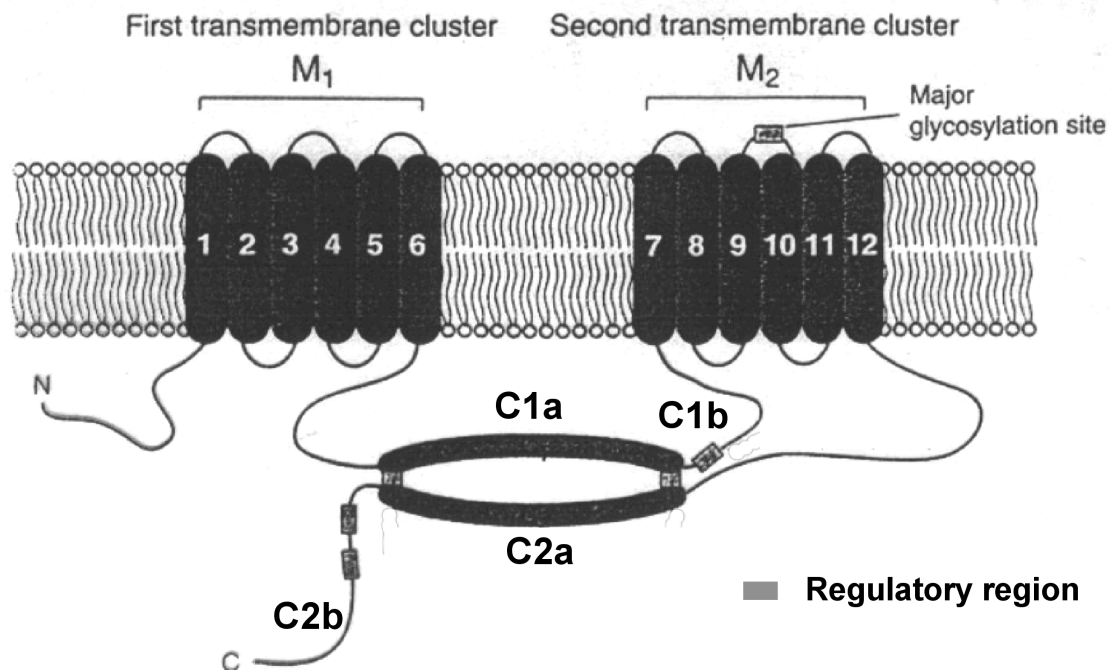
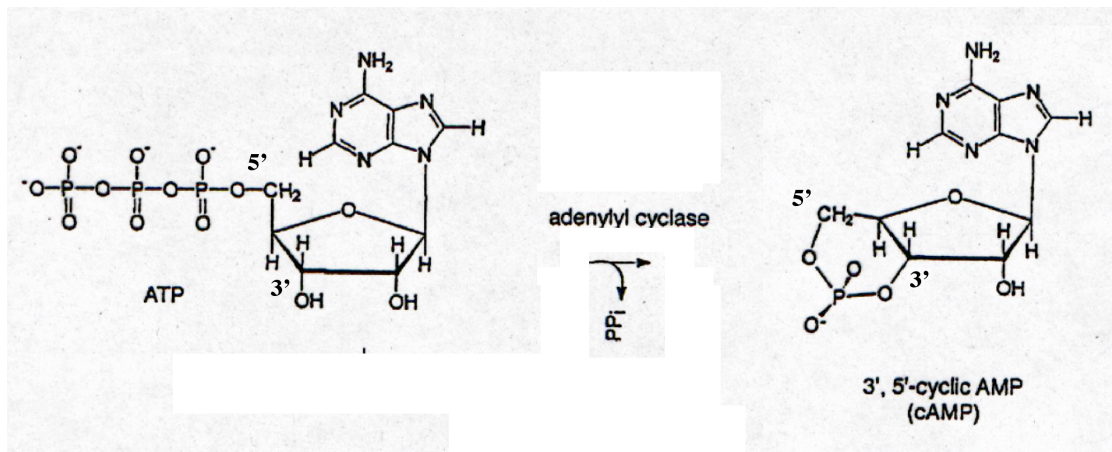


Adenilato ciclasi



Structure of Adenylate Cyclases (ACs)

ACs can be divided into 5 major domains:

1. The N-terminus).
2. The first Tm cluster (*M1*).
3. The first cytoplasmic loop (*C1*).
4. The second transmembrane cluster (*M2*).
5. The second cytoplasmic loop (*C2*).

