

Tutorial 3

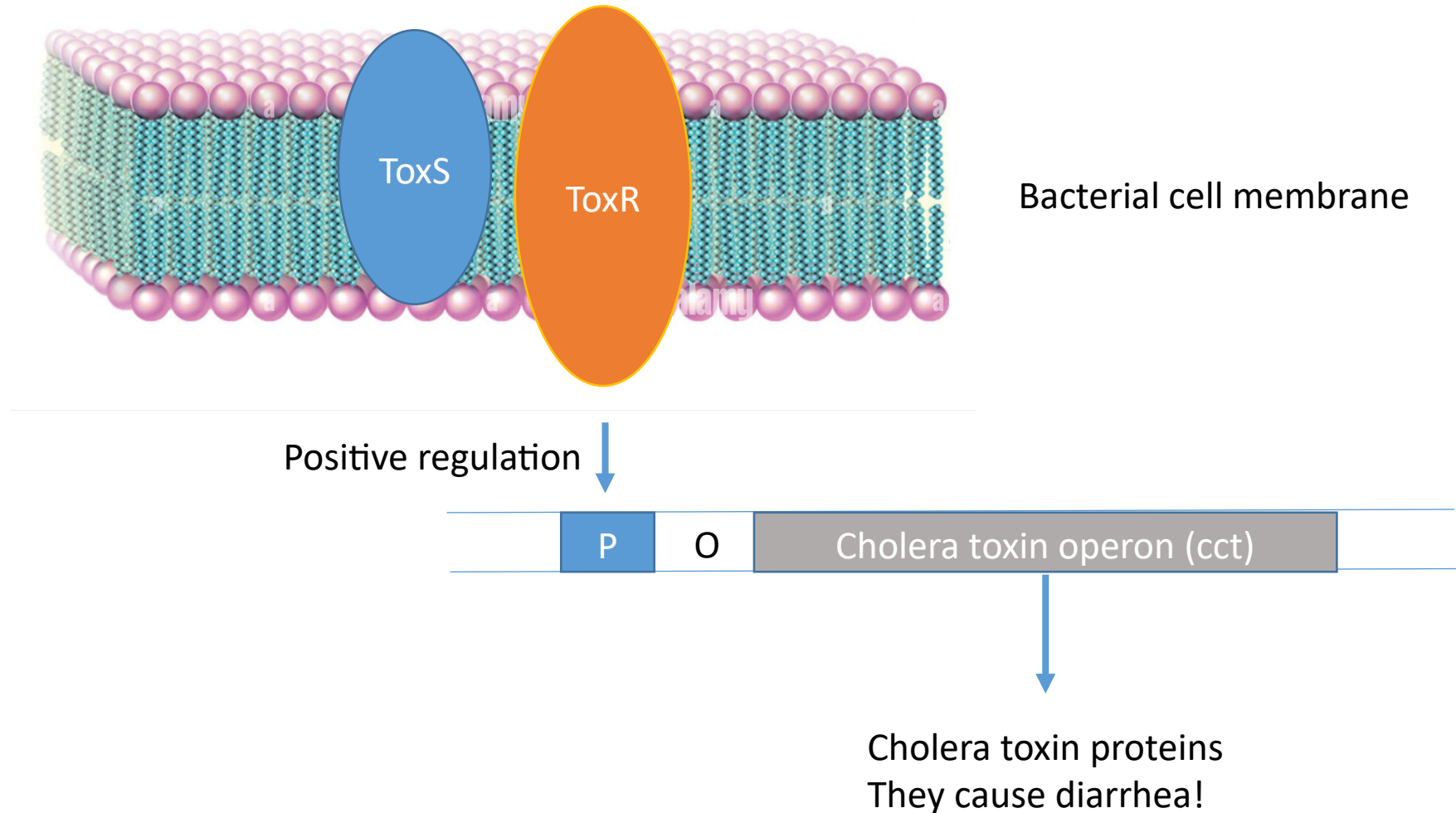
Regulation of gene expression
Cell communication



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How will you use your newly acquired knowledge of these two topics to treat cholera?

