Hierarchical Virtual Screening from Rocaglamide Derivatives to Discovery New Potential Anti-Skin Cancer Agents

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SUPPLEMENTARY MATERIAL

Figure S1 Redocking validation using Chk1 (PDB ID 2CGX) and its native ligand 3D3 showing poses obtained by software (a) GOLD, (b) FRED, and (c) Dockthor. Respective RMSD values are shown in each figure. Crystallographic pose of native ligands is shown in green, while docking poses from software are in gray, purple, and light blue, respectively. Figures were prepared using Maestro.

Figure S2. 2D diagram of the interactions of the 3D3 ligand and training set compounds. *: Pivot Molecule

Figure S3. 2D diagram of the interactions of the promissing compounds. PC: PubChem

Figure S4. Promising compounds overlap with Rocaglamide-A (yellow). PC: PubChem.

Figure S5. Overlays of the crystallographic ligand poses (in green) with the computational poses (in red): (A) 3D3 (PDB ID 2CGX), (B) RCG (PDB ID 5ZC9) and (C) V1Y (PDB ID 6XFP).

Figure S6. Results of binding affinity of the complex (3D3), control (Roc-A) and promising compounds with Chk1 receptor (PDB ID 2CGX).

Figure S7. Results of binding affinity of the complex (RCG), control (Roc-A) and promising compounds with elF4A1-ATP receptor (PDB ID 5ZC9).

Figure S8. Results of binding affinity of the complex (V1Y), control (Roc-A) and promising compounds with BRAF receptor (PDB ID 6XFP).

Figure S9. Interactions of complexed inhibitors with amino acid residues at the respective active sites. (A) 3D3 (PDB ID 2CGX), (B) RCG (PDB ID 5ZC9) and (C) V1Y (PDB ID 6XFP).

Figure S10. Interaction of promising compounds with amino acid residues in the active site of the Chk1 receptor (PDB ID 2CGX). (A) PC-135638768, (B) PC-53093220 and (C) PC-7581023.

Figure S11. Interaction of promising compounds with amino acid residues in the active site of the elF4A1-ATP receptor (PDB ID 5ZC9). (A) PC-18582767, (B) PC-16903784 and (C) PC-53093220.

