CONCEPT: STIMULATORY ADENYLATE CYCLASE GPCR SIGNALING

●*Adenylate Cyclase GPCR System*: a classic _____ step example/prototype of a GPCR signal transduction pathway.

□ Allows cells to generate a "fight or flight" response to the hormone _____ (*adrenaline*).

1) Hormone signaling ligand (*epinephrine*) binds GPCR (*β-adrenergic GPCR*) causing a _____ *shift*.

2) GPCR conformational shift _____ G protein (G_s) by promoting α subunit to *release* GDP & bind GTP.

3) With bound GTP, ___ subunit of G_s _____ from β-γ subunits & *diffuses* to nearby *effector enzyme*.

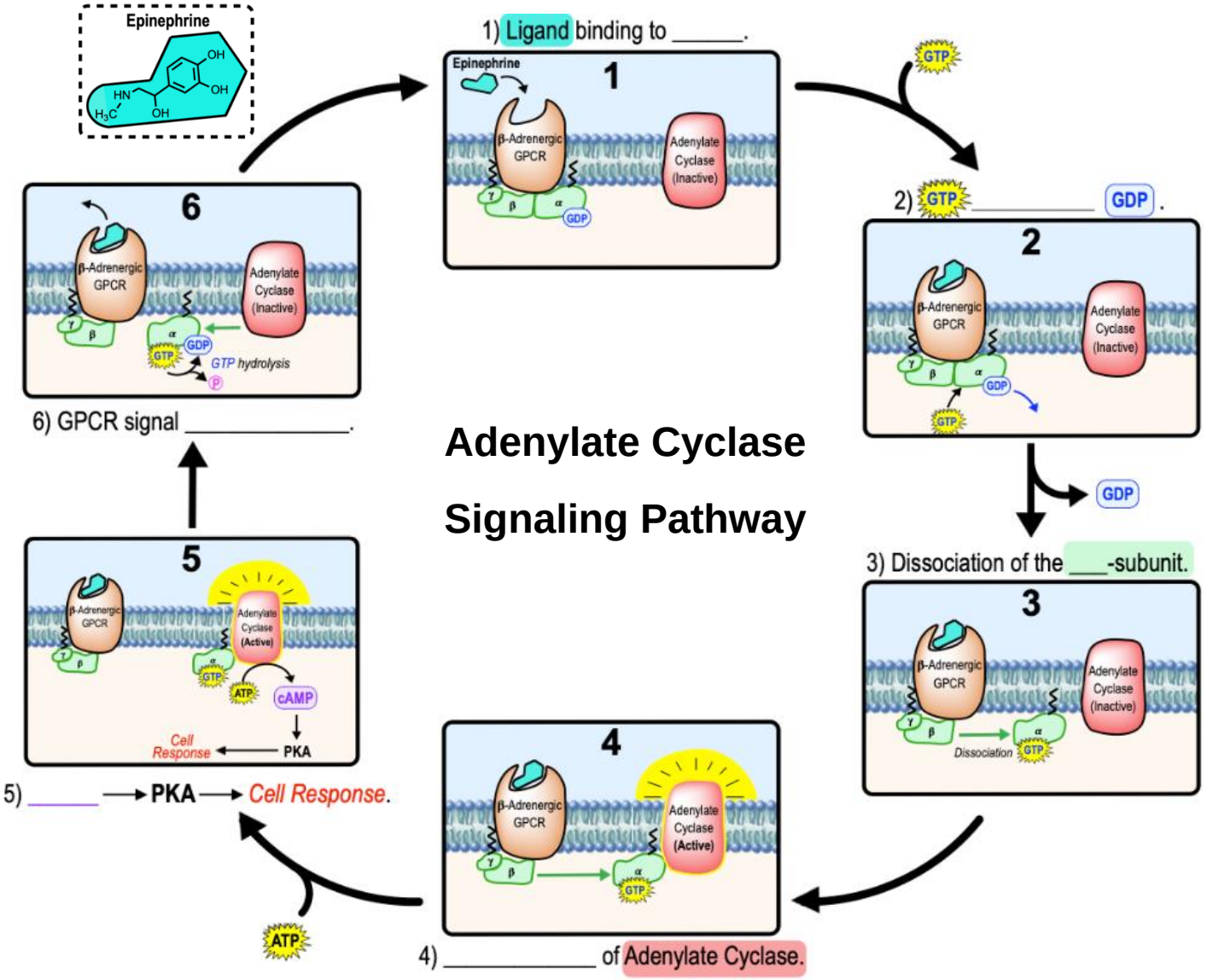
4) Activated/GTP-bound α-subunit of G_s binds & _____ the effector enzyme (*adenylate cyclase*).

