Name: _____
Class: _____

Structure-Based Virtual Screening Worksheet

Warm-Up Questions:

Read the article "Structure-Based Virtual Screening: From Classical to Artificial Intelligence" and answer the following questions.

1) What is a typical drug development timeline from drug target identification to clinical trials?

2) What are some advantages and disadvantages to performing structure-based virtual screens?

Question #1:

Why is it necessary to generate a receptor grid? What would happen if you proceeded with docking a ligand without a receptor grid?

Question #2:

Preparing a ligand using LigPrep may produce multiple output structures for each input structure by generating different protonation states, stereochemical outcomes, tautomers, and ring conformations. Why is it important to prepare a ligand before proceeding with docking?

Question #3:

What important protein-ligand interactions do you see when the cognate ligand is docked? List specific residues and define specific interactions that may play an important role in binding.

Question #4:

In the table below, select your top 5 ligands with the best docking scores. Remember that the lower the value, the better the docking score. For each ligand, i) write the ligand name and take a screenshot of the pose, ii) list the docking score that can be found in the Project Table, and iii) identify at least 2 types of protein-ligand interactions between that particular ligand and residues within the active site.

Ligand Name & a Screenshot of the Pose	Docking Score (found in Project Table)	Protein-Ligand Interactions

Question #5:

SiteMap visualization uses a grid of points to identify potential hydrophobic and hydrophilic regions; the hydrophilic regions are further classified into hydrogen-bond donor, hydrogen-bond acceptor, and metal-binding regions, and the surface of the protein is contoured. Take a screenshot of your SiteMap results. Identify which regions of your receptor are hydrophilic and hydrophobic.

Individual Exercise:

Using the information that you gained from docking the screening ligands, design a new inhibitor that may have a better docking score. Perform LigPrep on your molecule and use Glide to obtain its docking score. Take a screenshot of its pose and paste it below. Then list its docking score. Provide analysis as to why you chose to design this particular inhibitor.