The C1 and C2 regions are further subdivided into the highly conserved catalytic C1a and C2a regions, which dimerize to form the catalytic site (stippled areas) and the less conserved C1b and C2b domains.

Struttura tridimensionale dell'adenilato ciclasi

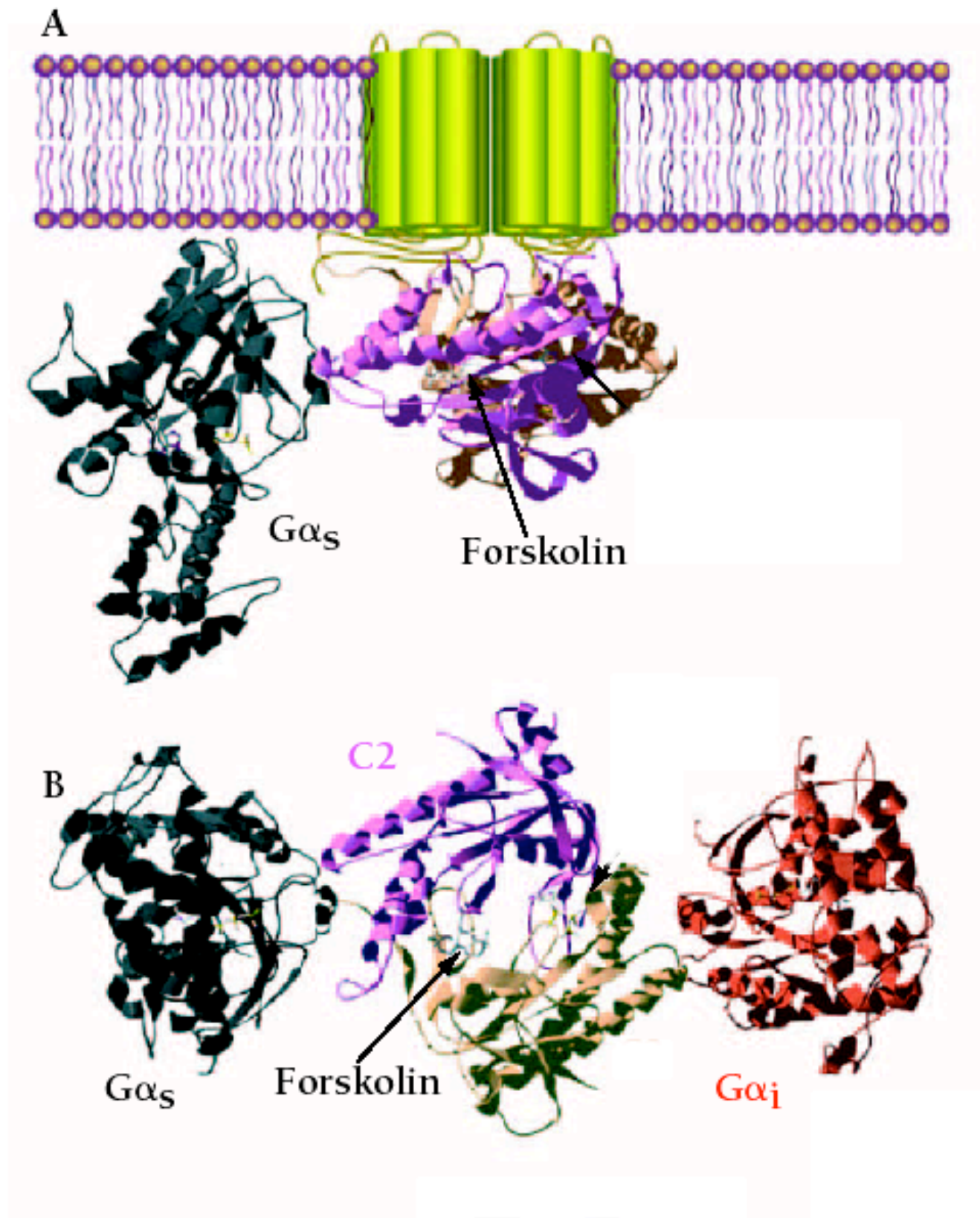


TABLE 1. REGULATORY PROPERTIES OF MAMMALIAN ADENYLYL CYCLASE ISOFORMS

AC Isoform ^{a,b}	Tissue Distribution	Regulation by G Protein Subunits	Protein Kinases	Calcium Effects	Putative Function
AC1	Brain adrenal medulla	Stimulated by $G\alpha_s$ Inhibited by $G\beta\gamma$ Inhibited by $G\alpha_o$	PKC: weak stimulation CaMKIV: inhibition	Stimulated by Ca^{2+} -CaM inhibition	Learning, memory, LTP Synaptic plasticity
AC2	Brain, skeletal muscle, lung, heart	Stimulated by $G\alpha_s$ Stimulated by $G\beta\gamma$ ^d	PKC: stimulation		
AC3	Brain, olfactory epithelium	Stimulation by $G\alpha_s$	PKC: weak stimulation CaMKII: inhibition	Stimulated by Ca^{2+} -CaM	Olfaction
AC4	Brain heart, kidney, liver, lung, BAT, uterus	Stimulation by $G\alpha_s$ Stimulated by $G\beta\gamma$ ^d	PKC: inhibition		
AC5	Heart, brain, kidney, liver, lung, uterus, adrenal, BAT	Stimulation by $G\alpha_s$ Inhibited by $G\beta\gamma$ ^e Inhibited by $G\alpha_i$ ^f	PKA: inhibition PKC α,ζ : stimulation	Inhibited	