Vibrio cholerae has two regulators (ToxR and ToxS) of the cholera toxin operon (*cct*)



How does the ToxR protein turn the *cct* operon on?

What do you know already? How the Lac and Trp repressors turn off their respective operons.

- Concept to recall: The repressors bind to the operators, which are strategically placed downstream of the promoter. Therefore, the repressors block the RNA polymerase from elongating.

The ToxR protein helps the RNA polymerase to do its job better. The way it works is that the ToxR protein helps RNA polymerase to bind and initiate transcription better.

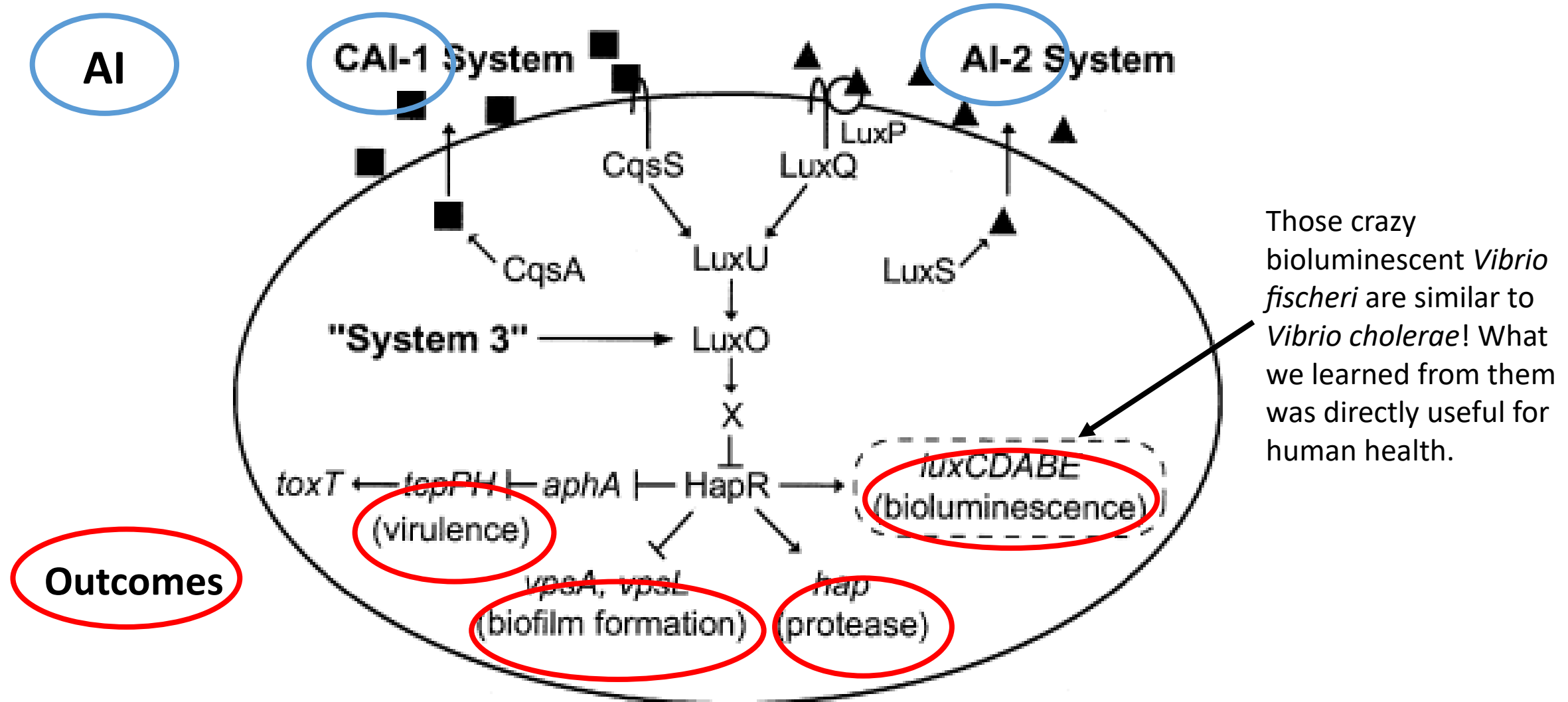
This is an example of a transcriptional regulator that is found on the bacterial membrane

Do you think that eukaryotes could use this strategy of having a transcriptional activator on their cell membrane?