Figure S12. Interaction of promising compounds with amino acid residues in the active site of the BRAF kinase receptor (PDB ID 6XFP). (A) PC-53093220, (B) PC-7581023 and (C) PC-9115580.
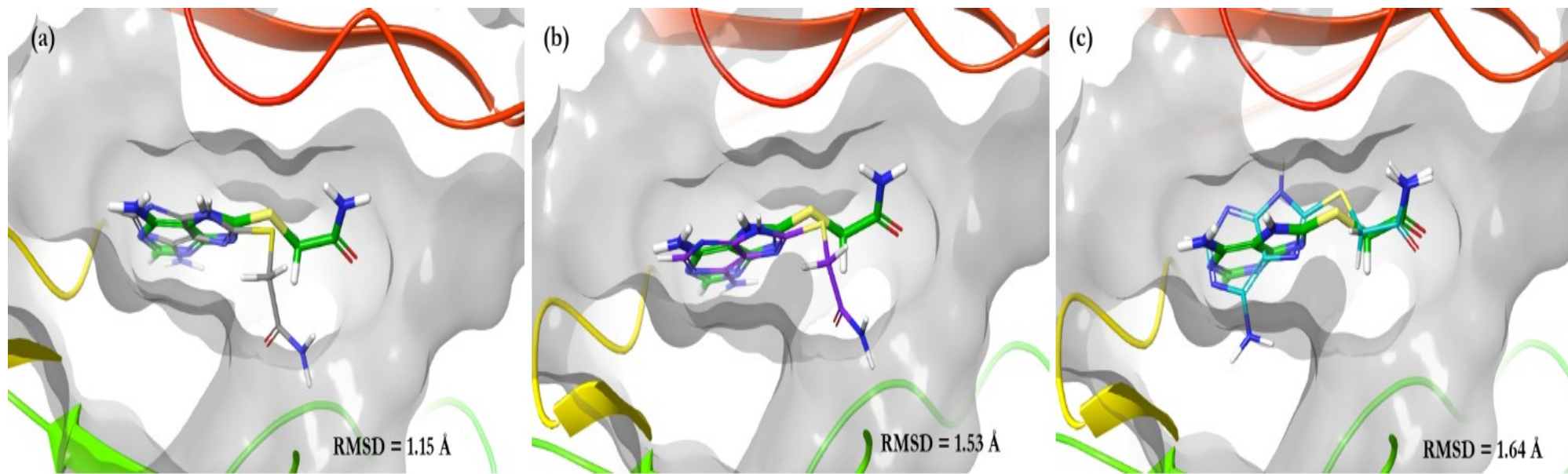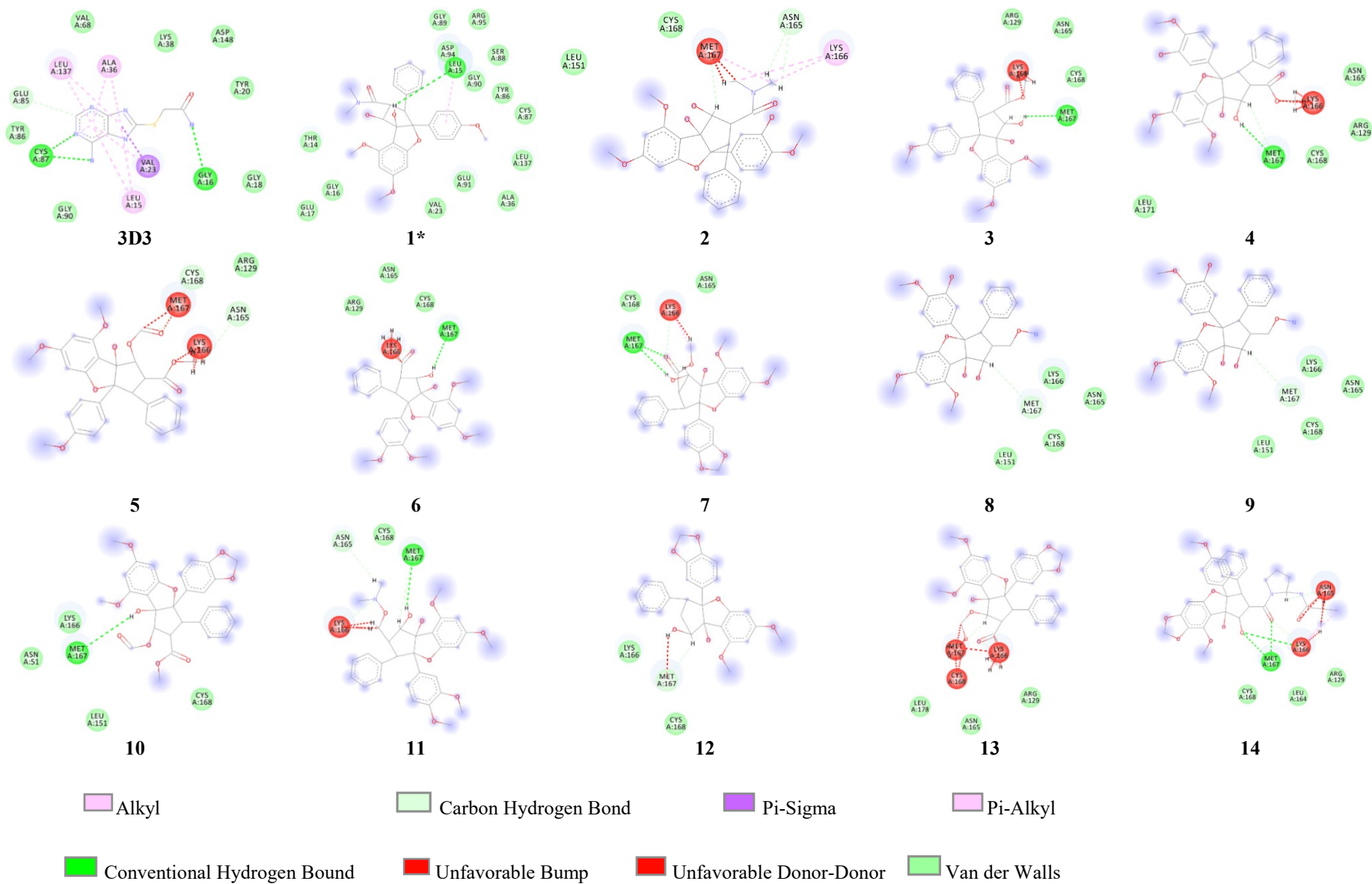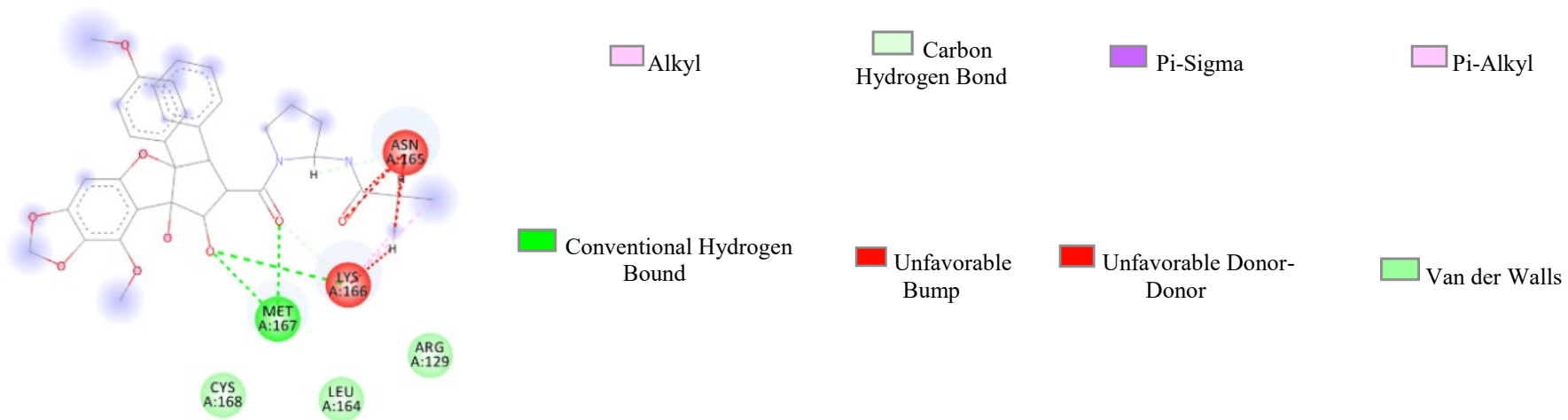
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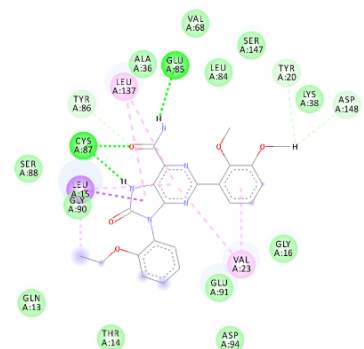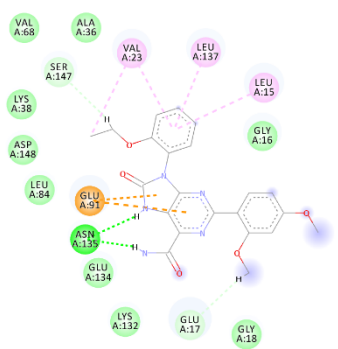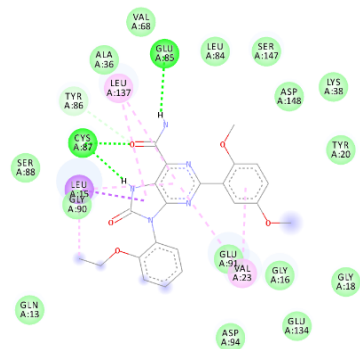
Figure S2. 2D diagram of the interactions of the 3D3 ligand and training set compounds. *: Pivot Molecule.