AC6	Ubiquitous	Stimulation by $G\alpha_s$ Inhibited by $G\beta\gamma$ ^e Inhibited by $G\alpha_i$ ^f	PKA: inhibition PKC: inhibition	Inhibited	
AC7	Ubiquitous, highly expressed in brain	Stimulation by $G\alpha_s$ Stimulated by $G\beta\gamma$ ^d	PKC: stimulation		Drug dependency
AC8	Brain, lung (testis, adrenal, uterus, heart)	Stimulation by $G\alpha_s$		Stimulated by Ca^{2+} -CaM	Learning, memory, LTP, Synaptic plasticity
AC9 ^g	Brain, skeletal muscle	Stimulation by $G\alpha_s$			
SAC ^h	Testis	Not regulated by G protein subunits			Sperm capacitation

BAT, brown adipose tissue; LTP, long-term potentiation.

^a All isoforms except SAC are inhibited by P-site inhibitors.

^b Forskolin stimulates human AC1-AC8, whereas AC9 is weakly stimulated by forskolin. SAC is not affected by forskolin.

^c Cited reference numbers.

^d $G\beta\gamma$ stimulation of AC isoforms is conditional upon $G\alpha_s$ co-activation.

^e Inhibition determined by transfection only and could be an indirect $G\beta\gamma$ effect.

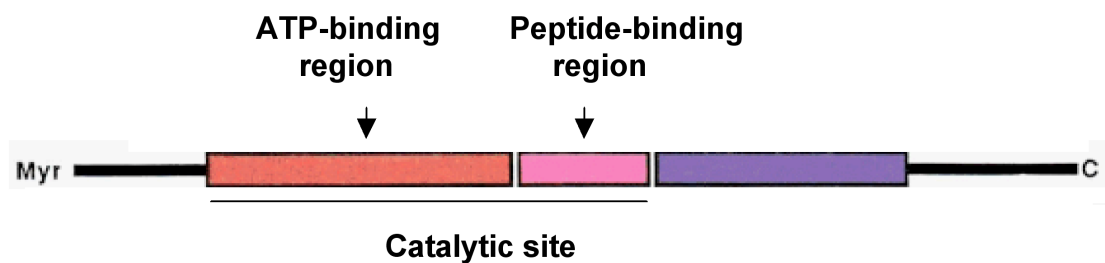
^f Denotes $G\alpha_i$ family members $G\alpha_{i1}$, $G\alpha_{i2}$, $G\alpha_{i3}$, and $G\alpha_{i4}$.