- Concept to recall: Eukaryotes are compartmentalized and have a nucleus. The transcriptional activator has to eventually enter the nucleus to work.

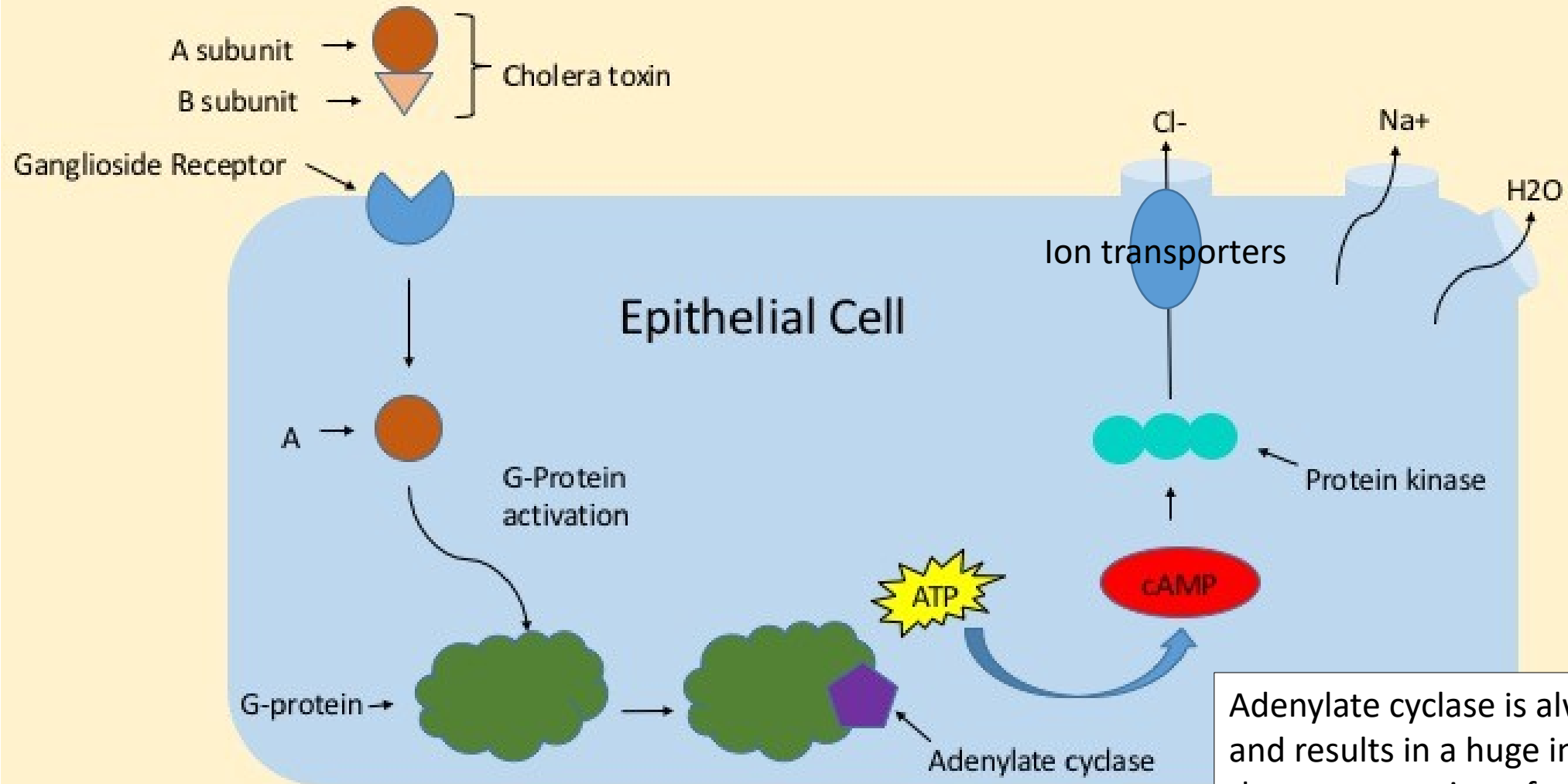
As they are compartmentalized, eukaryotes use the signal transduction cascades to transmit the signal from the cell membrane to the nucleus and would not use this strategy.