Alkyl

Carbon Hydrogen Bond

Pi-Sigma

Pi-Alkyl

Conventional Hydrogen Bound

Unfavorable Bump

Unfavorable Donor-Donor

Van der Walls

15

Figure S2 (*cont.*). 2D diagram of the interactions of the 3D3 ligand and training set compounds. *: Pivot Molecule

Figure S3. 2D diagram of the interactions of the promissing compounds. PC: PubChem

Compounds	Overlap		
	50ste	70ste/30elt	100ste

PC-135638768

PC-18582767

PC-53093220

PC-16803784

PC-16811025
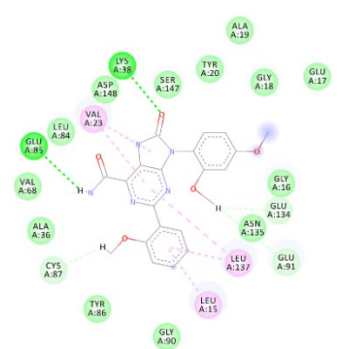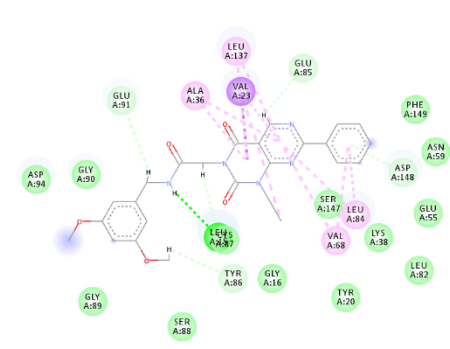
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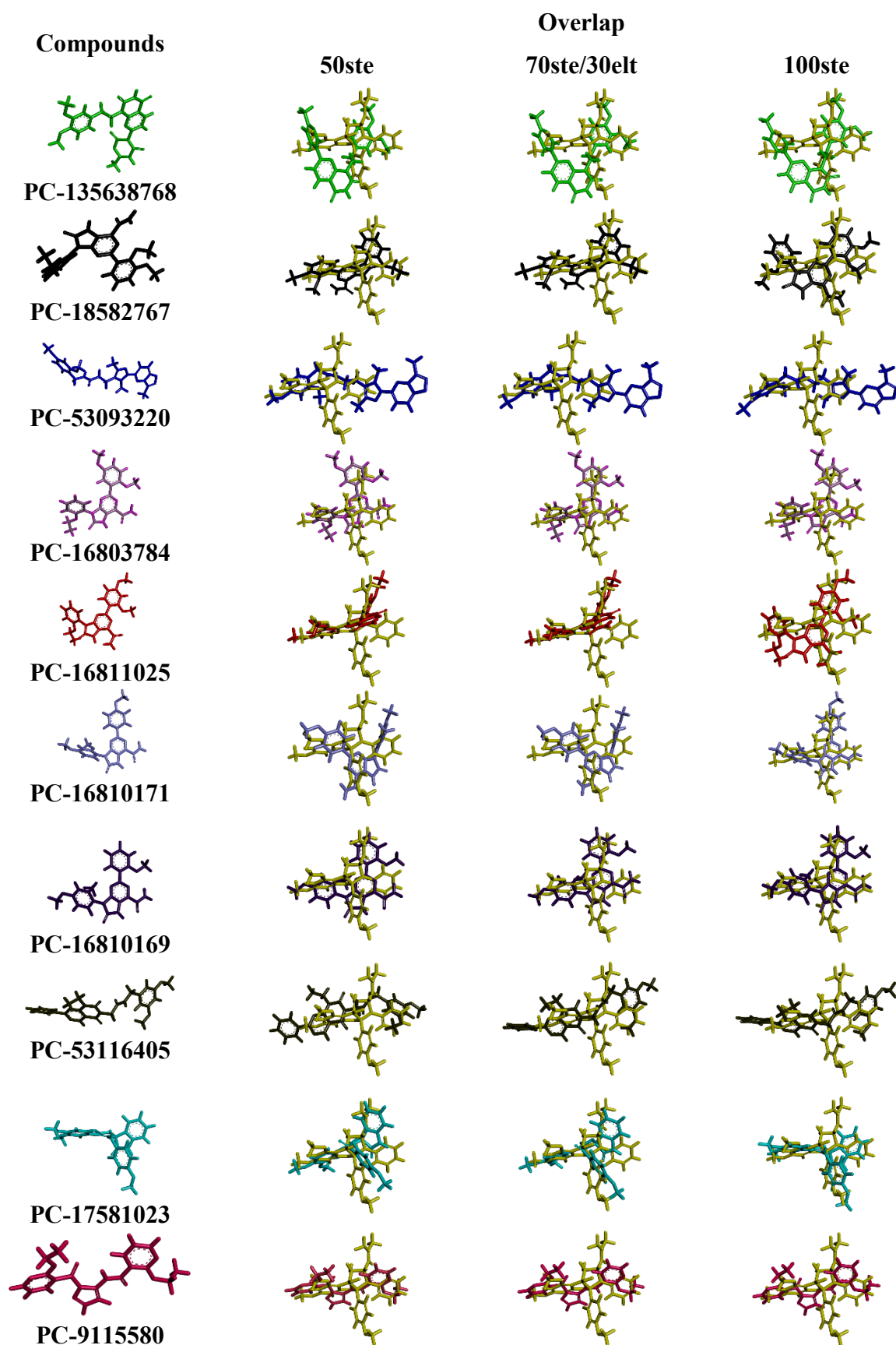
PC-16810169

