Neonatal severe hyperparathyroidism	Autosomal recessive

INOSITOL-PHOSPHATE DEPENDENT SIGNALLING

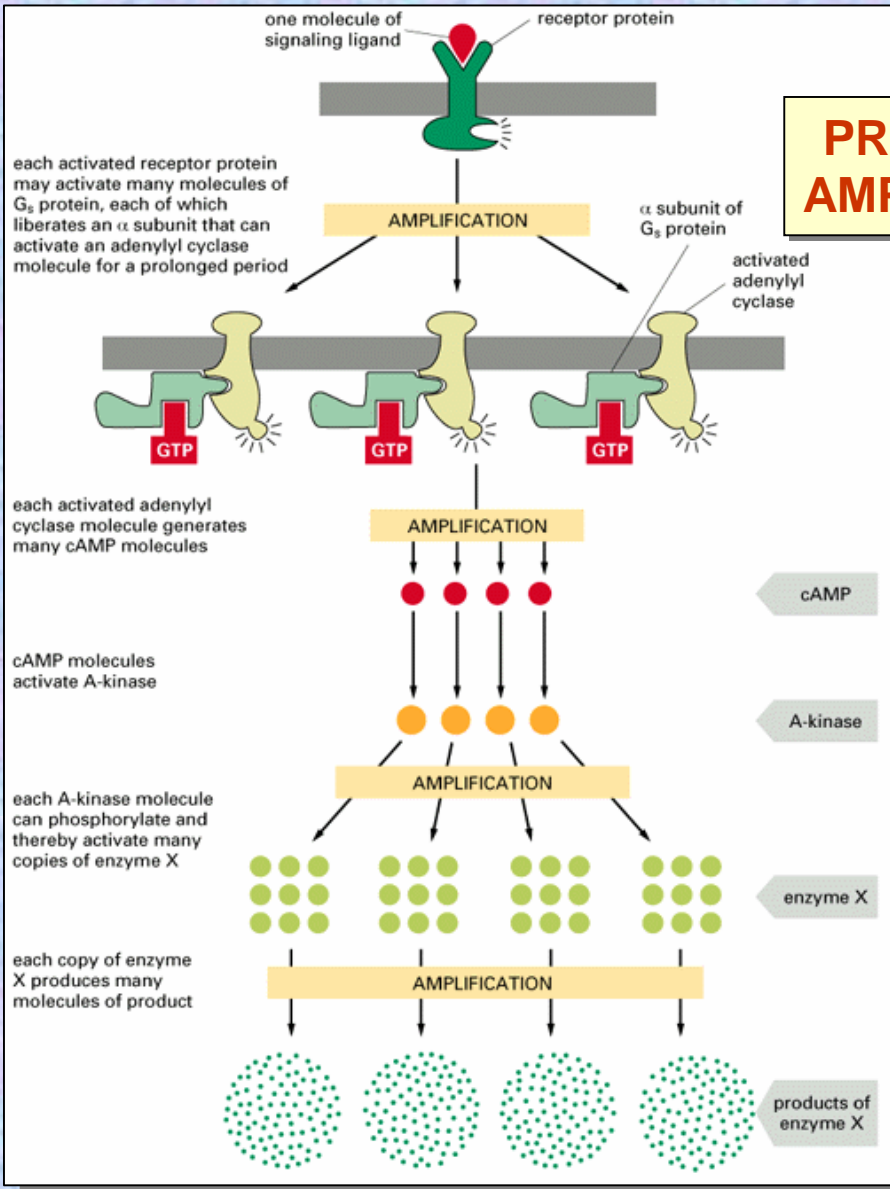
Substance	Receptor	Transduction
Acetylcholin	→ M ₁ , M ₃ , M ₅	<p>G_{q/11} (R) → IP₃/DAG</p>
Catechoamines	(R) α _{1A,1B,1C,1D}	
Serotonin	(R) 5-HT _{2A,2B,2C}	
Histamin	(R) H ₁	
Adenosin	(R) A ₁ , A ₃	
Purines	(R) P _{2U} , P _{2Y}	
EAMA	(R) mGlu ₁ , mGlu ₅	
Vasopressin	(R) V _{1A} , V _{1B}	
Oxytocin	(R) Oxy	
Cholecystokinin	(R) CCK _A , CCK _B	
Melanin	(R) ML ₂	
Angiotensin	(R) AT ₁	
Bradykinin	(R) B ₁ , B ₂	
Tachykinins	(R) NK ₁ , NK ₂ , NK ₃	
Bombesin	(R) BB ₁ , BB ₂	
Endothelin	(R) ET _A , ET _B , ET _C	
Prostanoids	(R) EP ₁	
Leukotriens	(R) LTB ₄ , LTD ₄	
PAF	(R) PAFR	