Vibrio cholerae has two auto-inducers for quorum sensing



How does the cholera toxin act on our intestine cells to cause diarrhea?

Intestinal lumen

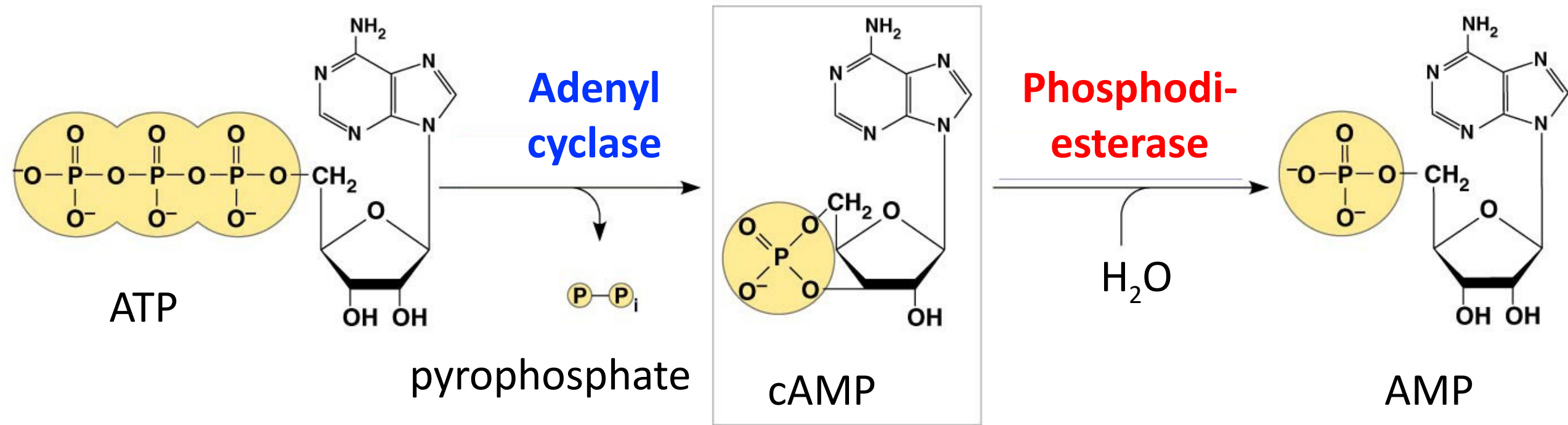


Adenylate cyclase is always ON and results in a huge increase in the concentration of cAMP