PC-53116405
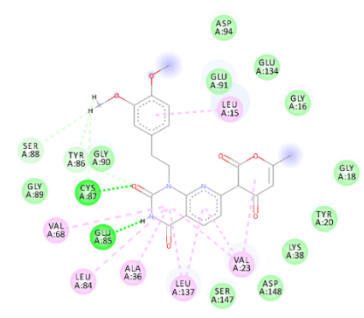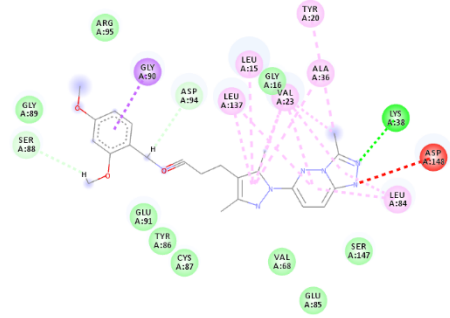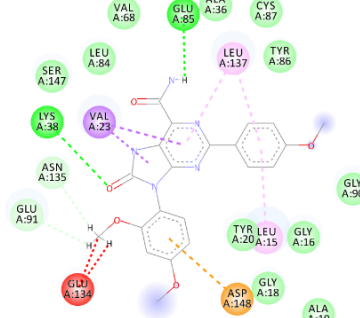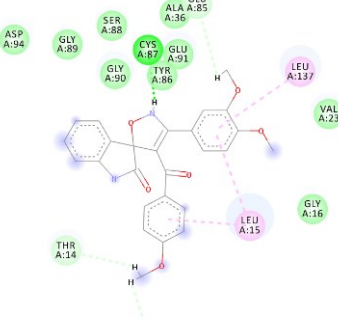
PC-17581023
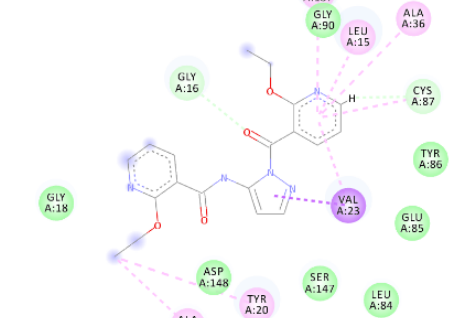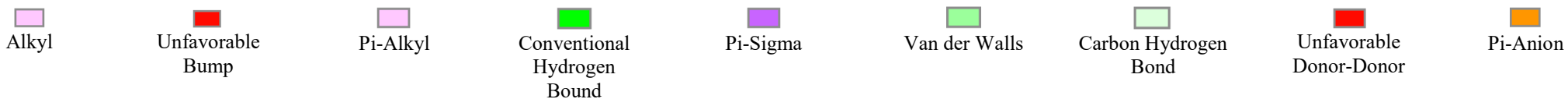
PC-9115580

