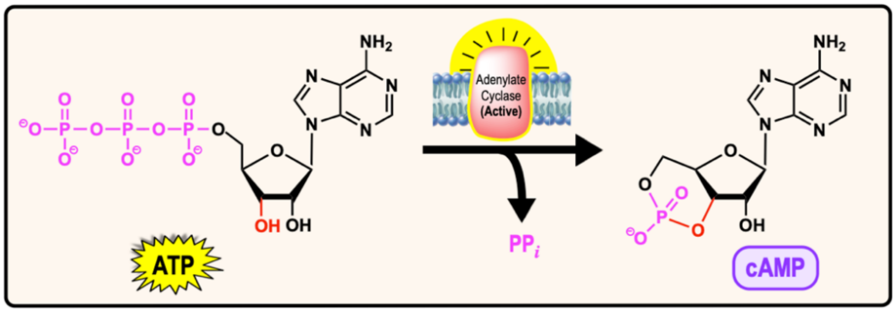
CONCEPT: cAMP & PKA

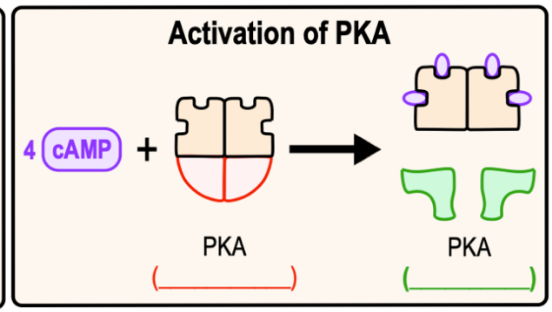
Production & Function of cAMP

●Recall: the effector enzyme, *adenylate cyclase*, converts ATP to **C**yclic **A**denosine **M**ono-**P**hosphate (________).

□ *cAMP*: *secondary messenger* that _______________ *cAMP-dependent **P**rotein **K**inase **A*** (______).

□ Therefore, cAMP functions as an *allosteric* ________________ (+) of PKA.





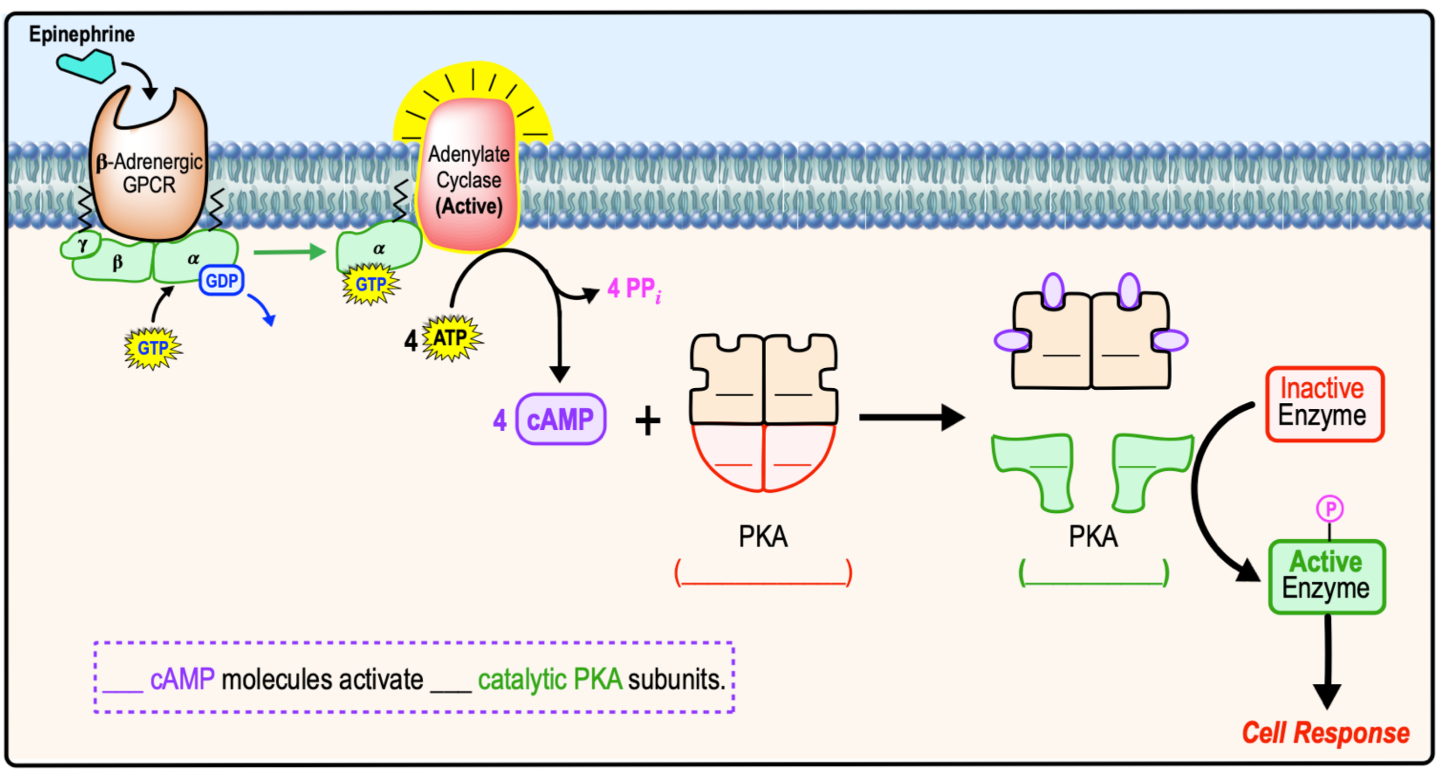
Activation of cAMP-Dependent Protein Kinase A (PKA)