^g Inhibited by cactinurin.

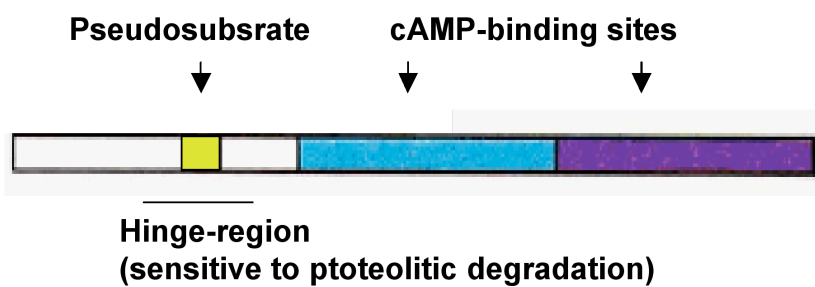
^h Stimulated by bicarbonate.

Cyclic-AMP-dependent protein kinase (PKA) structure

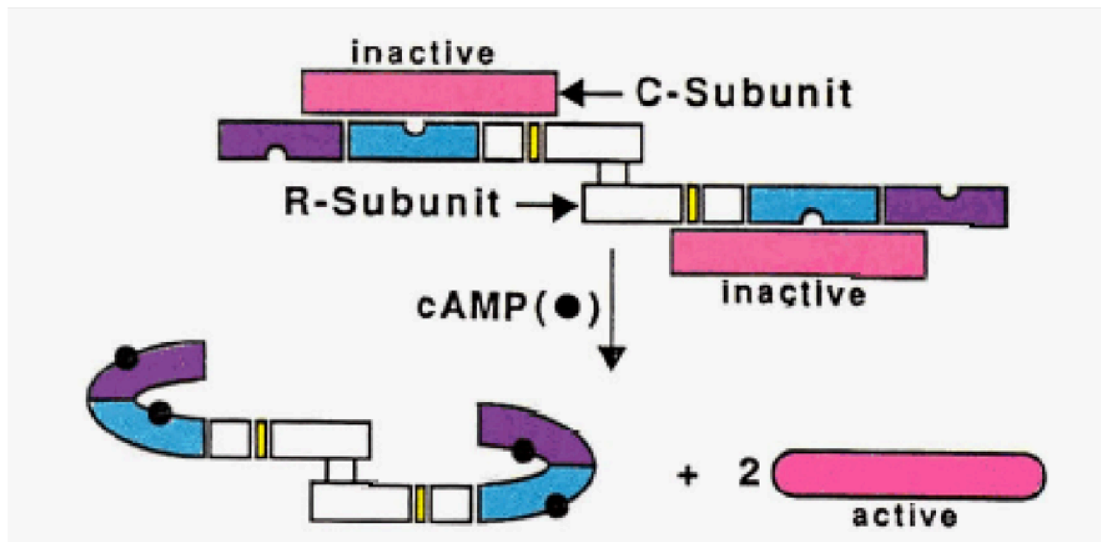
Catalytic subunits - Three subtypes: C, C α , C β