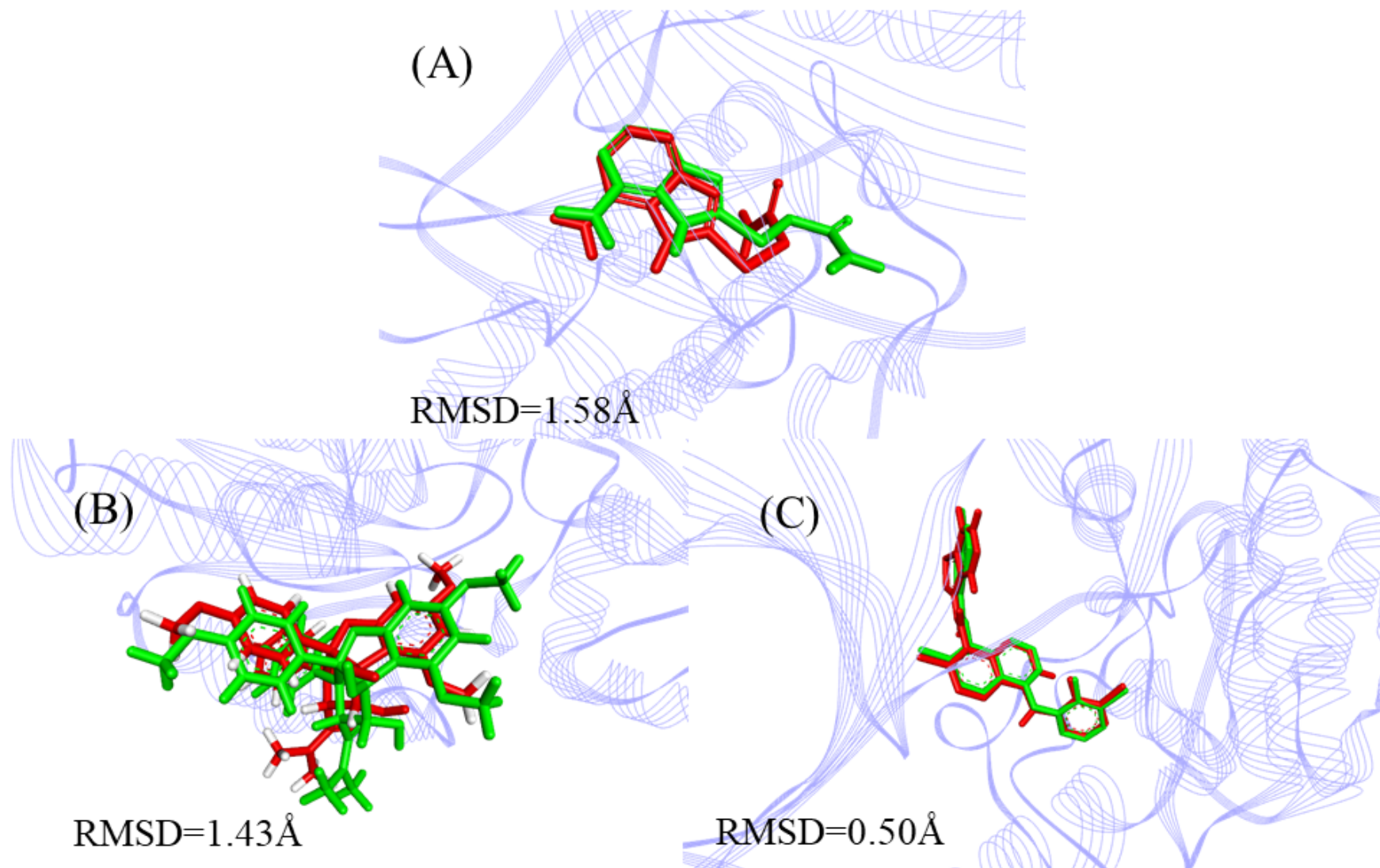**Figure S4**. Promising compounds overlap with Rocaglamide-A (yellow). PC: PubChem.

Figure S5. Overlays of the crystallographic ligand poses (in green) with the computational poses (in red): (A) 3D3 (PDB ID 2CGX), (B) RCG (PDB ID 5ZC9) and (C) V1Y (PDB ID 6XFP).
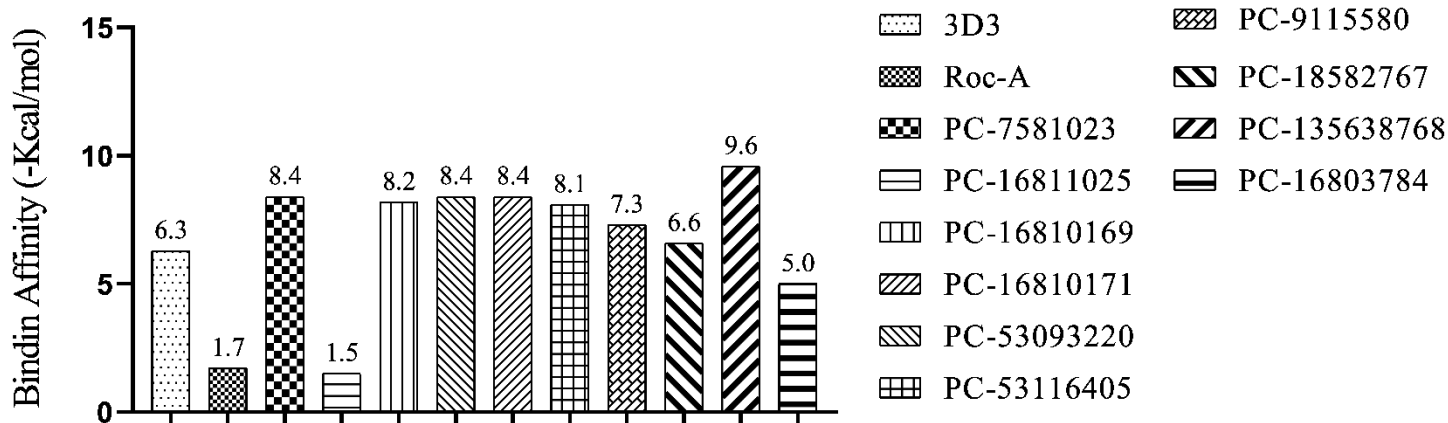
Chk1