c-AMP DEPENDENT SIGNALLING

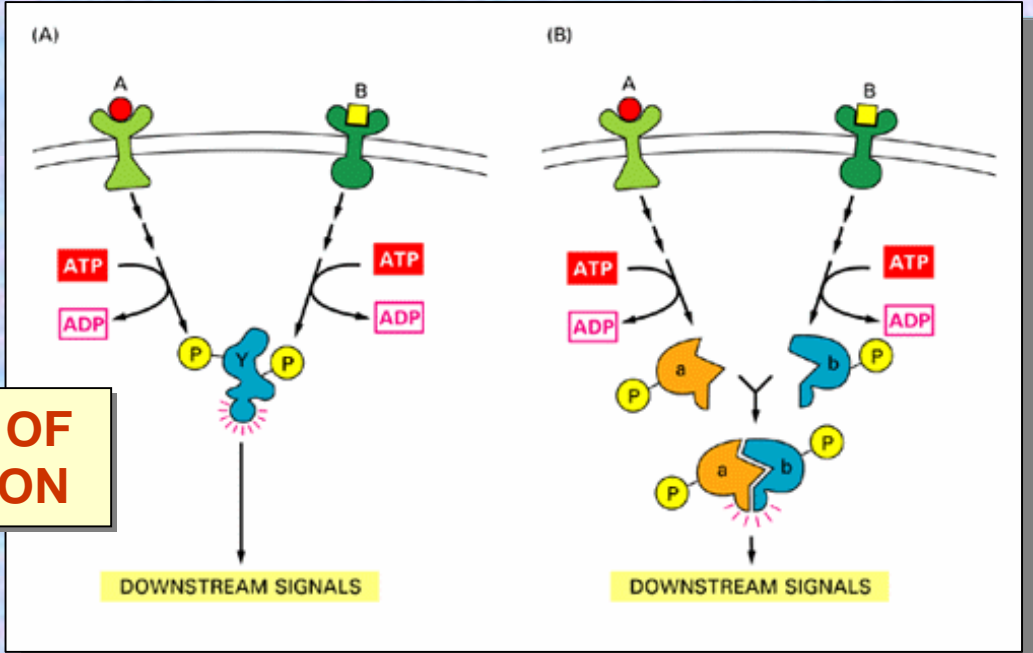
Substance	Receptor	Transduction
Catecholamines	Ⓡ $\beta_{1,2,3}$	<p style="text-align: center;">Gs Ⓡ ñ cAMP</p>
Serotonin	Ⓡ 5-HT _{4,5,6,7}	
Dopamin	Ⓡ D ₁ (D _{1A}),D ₅ (D _{1B})	
Histamin	Ⓡ H ₂	
Adenosinn	Ⓡ A _{2A} ,A _{2B}	
Vasopressin	Ⓡ V ₂	
VIP	Ⓡ VIP _{1,2} ,GRF	
Prostanoidy	Ⓡ EP ₂ ,EP ₄	
Octopamin	Ⓡ OA _{2A} ,OA ₃	
CGRP	Ⓡ CGRP	