Regulatory subunits - Two types: R I, R II

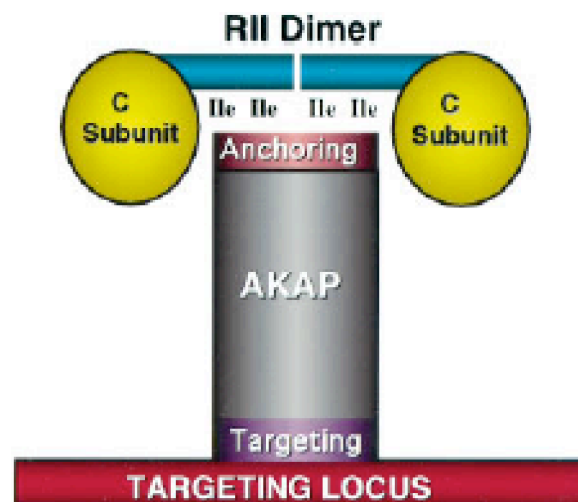


Mechanism of PKA activation

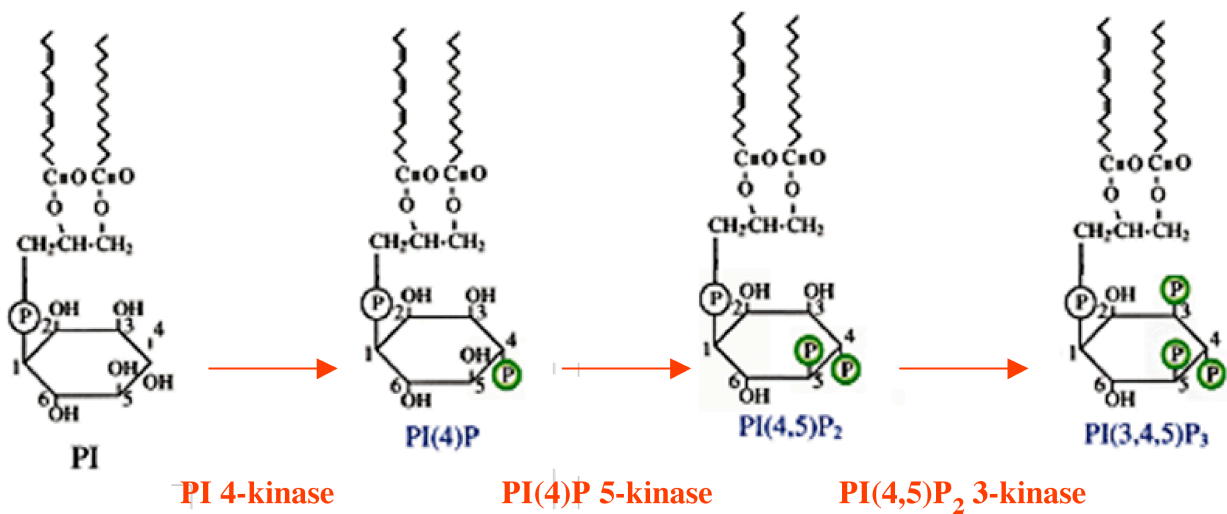
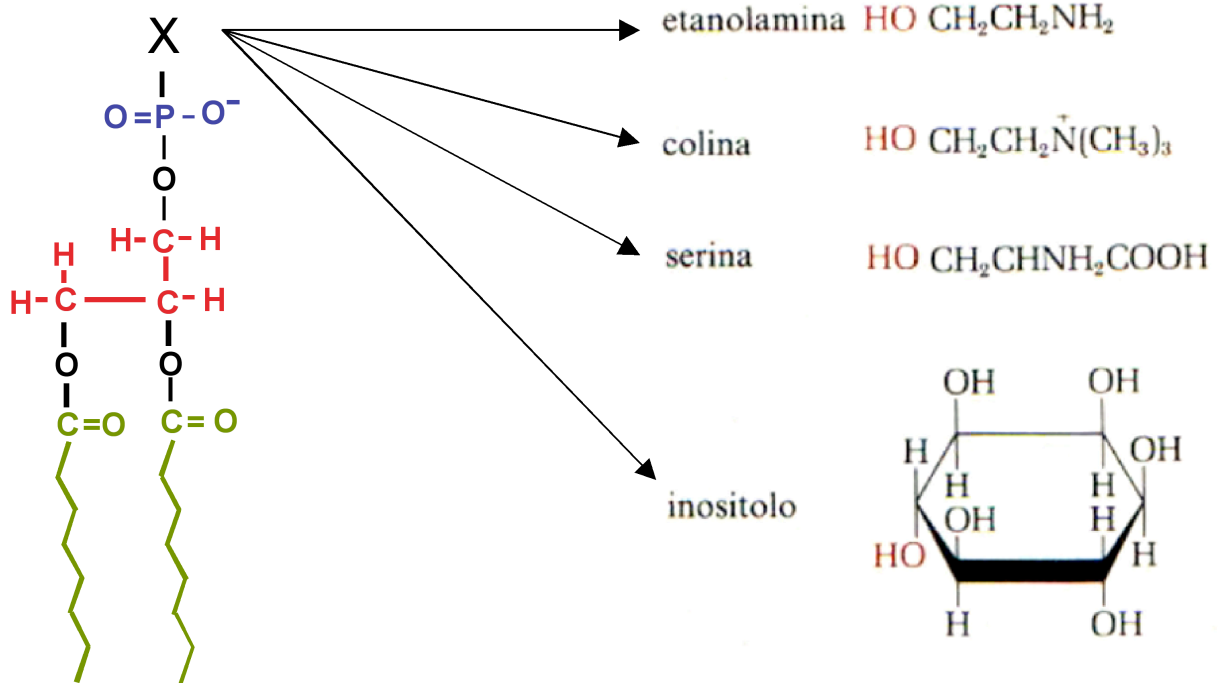


