**Question 1: How do mutations in the N-terminal domain of CCK1R affect ligand-binding specificity and efficacy?**

* **Need to Knows**:
  + How do specific mutations influence the ligand binding affinity of CCK1R?
  + Which regions in the N-terminal domain are critical for ligand selectivity and binding strength?
  + What insights can molecular docking and affinity prediction tools provide for these mutations?

**Question 2: How does CCK1R interact with other signaling molecules in PPIs, and what are the implications of these interactions for gastrointestinal function?**

* **Need to Knows**:
  + Which protein-protein interaction partners are most relevant to CCK1R’s role in gastrointestinal signaling?
  + What experimental or computational tools can best analyze these interactions in a pathway-specific manner?
  + How do known PPIs contribute to receptor stability and function, and how might mutations alter these interactions?

**Question 3: What are the potential pathophysiological consequences of destabilizing mutations within CCK1R in relation to receptor signaling?**

* **Need to Knows**:
  + Which downstream signaling pathways are affected by mutations in CCK1R, particularly those related to gastrointestinal physiology?
  + How does structural stability correlate with receptor function in a physiological context?
  + What structural features are responsible for activation and deactivation cycles in the receptor, and how do mutations impact these?

**200-Word Annotation**

This project explores the effects of key mutations on the structure and function of CCK1R, a receptor integral to gastrointestinal physiology. Prior structural analysis (Part I) covered mutation stability and structural integrity using homology modeling and molecular dynamics. Tools like SWISS-MODEL, I-Mutant, and RMS analysis provided foundational insights, while sequence alignments helped identify critical binding motifs within the receptor. Moving into functional analysis, additional insights will be gathered through protein-protein interaction networks to assess how mutations impact signaling pathways, particularly in ligand binding and downstream signal propagation. While initial “Need to Knows” related to structural stability were addressed in Part I, computational tools to simulate receptor function and analyze PPIs, such as BioPlex and molecular docking, will be applied in Part II. External resources, including primary literature on gastrointestinal signaling, will assist in understanding broader physiological implications. The questions posed aim to link mutation-induced structural changes with alterations in receptor efficacy and potential disease associations, creating a comprehensive perspective on CCK1R’s role in digestive health.