5) Activated effector enzyme (*adenylate cyclase*) converts ATP → _____ *messenger* (*cAMP*).

□ cAMP Activates → ***p**rotein **k**inase **A*** (_____) → *Cell* _____ (ex. ↑ breakdown of glycogen/fat).

6) G protein α subunit slowly _____ itself (& the effector enzyme) by *hydrolyzing* its GTP → GDP.

□ α subunit assembles its original, *inactive* form & ligand *dissociates* from GPCR to _____ pathway.



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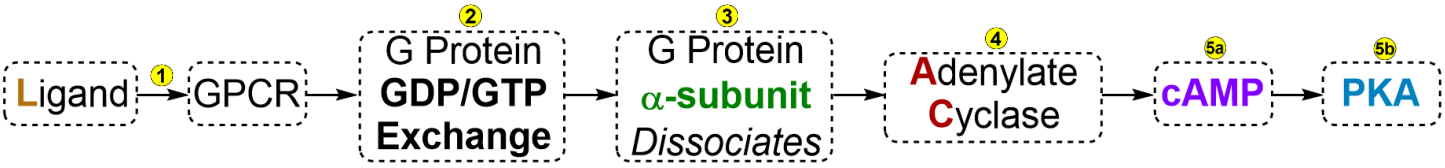
How to Remember Stimulatory Adenylate Cyclase GPCR Signaling?