Activation of cAMP-dependent protein kinase. The domain structure of the R-subunit is summarized with cAMP binding sites A and B shown in turquoise and purple, respectively, and the hinge region in yellow. Two disulfide bonds link the R1 protomers at the amino terminus. The C- subunit is indicated in pink.

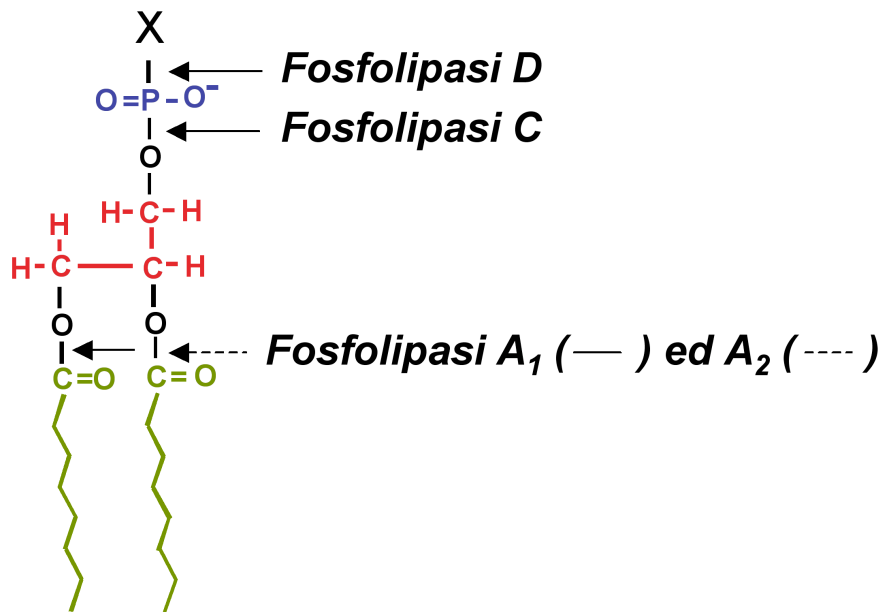
A-kinase anchoring protein (AKAP)



