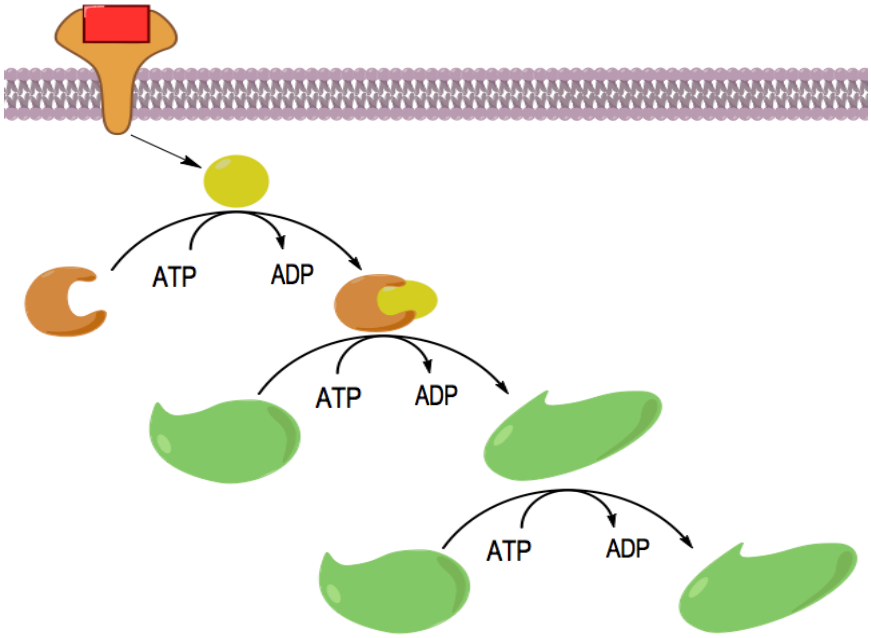
CONCEPT: BIOSIGNALING

- cAMP – secondary messenger that activates protein kinase A (PKA) by allosterically binding to the regulatory subunit
    - □ Binding causes the regulatory subunit to release from the catalytic subunit, allowing catalysis to occur
    - □ Used as secondary messenger for MANY systems, hormones, and neurotransmitters
    - □ Broken down by cyclic nucleotide phosphodiesterase (PDE) cAMP → AMP
- Protein kinase A regulates many enzymes and proteins by covalently modifying S or T residues with phosphate group
- Anchoring proteins hold together the receptor, PK, and adenylyl cyclase
- Phosphorylation cascades activate and deactivate a series of proteins through the transfer of phosphate groups
- Epinephrine – hormone synthesized from tyrosine that binds to a GPCR and leads to the activation of PKA
    - □ PKA phosphorylates phosphorylase b kinase b to the active form, phosphorylase b kinase a
    - □ Phosphorylase b kinase a phosphorylates glycogen phosphorylase b to glycogen phosphorylase a
    - □ Glycogen phosphorylase a breaks down glycogen to glucose 1-phosphate, that is released as glucose into blood



- 1 molecule of epinephrine → 100,000 molecules of glucose
- ß adrenergic receptor kinase (ßARK) – binds and phosphorylates epinephrine receptor so it won't work
    - □ ß-arrestin binds to phosphorylated terminal of receptors, signals the membrane trafficking system to pull receptors back into the cell, where they're stored in endosomes
- Cholera toxin causes NAD+ to be broken down and covalently linked (as ADP-ribose) to G protein
    - □ Covalent modification causes G protein to be stuck in active form
    - □ Leads to far too much cAMP being produced, resulting in pumping out excess Cl^- and Na^+, water follows solutes