●Recall: _______________: enzymes that utilize energy (ex. ATP) to *phosphorylate* a substrate.

□ In absence of cAMP, PKA is an inactive *heterotetramer* (2 **R**egulatory & 2 **C**atalytic subunits: R_2C_2).

□ ______ *cAMPs* bind regulatory PKA subunits to release ______ *catalytically active PKA subunits.*

□ Catalytically active PKA subunits ___________________ Ser/Thr residues on target proteins to alter their activity.



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EXAMPLE: Order each of the steps in the activation of PKA (by numbering them 1-4 ; first step is already numbered for you) starting after adenylate cyclase activation.

a) Cytosolic cAMP concentration increases. ___1___
b) The free catalytic subunits phosphorylate proteins on their Ser of Thr residues. ______
c) The regulatory subunits of PKA dissociate from the catalytic subunits. ______
d) Two cAMP molecules bind to each PKA regulatory subunit. ______

PRACTICE: Which of the following statements about protein kinase A (PKA) is false?

a) PKA binds a total of four molecules of cAMP, two molecules on each of the regulatory (R) subunits.
b) PKA binds a total of four molecules of cAMP, one on each of the four subunits.
c) Once active, the catalytic (C) subunits dissociate and phosphorylate target proteins.
d) When inactive, PKA is a tetramer of two regulatory (R) and two catalytic (C) subunits.