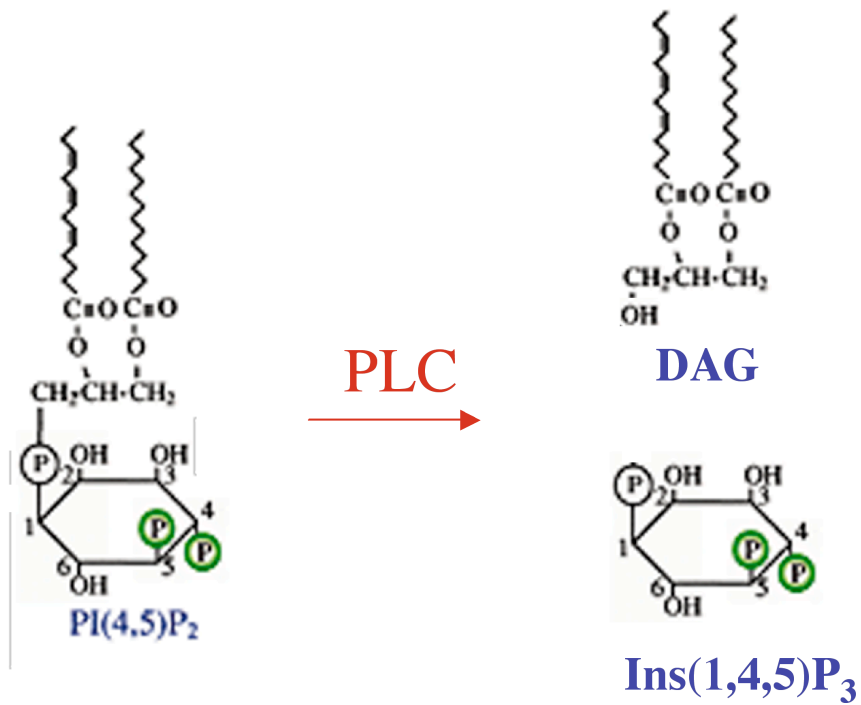
Glicerofosfolipidi e fosfoinositidi



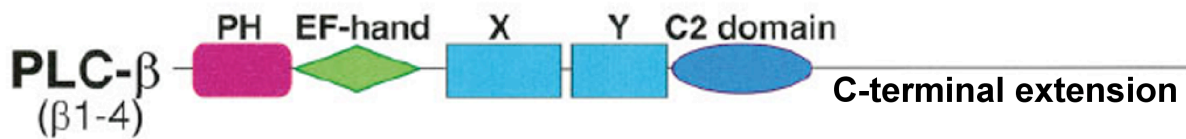
I diversi tipi di fosfolipasi



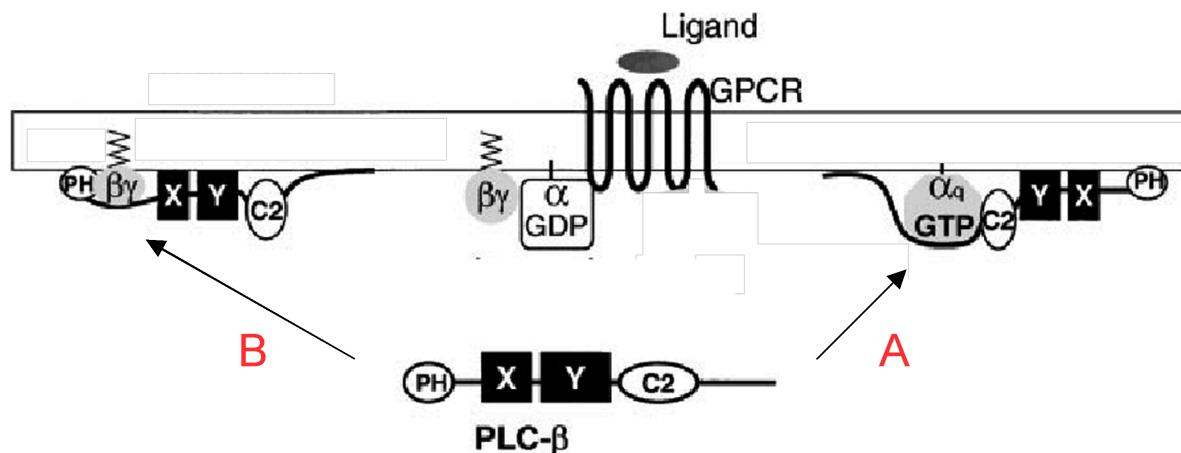
Prodotti dell'idrolisi del PIP₂ operata dalla fosfolipasi C



Struttura ed attivazione della fosfolipasi C- β



Dominio	Funzione
PH	Interagisce con PIP_3 , PIP_2 , IP_3 e con la subunità β della proteina G
EF-hand	Lega il Ca^{2+}
X ed Y	Domini del sito attivo
C2	Lega il Ca^{2+}
C-terminal extension	Interagisce con la subunità α_q della proteina G

