**Waking Up Anna**

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**Part 6: Waking up Anna**

The substance in Anna’s CSF was making her sleepy just like the action of benzodiazepine, so her doctors considered testing Flumazenil, a competitive inhibitor of benzodiazepine, to treat her. It worked and Anna woke up (for the first time in many years). Explore the structure of the GABA-A receptor in complex with GABA and Flumazenil to understand where it binds and how it regulates the receptor function.

* Open the file PDB ID 6d6t in RCSB and explore the structure.

Q1 (2 pts). Scroll down in the Structure Summary to find Small Molecules and complete the table below.

|  |  |  |  |
| --- | --- | --- | --- |
| **Small molecule abbreviation** | **Chains that it interacts with** | **Complete chemical name** | **Identify which complete chemical name indicates GABA and which is Flumazenil** |
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Q2 (1 pt). Click on flumazenil and include a picture of the molecule below.

* From the Structure Summary page (RCSB), click on Ligand Interaction for flumazenil.
* Click on the arrow (right side toolbar) and then click on the flumazenil molecule to highlight.
  + Make the flumazenil molecule space filling (Ligand > … > Add representation > spacefill)
  + Color the flumazenil molecule light blue (cyan)

Q3 (1 pt). Between what two polypeptides does the flumanezil bind?

Similarly to Part 5 of the worksheets, color all of the protein subunits gray and color the GABA molecules yellow. *If you wish, you can hide the antibody polypeptides from this structure and the carbohydrate small molecules.*

Q4 (2 pts). Where in the structure are the GABA and Flumazenil molecules bound? Which GABA-A receptor chains are they bound to? Support your answer with a publishable figure drawn using Mol\* (in RCSB).

Q5 (2 pts). Based on your explorations of these structures, can you explain the mechanism of Flumazenil’s action in waking up Anna (*Hint: Think about what might be in the CSF.)*.

Q6 (2 pts) With a hand drawn model summarize the structure of the GABA-A receptor (as seen from the outside of the cell). You may use the pentameric structure shown below to draw and mark in the model where GABA, benzodiazepine, and Flumazenil bind. Remember to label the alpha, beta, and gamma chains of the GABA-A receptor.