Electronic Supplementary Material (ESI) for RSC Advances.

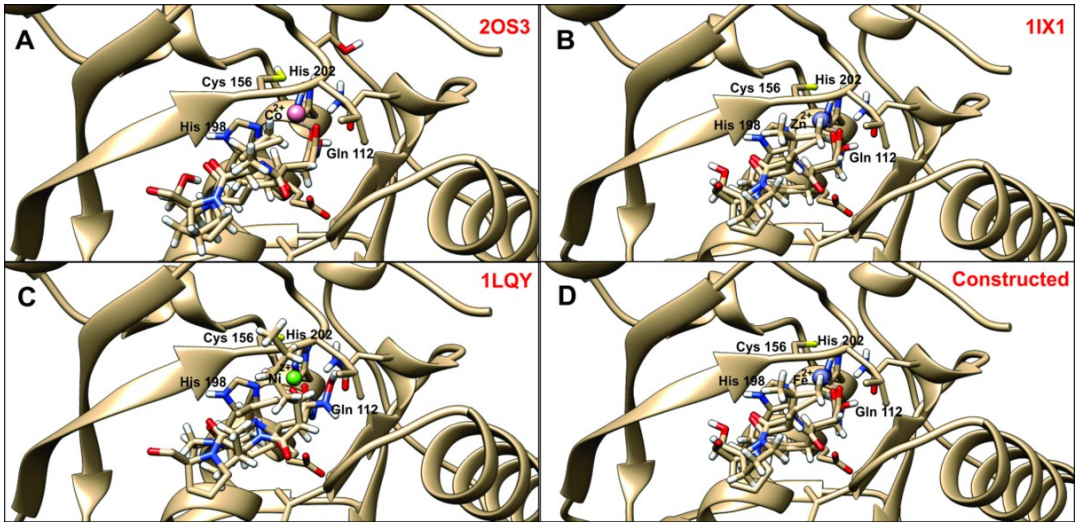
Electronic Supplementary File

Molecular Modeling of *Plasmodium falciparum* Peptide Deformylase and Structure-based Pharmacophore Screening for Inhibitors

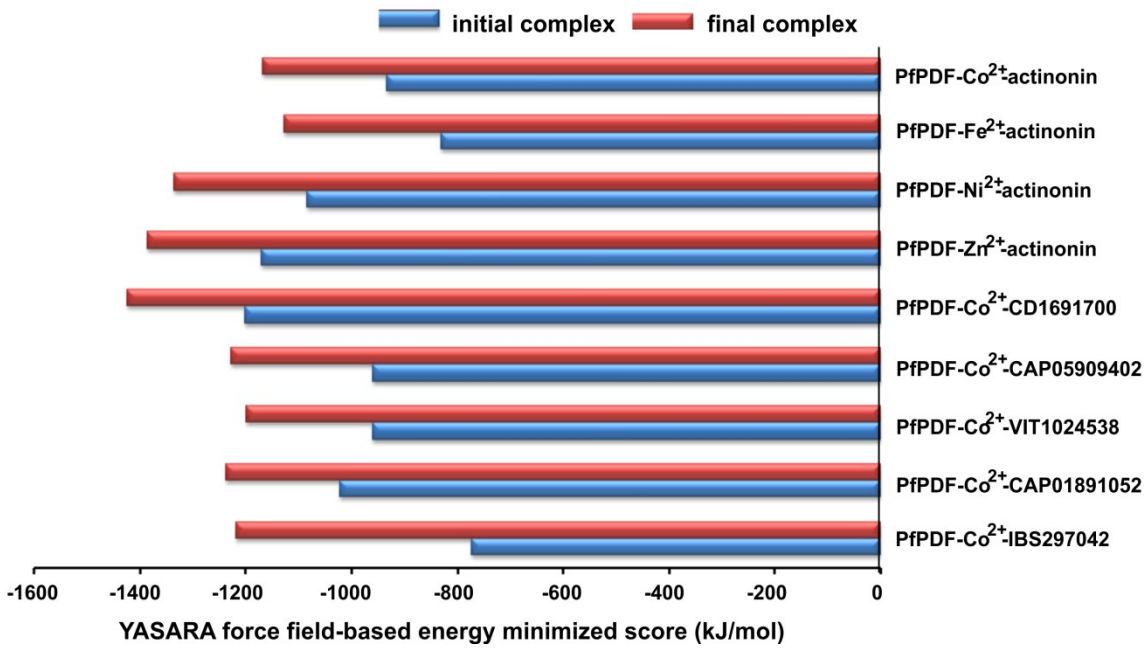
Anu Manhas, Sivakumar Prasanth Kumar and Prakash Chandra Jha*