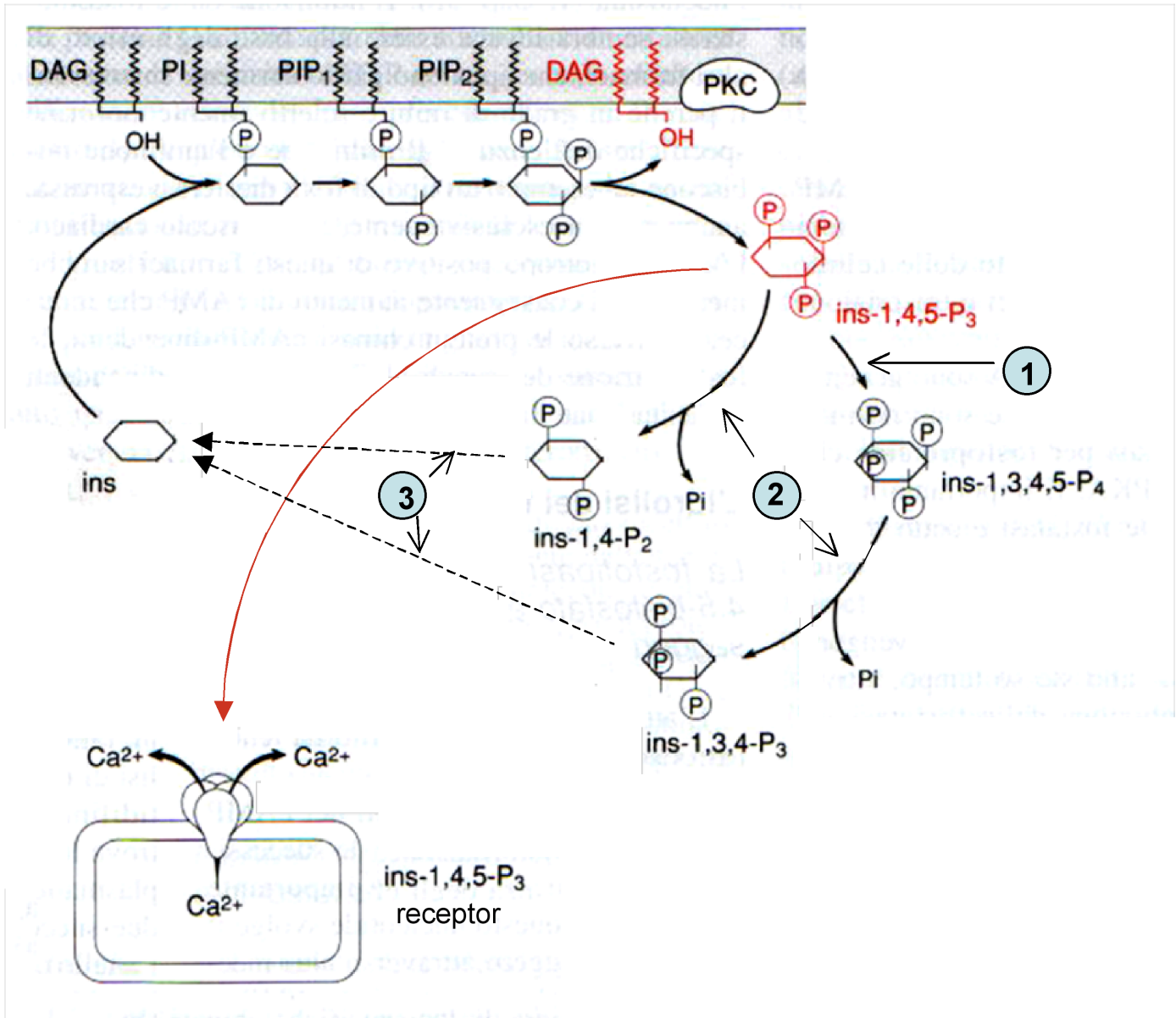


A) La PLC- β è reclutata in membrana dall'interazione tra l'estensione C-terminale e la subunità α_q della proteina G.

B) La PLC- β è reclutata in membrana dall'interazione tra il dominio PH e la subunità β della proteina G. I dimeri $\beta\gamma$ che reclutano la PLC-beta possono provenire non solo dalle G_q ma anche da altri tipi di proteina G

Nel disegno non sono mostrati i domini EF-hand della PLC- β .

Metabolismo dell'inositolo 1,4,5- trisfosfato



- ① Ins 1,4,5 P₃ 3-kinase (activated by the Ca²⁺/ calmodulin complex)
- ② Ins 1,4,5 P₃ / Ins 1,3,4,5 P₄ 5-phosphatase (activated by PKC)
- ③ Ins 3- , 1- and 4- phosphatases

Destino metabolico del DAG