Substance	Receptor	Transduction
Acetylcholin	Ⓡ M ₂ ,M ₄	<p style="text-align: center;">Gi/o Ⓡ ò cAMP</p>
Catecholamines	Ⓡ $\alpha_{2A,2B,2C,2D}$	
Serotonin	Ⓡ 5-HT _{1A,1B,1D,1E,1F}	
Dopamin	Ⓡ D ₂ ,D ₃ ,D ₄	
GABA	Ⓡ GABA _B	
Adenosinn	Ⓡ A ₁ ,A ₃	
Purines	Ⓡ P ₁ , P _{2T}	
EAMK	Ⓡ mGlu _{2,3,4,6,7,8}	
Opioides	Ⓡ μ,δ,κ	
Somatostatin	Ⓡ SST _{2,3,4}	
Melanin	Ⓡ ML _{1A,1B}	
Intereleukines	Ⓡ IL _{8A} ,IL _{8B}	
Chemokines	Ⓡ CCCK _{1,2,3}	
Protease	Ⓡ PAR ₁	
NPY	Ⓡ Y ₁ ,Y ₂ ,Y ₃	
Galanin	Ⓡ Gal	
Prostanoids	Ⓡ EP ₃	

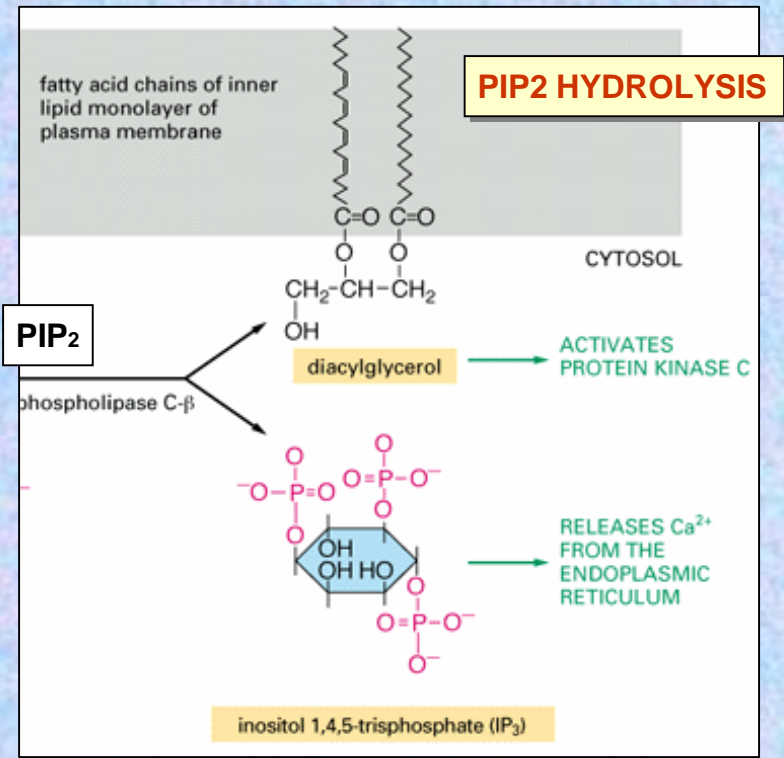
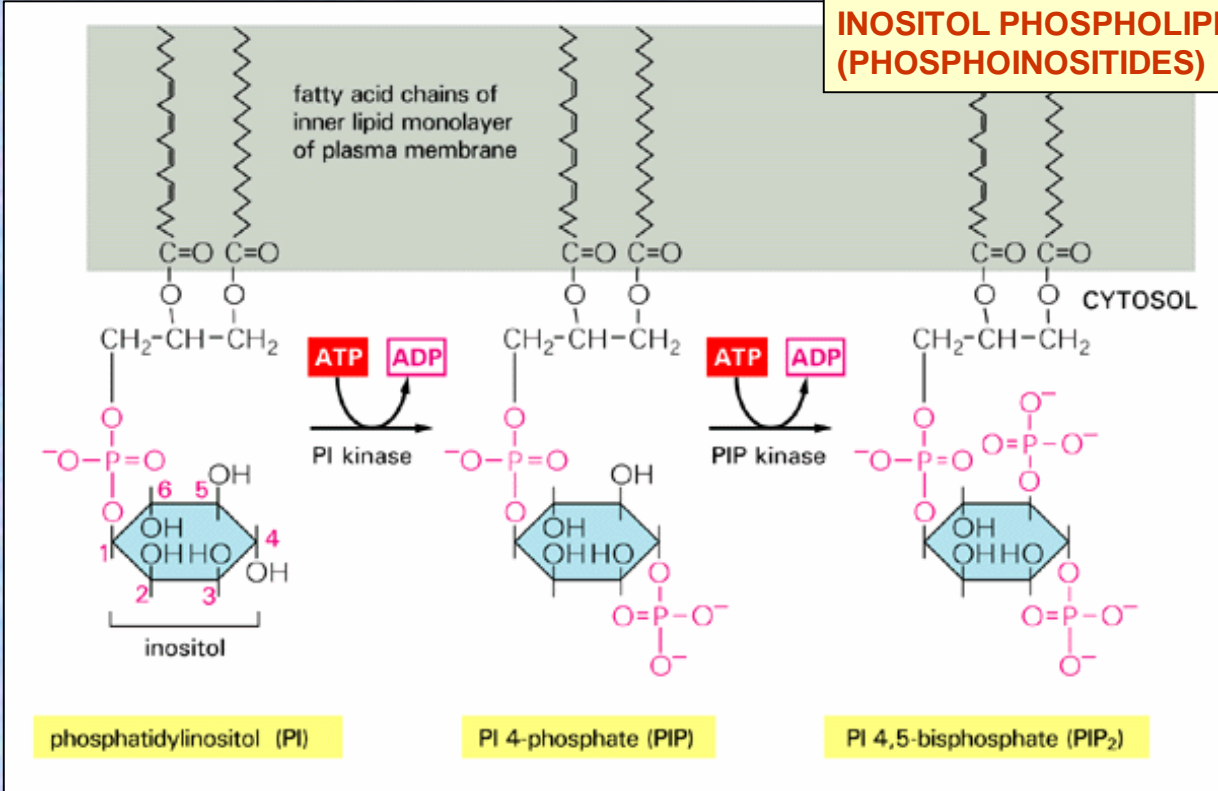
PRINCIPLE OF AMPLIFICATION