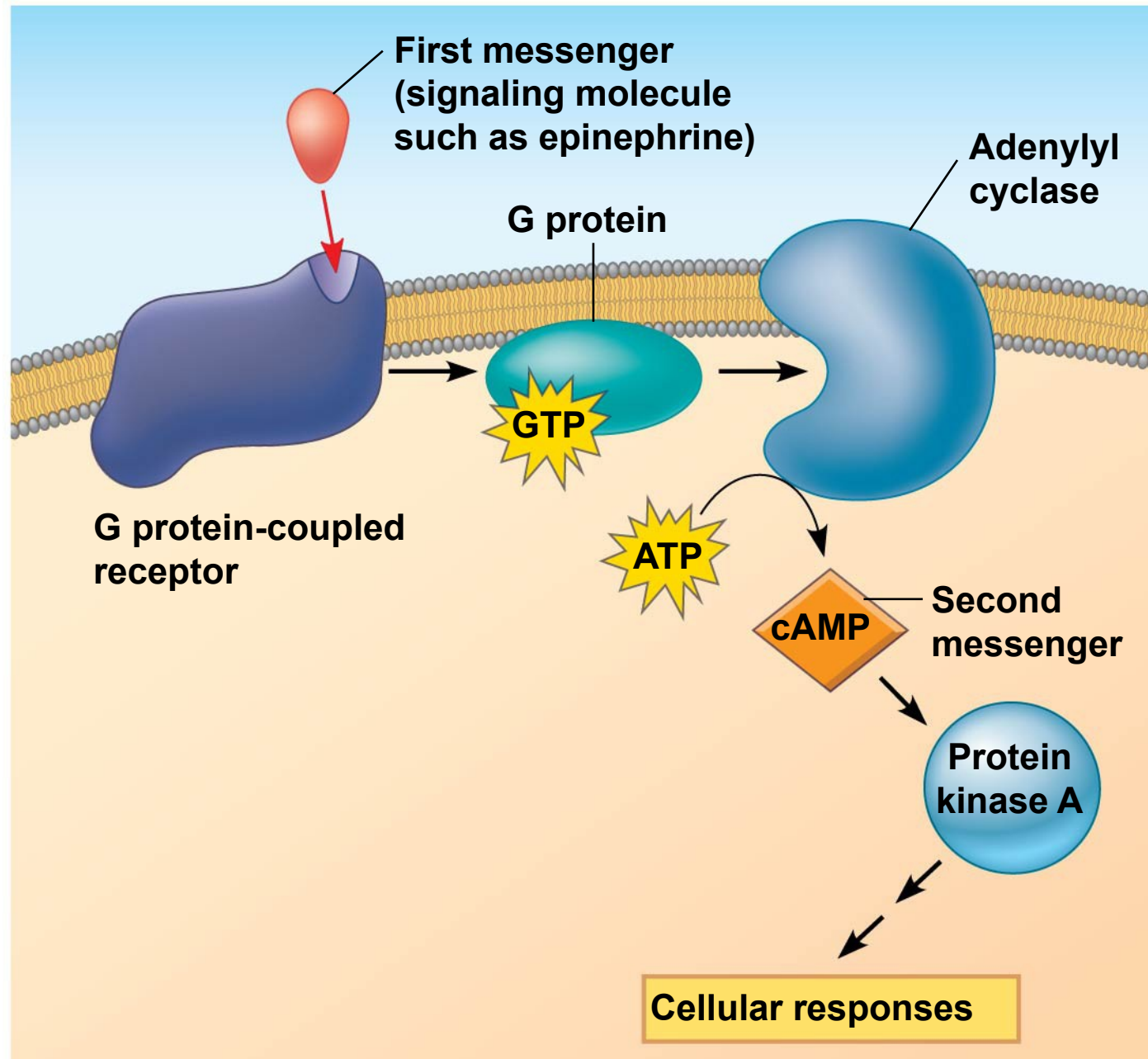
Cyclic AMP is a second messenger

AMP: adenosine monophosphate

cyclic AMP: cAMP



cAMP and G protein signaling pathway



You are now an expert in biology and want to treat the symptoms of cholera

How will you treat diarrhea using your knowledge of GPCRs?

- Concept to recall: GPCRs activate G proteins and also second messengers like cAMP
- Concept to recall: there are many drugs that target GPCRs and reduce the activation by GPCRs; maybe one of them will reduce the activation of G proteins and production of cAMP caused by cholera toxin (actually enkaphalins do exactly this)

NOTE: the best treatment for cholera dysentery is oral rehydration salts and rest!

You are now an expert in biology and want to treat the symptoms of cholera

How will you treat diarrhea using your knowledge of operons?

You want to design a switch in *Lactobacillus* (normally found in probiotics like yoghurt) that will sense the cholera toxin in the intestine and kill *Vibrio cholerae*. The idea is to have genetically modified *E. coli* in our intestines that are natural killers of *Vibrio cholerae* when they detect these bacteria. Discuss with your classmates and your TA and come up with such a switch.