Ensemble docking of Palbociclib using all similar structures starting from apo CDK structure

- 1. Open Orbital from the desktop. In the File dropdown menu, select Open PDB ID (Ctrl+P).
- 2. In the Open PDB ID popup window, enter the PDB ID **1BI8-A** and select OK in order to open the Crystal structure of the CDK6-P19^{INK4D} inhibitor complex.

	Orbital		
File	General	Protein	Li
	Open	Ctrl+0	
	Open Recent	•	
	Open PDB ID	Ctrl+P	
	Open PDB Redo	Ctrl+Shift+P	
	Open ZINC ID	Ctrl+Shift	+L
	Open Pubchem ID	Ctrl+L	
	Open Ideal Ligand	Ctrl+I	
	Open COD ID	Ctrl+Alt+	L
	Open Density Map	Ctrl+D	
	Save Session	Ctrl+S	
	Save All Files		
	Help	•	
	Exit	Ctrl+Q	

3. Under the **General** tab select the **Cartoon** setting in the **Display** panel and deselect the **Sticks** icon in order show the protein in its cartoon structure.



4. Next, select the Ligand tab and open the dock wizard



5. In the dock wizard, select **Switch to SMILES input.** Next, copy and paste the SMILES value for the ligand **LQQ** from the ligand summary on the RCSB PDB web page in the the Ligand Input in the Dock Wizard. (SMILES input:

CC(=O)c1c(C)c2cnc(Nc3ccc(cn3)N3CCNCC3)nc2n(C2CCC2)c1=O http://www.rcsb.org/pdb/ligand/ligandsummary.do?handler=biologyChemistry&hetId=LQQ)

6. Under Advanced Options check the dock all box and select Dock Begin.



 After the calculation is complete, select all docked conformations in the **Object Manager**, right click and change the color of the ligands to blue under **Color Manager**.

■ ~ All → 4 ²	1BI8-A_RCS	8	^					
	dock_ Z dc	Center		F				
	e de de X	Clone Object(s) Delete Selection		Ctrl+Shift+C Del	By Object By Chain Mode Spectrum			
	ar ar ar	Save as Color Manager	pt Selection	s •		By Object By Chain Mode Spectrum		$\sum_{i=1}^{n}$
	de de de de de	Delete All Except Merge Ligands Dissolve Groups Rename Group		Ctrl+D			,	P S
	dock11, dock12, dock13	0.000328_CC(0.000291_CC(0.000227_CC(*			Orange Yellow Green Cyan	, , , ,	/
Orbital Logger		80	ĸ			Blue		Blue
0 ligand dock do	one.					Magenta Gray	;	Blue Ribbon Dark Blue
					Ator	726		Blue Violet Jacksons Purple

- 8. Use the scroll button on the mouse to select the first calculated ligand in the **Object Manager**. This action will center the ligand in the viewport.
- Under the Docking Wizard in Advanced Settings, select the Ensemble dock button and in Pocket Sequence Similarity input a value of 0.99. Hide the all currently selected ligands before pressing Dock Begin.



Dock Wizard	Β×
Protein :	
1BI8-A_RCSB	~ 씁
SMILES :	
c3ccc(cn3)N3CCNCC3)nc2n(C2CCCC	2)c1=O
Single	
Switch to ligand input	
Dock Begin	
 Advanced Options 	
Ligand Options :	
Flexible dihedral	
✓ Flexible within ring structure	
Receptor Options :	
🗹 Dock all	
Ensemble dock	
Pocket Sequence Similairty	
0.99	*
Pocket Structure RMSD	
0.50	
Early Stop	



10. Next, in the object manager delete all docked ligands except for the first output (shown in blue). In addition, hide all **sticks** and show **cartoon** in the display panel as before. Next, hide the original protein (in green) by checking the box next to the name in the **object manager**.



- 11. Open the File menu and select Open PDB ID (Ctrl+P) to open the protein 5L2I as shown in step 1.
- 12. First, select the protein that is moving in the **object manager**, second, select the reference protein and then click **Align** in the General tab in order to finish the structure alignment.



 Select both ligands with the middle scroll button using the **Object Manager** in order to zoom in on the selection. From here, RMSD can be calculated as shown in previous tutorials. (RMSD = 2.05 Angstroms).