School of Chemical Sciences, Central University of Gujarat, Gandhinagar - 382030, Gujarat, India.

*Corresponding Author, email: prakash.jha@cug.ac.in, Tel.: +91 8866823510



Supplementary Fig. 1 The comparative view of crystal (H depleted) and dock (H shown) conformations of actinonin in the PfPDF morph proteins.



Supplementary Fig. 2 The comparative view of initial and final minimized energy details of PfPDF-ligand complexes having various metal cofactors.

Supplementary Table 1 List of metal coordinating residues and its distance from selected PDF proteins.

S. No	PDB entry	Organism	Metal ion	Metal coordinating amino acids	Distance (Å)
I	1RL4	*P. falciparum*	Co^{2+}	Cys 156	2.44
				His 198	2.15
				His 202	2.04
				Gln 112	3.86
II	1IX1	*P. aeruginosa*	Zn^{2+}	Cys 92	2.35
				His 134	2.12
				His 138	2.13
				Gln 51	3.32
III	1LQY	*B. stearothermophilus*	Ni^{2+}	Cys 110	2.69
				His 153	2.13
				His 157	2.17
				Gln 65	3.06
IV	2OS3	*E. faecalis* and *S. pyogenes*	Co^{2+}	Cys 131	2.30
				His 174	2.42
				His 178	2.21
				Gln 77	3.06

Supplementary Table 2 Distance of metal coordinating residues with metal ions of PfPDF proteins.

S. No	PfPDF morph proteins[a]	Metal coordinating residues (triad)	Distance (Å)
I	Co^{2+}	Cys 156	2.39
		His202	2.47
		His198	2.66
II	Zn^{2+}	Cys 156	2.51
		His202	1.96
		His198	2.24
III	Ni^{2+}	Cys 156	2.74
		His202	2.38
		His198	2.54
IV	Fe^{2+}	Cys 156	2.51
		His202	1.96
		His198	2.24

Supplementary Table 3 The energy details of the PfPDF-ligand complexes with various metal cofactor obtained using YASARA force field-based energy minimization.

Enzyme-inhibitor complex	Initial Energy (kJ/mol)[a]	Final Energy (kJ/mol)[a]
PfPDF-Co^{2+}-actinonin	-772.45	-1216.8
PfPDF-Fe^{2+}-actinonin	-959.66	-1227.63
PfPDF-Ni^{2+}-actinonin	-960.23	-1198.19
PfPDF-Zn^{2+}-actinonin	-1020.47	-1237.63
PfPDF-Co^{2+}-CD1691700	-1200.55	-1423.15
PfPDF-Co^{2+}-CAP05909402	-1170.66	-1384.14
PfPDF-Co^{2+}-VIT1024538	-1083.44	-1335.53
PfPDF-Co^{2+}-CAP01891052	-829.83	-1127.71
PfPDF-Co^{2+}-IBS297042	-933.25	-1167.35

[a]Computed using YASARA force field

Supplementary Table 4 The spatial coordinates and orientation details of pharmacophore features in the selected model.