Inactivation of cAMP & PKA

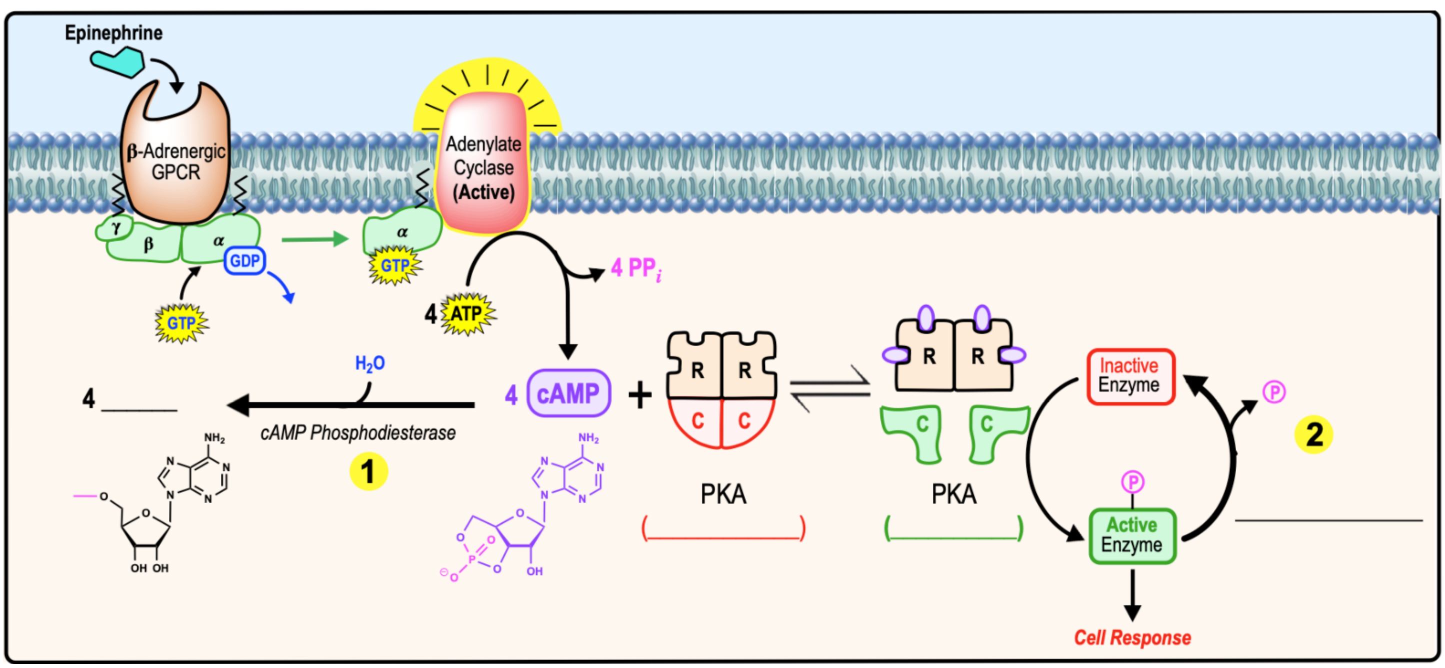
●Recall: ______________ activity in the G protein α-subunit _______________/*terminates* GPCR signaling pathways.

●______ other events also allow termination of GPCR signaling:

(1) cAMP's signaling affect is "*turned* _______" by ↓ [cAMP] using the enzyme *cAMP phosphodiesterase*.

□ *cAMP* _______________________: converts cAMP → ________ (AMP does *not* activate PKA).

(2) PKA's activity is *reversed* by *Ser/Thr* __________________ (which remove phosphate groups from substrates).



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PRACTICE: Which of the following is/are associated with cAMP binding to cAMP-dependent protein kinase A (PKA)?

I. cAMP binds to the regulatory subunits.

II. Tetrameric regulatory subunits and catalytic subunits dissociate.

III. Catalytic subunits phosphorylate proteins with specific Ser and Thr residues.

IV. cAMP is membrane bound via a phosphoinositol covalent attachment.

a) III and IV.
b) II, III, and IV.
c) I, II, III, and IV.
d) I and II.
e) I, II, and III.

PRACTICE: What is the function of a phosphatase?

a) A phosphatase removes phosphorylated amino acids from proteins.
b) A phosphatase removes the phosphate group from phosphorylated amino acid residues in a protein.
c) A phosphatase phosphorylates serine, threonine, and tyrosine residues in a protein.
d) A phosphatase degrades secondary messengers in the cell.

PRACTICE: What could be the result of a mutation in the R subunits of cAMP-dependent protein kinase A (PKA) that inhibits formation of the R_2C_2 protein complex?

a) PKA will always remain in the inactive state.
b) cAMP would drastically decrease PKA activity.
c) PKA will always remain in the active state.
d) No effective change occurs.

PRACTICE: The image below is a schematic representation of PKA activation from epinephrine binding. Based on the provided numbers in the diagram, how many subunits of catalytically active PKA will there be?

a) 1,000 molecules.
b) 200 molecules.
c) 100 molecules.
d) 50 molecules.
e) 400 molecules.