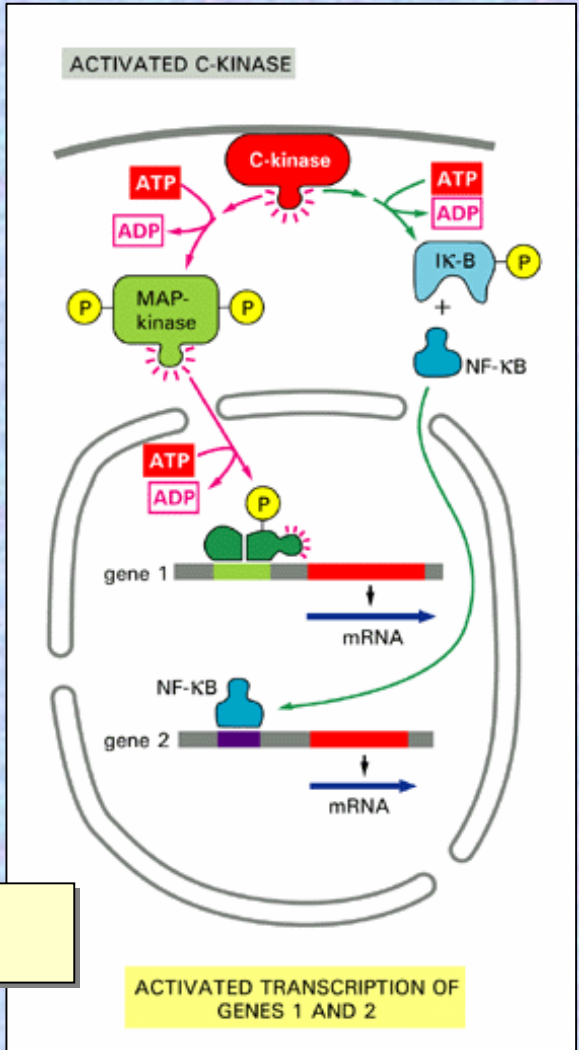
PRINCIPLE OF INTEGRATION



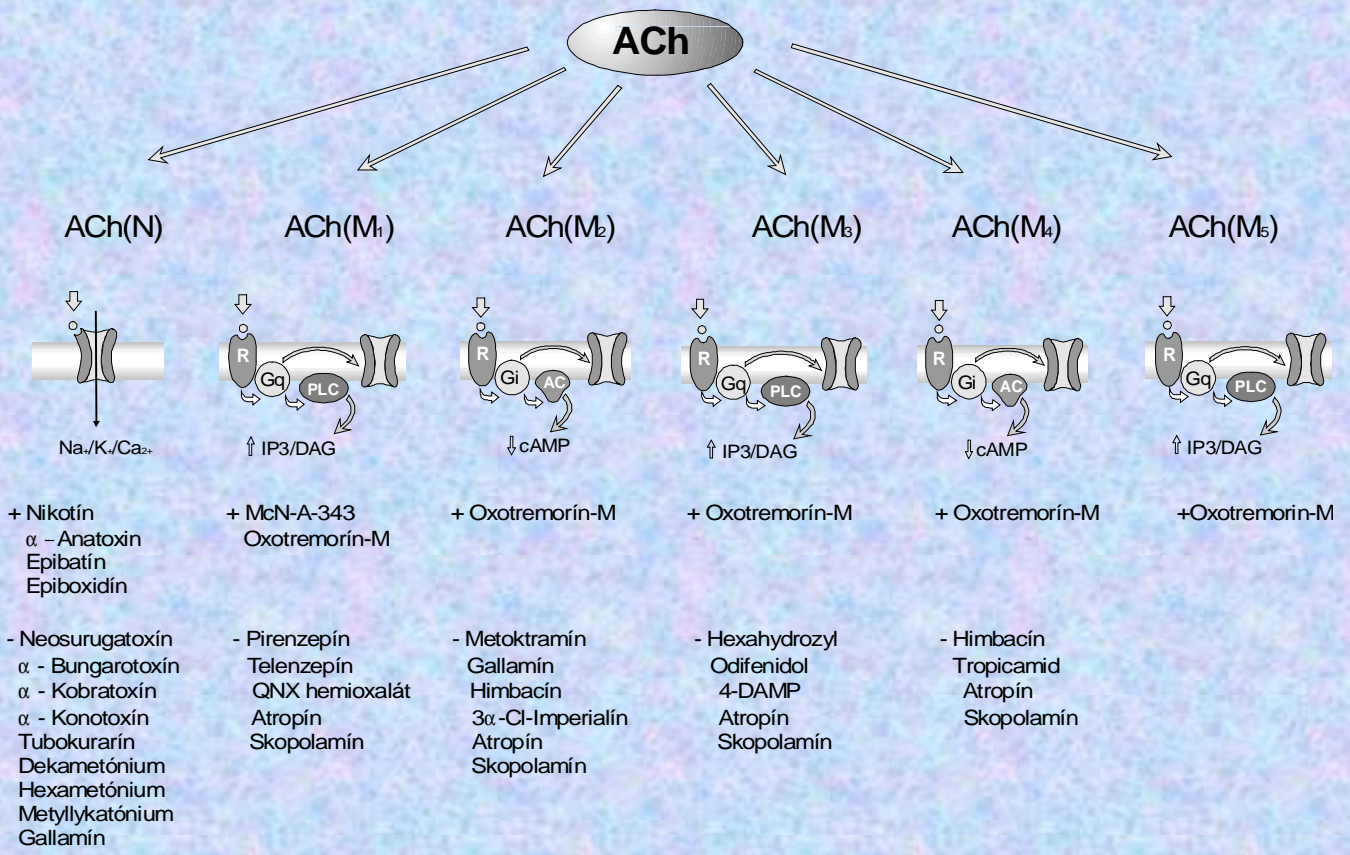
INOSITOL PHOSPHOLIPIDS (PHOSPHOINOSITIDES)



C-KINASE ACTIVATED GENE TRANSCRIPTION



Same ligand can bind to different receptors



Different Cells Can Respond Differently to the Same Chemical Signal