Figure S6. Results of binding affinity of the complex (3D3), control (Roc-A) and promising compounds with Chk1 receptor (PDB ID 2CGX).
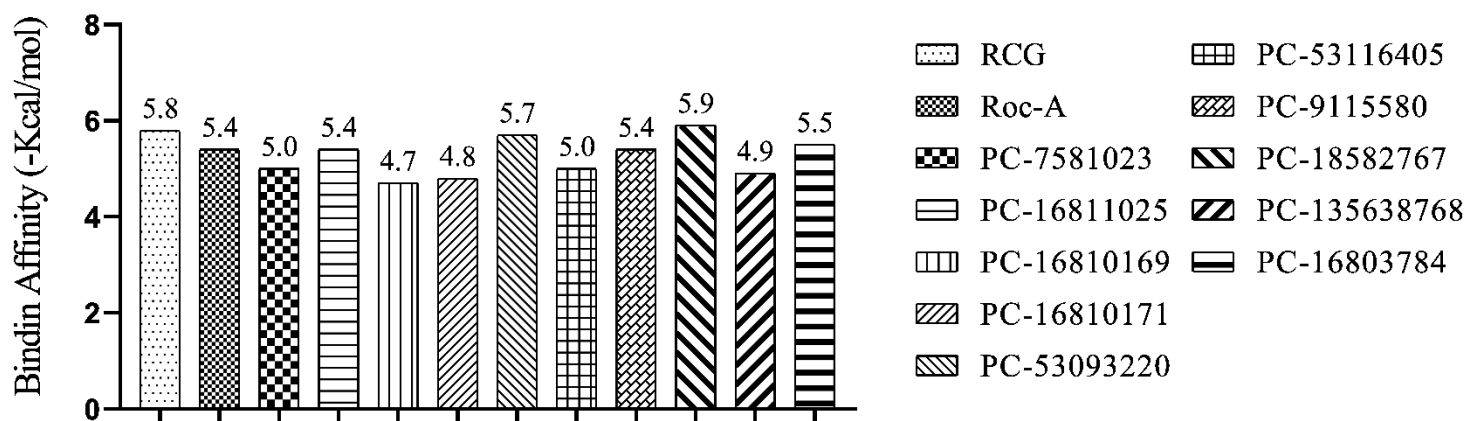
elF4A1-ATP

Figure S7. Results of binding affinity of the complex (RCG), control (Roc-A) and promising compounds with elF4A1-ATP receptor (PDB ID 5ZC9).
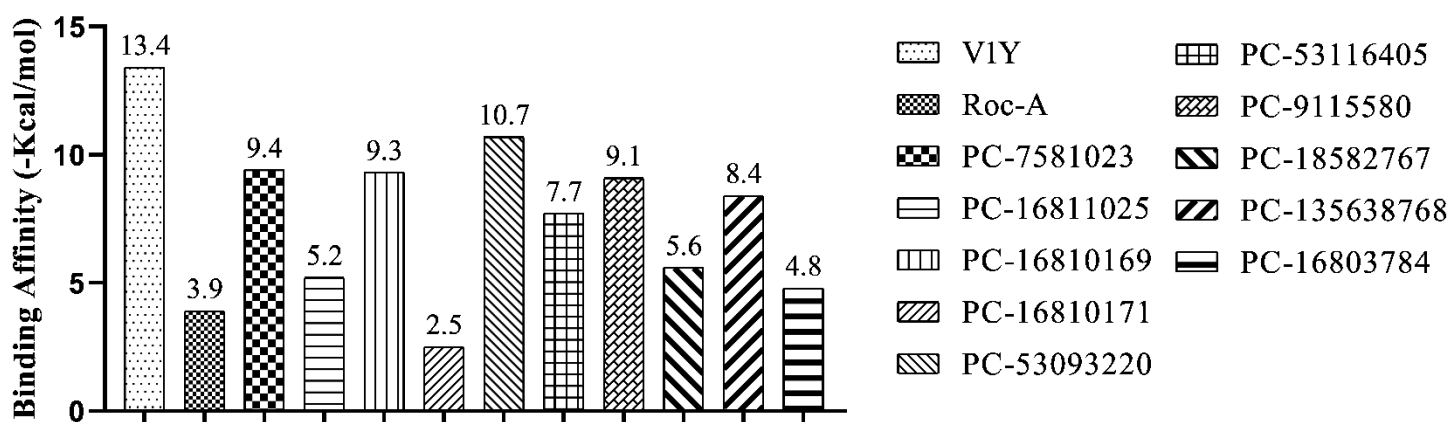
BRAF

