**Refined Complex Questions About Protein Structure:**

1. **How can we evaluate the structural changes in the N-terminal domain of CCK1R upon binding with CCK-8?**
   * **Need to Know**:
     + What simulation tools can assess structural changes in receptor-ligand interactions?
     + How do MD simulations reveal conformational changes upon ligand binding?
     + How can we evaluate binding stability using RMSD or other structural analysis metrics?
2. **What role does the N-terminal domain of CCK1R play in receptor-ligand selectivity?**
   * **Need to Know**:
     + How can homology modeling predict ligand selectivity in this domain?
     + How can sequence alignments between homologous receptors provide insight into selectivity?
     + What structural motifs in the N-terminal domain are critical for ligand binding?
3. **How do mutations in the N-terminal domain of CCK1R affect its structural stability and function?**
   * **Need to Know**:
     + How can we use MD simulations or stability prediction tools to evaluate the impact of mutations?
     + How do we assess changes in binding affinity due to mutations?
     + Can we predict destabilizing mutations using homology modeling or deep learning-based prediction tools?

**Revised 200-Word Annotation:**

The questions above focus on analyzing the N-terminal domain of CCK1R and its interaction with CCK-8. The material from Part I, such as structural and sequence data, can help answer questions on ligand selectivity by utilizing sequence alignments and homology modeling. The course material on MD simulations and homology modeling will provide computational answers to questions about structural changes upon ligand binding and the effects of mutations on receptor function. While we can infer structural insights from sequence data, external resources like docking simulations or mutational analysis datasets will be necessary to fully explore receptor selectivity and mutational effects. These "Need to Knows" align with previously taught tools like **PyMol** and **VMD** but will also guide further computational work to evaluate molecular interactions and structural predictions. I want to keep my medical relavency as part of this project, since that is my background. But I understand how complex this project can become so I have decided to see if I can identify potentially pathogenic mutations to analyze and then in my discussion, analysis and in the functional aspects of this project try and focus on the pathophysiological implications I can find.