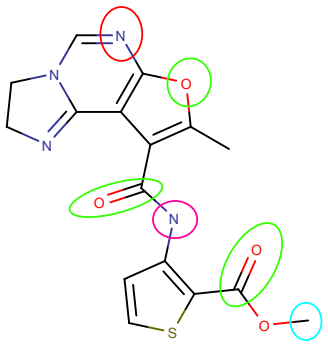
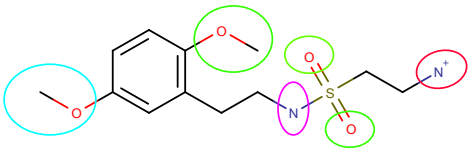
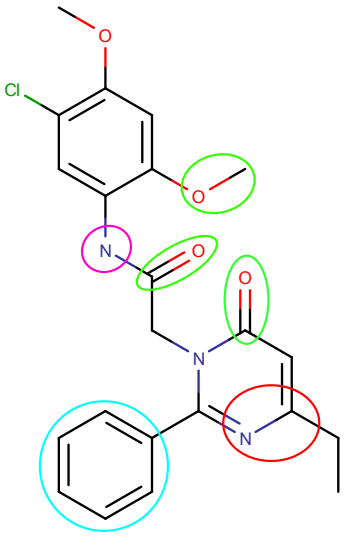
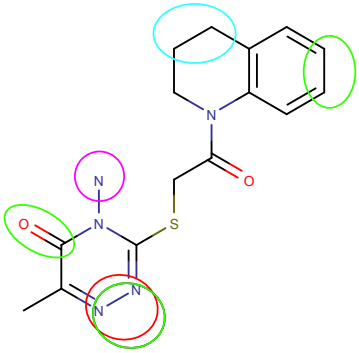
S. No	Features	Coordinates (x, y, z)	Type	Orientation
I	HBA1	-5.621, 40.93, 2.428	HBA	Projection
II	HBA3	-9.136, 32.615, 0.738	HBA	Projection
III	HBA5	-10.815, 38.879, -5.36	HBA	Projection
IV	HBD7	-9.061, 39.173, -3.787	HBD	Projection
V	HY8	-6.92, 33.74, -6.16	Hydrophobe	Point
VI	PI10	-5.083, 37.641, -0.013	Ionisable-Positive	Projection

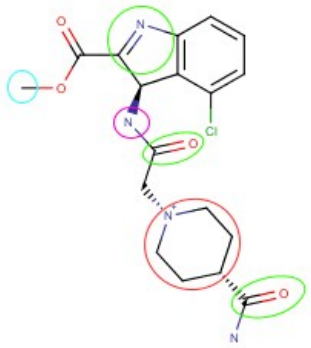
Supplementary Table 5 List of validation molecules with experimental activity and fit values.

Compound No./ Identifiers[a]	pIC_{50}	Fit value
Experimental validation set		
35	8.7	2.59768
15	9	2.55728
25	8.1	2.55343
11	8.15	2.42069
39[b]	7.68	1.88615
3	8.04	1.64671
10	7.8	1.58481
9	7.89	1.01207
37[b]	7.77	0.923234
23	8.1	0.852796
8	7.8	0.776071
7	7.89	0.430411
13	8.7	0.305794
14	8.7	0.305794
Randomized inactive set[c]		
ChEMBL25105	-	1.22491
ChEMBL30044	-	0.674728
ChEMBL55	-	0.427947

[a]Compounds were numbered according to Gao *et al*., 2012; molecules tested against *E. coli* PDF; molecules which secured fit values are only shown here.
[b]False positives from experimental set; $pIC_{50} < 7.8$ are regarded as experimental inactives
[c]False positives from randomized set

Supplementary Table 6 The 2D pharmacophore map projected above hit molecular structures.

S. No	Hits	Feature mapping on molecules 2D structure[a]
I	CD1691700	
II	CAP05909402	
III	VIT1024538	
IV	CAP01891052	

V	IBS297042	

[a]The pharmacophore features are mapped by encircling the corresponding functional groups, HBA – Green, HBA – Pink, HY – Blue and PI – Red.