Figure S8. Results of binding affinity of the complex (V1Y), control (Roc-A) and promising compounds with BRAF receptor (PDB ID 6XFP).
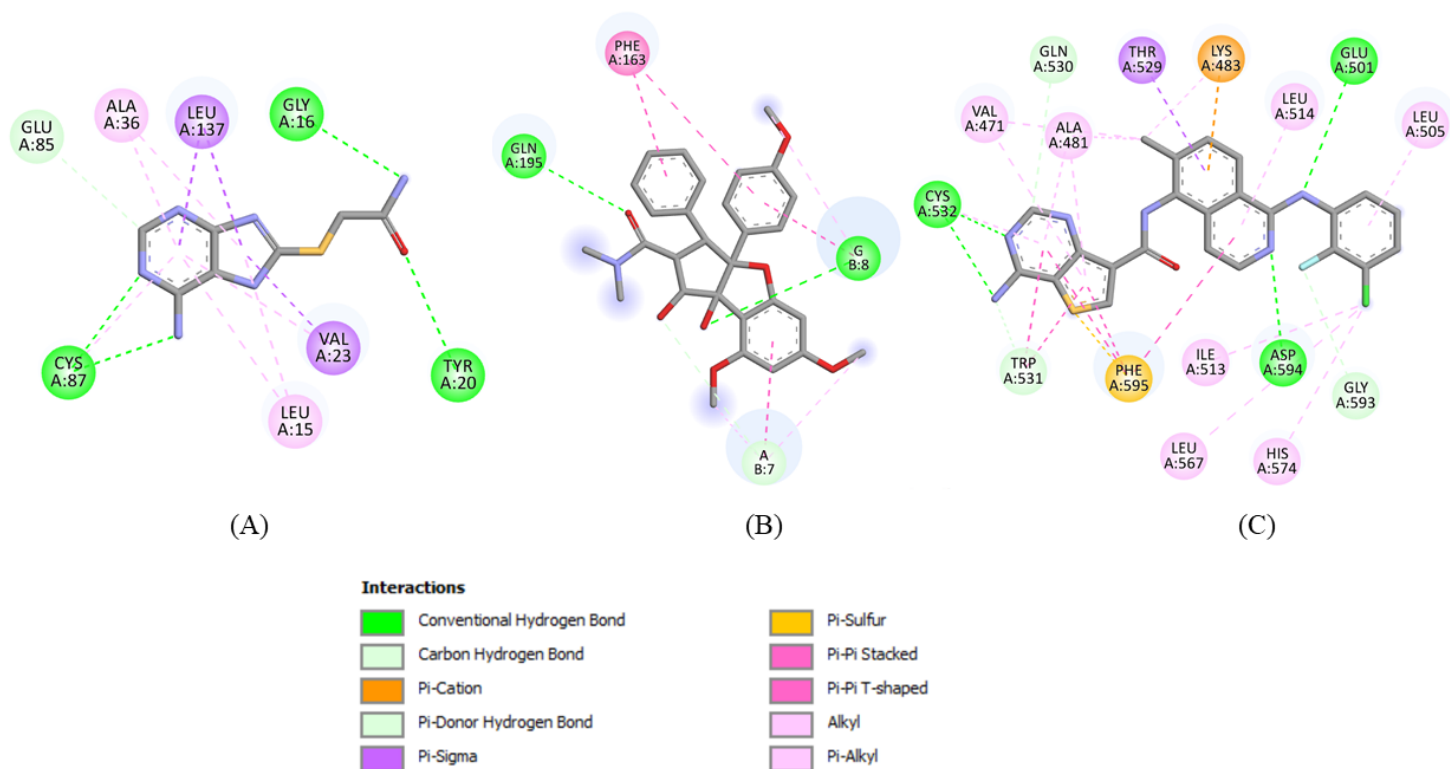
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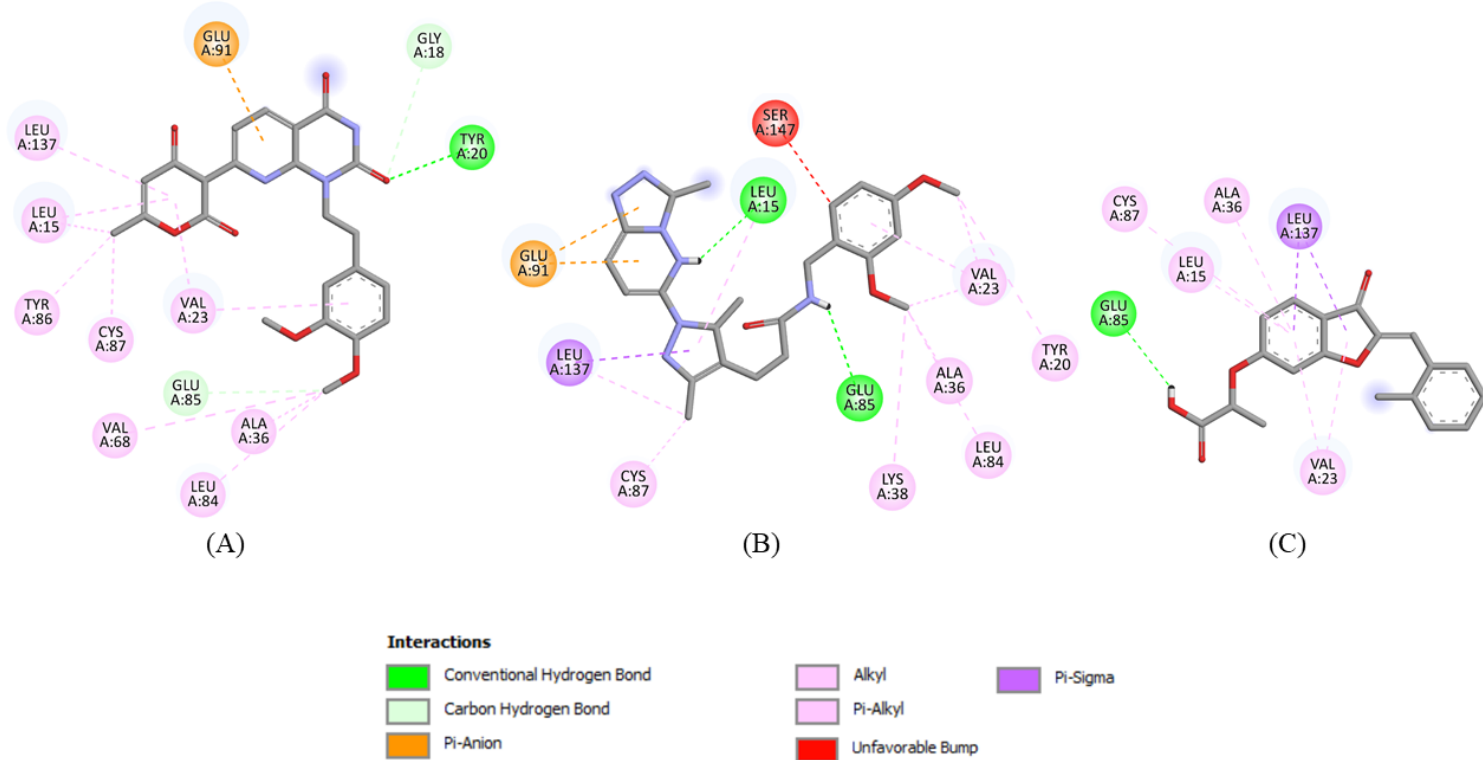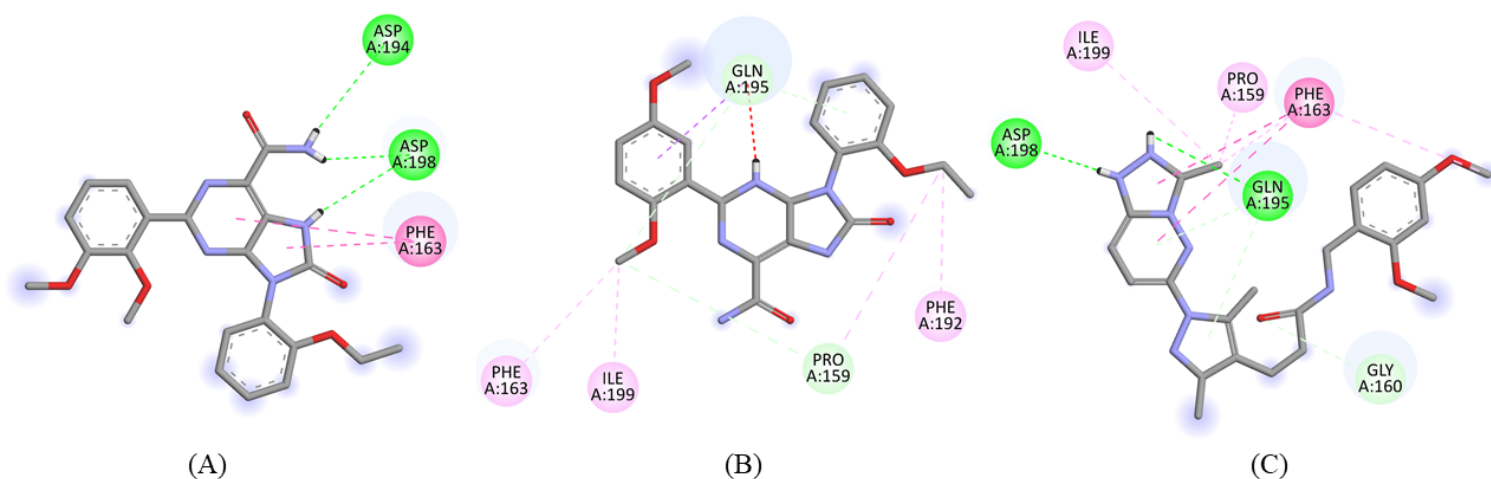