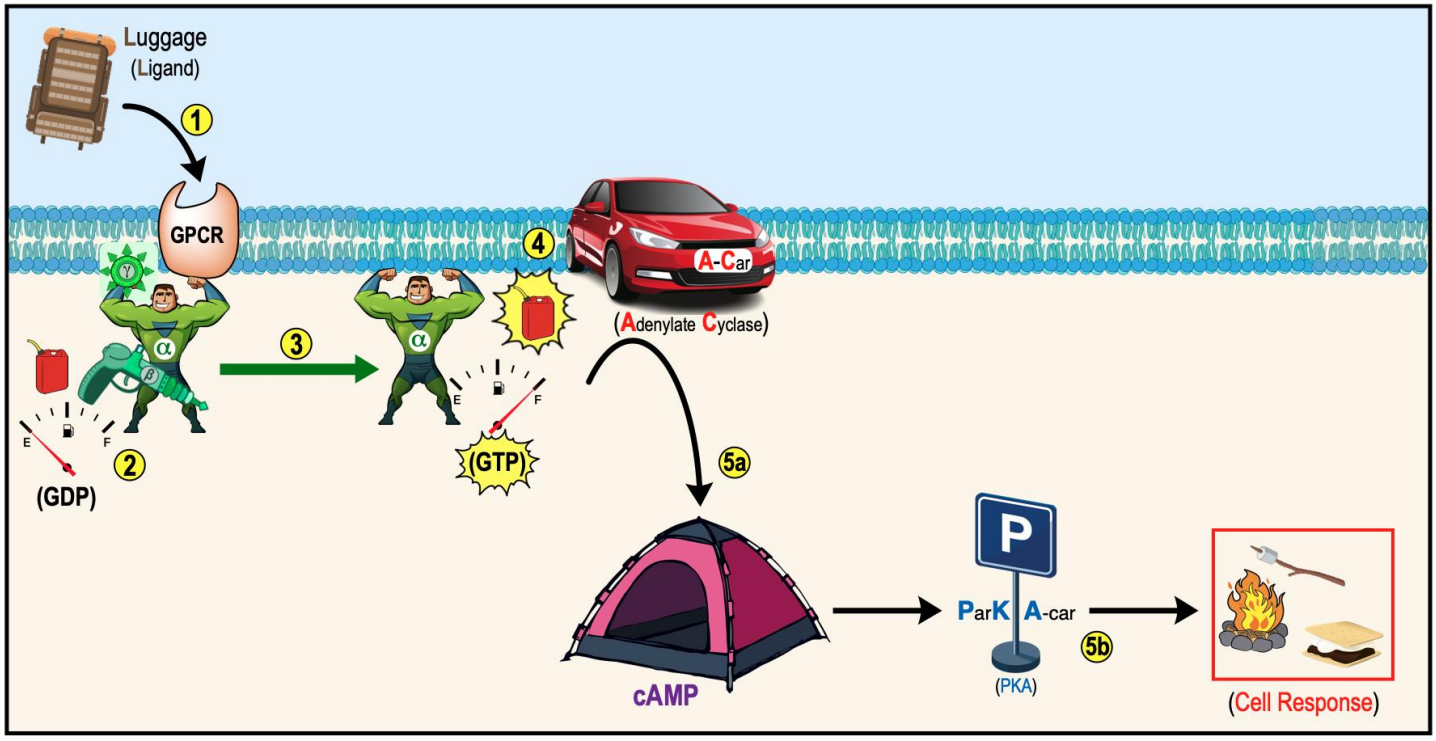


Story: Cell wants to go ***cAMP***ing (*secondary messenger*) & ***C****ook smores* (***C****ell response*)!

1. Pack the ***L***uggage (***L***igand binding to GPCR).
2. ***Alpha****-hero* (G protein α-subunit) takes charge, *exchanging empty* **G**as-can with *full* **G**as-can (**G**TP exchange).
3. *Alpha*-hero rents ***A-C***$_{ar}$ but *forgets* β-blaster & γ-gadget (G protein α-subunit dissociates to ***A***denylate ***C***yclase).
4. *Alpha*-hero fills-up ***A-C***$_{ar's}$ gas tank & *starts its engine* (***A***denylate ***C***yclase *activation*).

5a. ***A-C***$_{ar}$ goes to ***cAMP*** site (***cAMP*** production).

5b. Upon arrival to ***cAMP*** site, they ***P***$_{ar}$***K A***$_{-car}$ (***PKA***) & can now ***C****ook smores* (***C****ell Response*)!



PRACTICE: Which of the following represents the best order of signal transduction for the β-adrenergic receptor?

a) Hormone → receptor tyrosine kinase → G-protein → protein kinase A → cAMP → cellular effects.

b) Ligand → receptor → secondary messenger → G-protein → protein kinase A → cellular effects.

c) Hormone → G-protein → receptor → cAMP → protein kinase A → cellular effects.

d) Hormone → receptor → G-protein → second messenger → protein kinase A → cellular effects.

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PRACTICE: Which of the following molecules is NOT involved in signal transduction of the β-adrenergic GPCR?

a) GTP.
b) ATP.
c) cAMP.
d) cGMP.
e) GDP.

PRACTICE: Which of the following reactions does the enzyme adenylate cyclase catalyze?

a) cATP to cAMP.
b) GTP to cGMP.
c) ATP to cADP.
d) cGMP to GTP.
e) ATP to cAMP.

PRACTICE: In response to a ligand binding a GPCR, a particular G protein (G_s) activates adenylate cyclase. If a cell has a mutation where the G protein can no longer hydrolyze GTP, which of the following would be the result?

a) Cellular levels of cAMP would go down in response to ligand binding.
b) Cellular levels of cAMP would go up independent of ligand binding.
c) The ligand would not be able to bind to the receptor.
d) Cellular levels of cAMP would not change.
e) Adenylate Cyclase would always remain inactive.

PRACTICE: When epinephrine binds to its GPCR activating the cAMP cascade, all of the following happen EXCEPT:

a) GDP dissociates from the G protein as GTP associates.
b) The alpha-subunit of the G protein activates adenylate cyclase and cAMP is produced.
c) G protein is activated and diffuses away from the cell membrane into the nucleus.
d) The alpha-subunit of the G protein hydrolyzes GTP and becomes inactive.
e) The alpha-subunit of the G protein bound to GDP reassociates with the beta & gamma-subunits.