Introduction:  
For the assignment I chose the PDL1 protein in complex with PD1. The PDB id for this complex is 3BIK.   
I started by pulling this PDB into my MOE workspace and visually inspecting the structure. Then I ran QuickPrep protocol to energy minimize the structure. A blue and pink glowing lines

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Figure 1: Energy minimized structure of PDL1-PD1 complex from MOE. PD1 is in salmon color while PDL1 is in cyan.

Next I worked on identifying hotspot residues in the PDL1 protein in the interface of PDL1 and PD1 complex. I used the tool: Protein -> Contacts to identify the residues which are in contact.

A screenshot of a computer

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Figure 2: Protein Contact panel from MOE. It shows the interacting residues in PDL1 and PD1.

I will be using these residues in my RFDiffusion commandline script for hot spots. Next I removed the part of the PDL1 protein that was not interacting with PD1 and this truncated protein will be used as RFDiffusion input.

A blue and pink structure

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Figure 3: Truncated PDL1 protein in cyan and PD1 in salmon.

I saved from MOE the two individual pdb files as  
pdl1\_truncated.pdb

pd1.pdb  
These were used in the protocol described in my jupyter notebook: pdl1\_binder\_rfdiffusion.ipynb

Results:

I tried the scaffold guided binder design protocol in RFdiffusion and I thought that would generate the best designs. However 4 out of the 5 binder designs obtained from the alphafold2 with pAE\_interaction score came from unconditional RFdiffusion runs with hotspots specified.

Following are the top AF2 predicted structures that I obtained from running the dldesign protocol with pAE interaction scores < 20. According to the paper, the lower the value of this parameter the better they performed experimentally.

A group of blue and pink objects

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Figure 4: Top 5 binder structures generated after dldesign protocol with binder in salmon and PDL1 in cyan.

Observations: The dl\_binder\_design protocol discussed in the jupyter notebook ensured that the structures are not just helical bunches that are most commonly observed in RFDiffusion outputs. Also the binders look similar to the PDL1 binder in the native PDB. I ran the h-bonds and buried residue charges script but my ranking is based solely on the pAE interaction. I think this might be a better ranking method and proven through experimental results.