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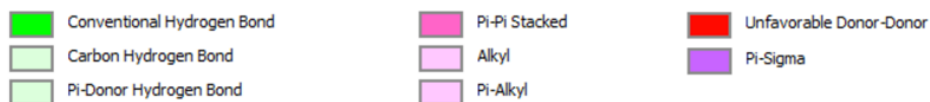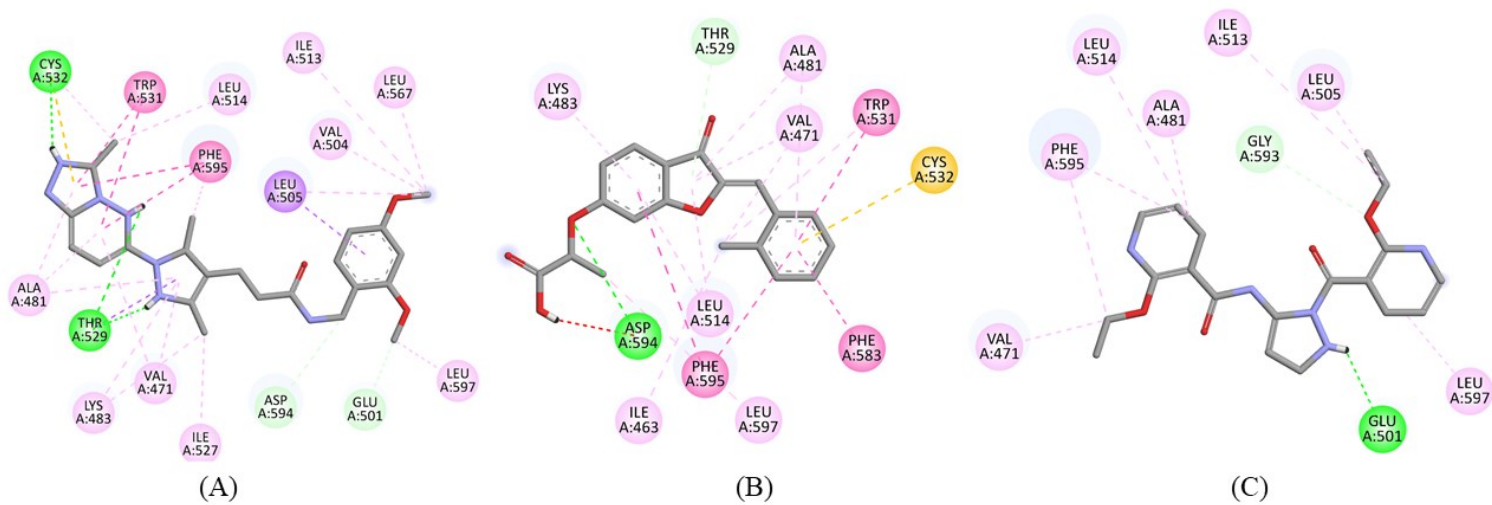
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