Comprehensive Screening of Marine Metabolites against Class B1 Metallo-β-Lactamases of *Klebsiella pneumoniae* Using Two-pronged *in silico* Approach

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SUPPLEMENTARY INFORMATION

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Table 1S: List of FDA-approved Drugs used in this study

S.No.	PubChem ID	Compound name
1	5742832	Azactam
2	9835049	Avibactam
3	77843966	Cefiderocol
4	54686904	Tigecycline
5	54726192	Eravacycline
6	123630	Tazobactam
7	44129647	Relebactam
8	5481173	Ceftazidime
9	5479537	Cefepime
10	76902493	Taniborbactam
11	77846445	Zidebactam
12	23653540	Enmetazobactam
13	130313	Sulbactam
14	89851852	Durlobactam
15	6335986	Cefpodoxime
16	129735677	Diazabicyclooctanone

S.No.	PubChem ID	Compound name
17	104838	Imipenem
18	6435415	Cilastatin
19	56649692	Vaborbactam
20	56843746	Ceftolozane
21	5282242	Cefibuten
22	5280980	Clavulanic acid
23	71339	Biapenem
24	5362065	Cefixime
25	9852981	Ceftaroline
26	73303	Doripenem
27	150610	Ertapenem
28	216262	Lenapenem
29	72015	Panipenem
30	10993211	Razupenem
31	9800194	Tebipenem
32	9809656	Tomopenem

Table 2S: List of PDB IDs of the structures with co-crystallized ligands

PDB IDs STRUCTURES WITH CO-CRYSTALLIZED LIGANDS									
1A63	2QDT	4PVO	5FQA	5N4T	5YPL	6F2N	6LJ2	6TMS	7A5Z
1A7T	2WHG	4RAM	5HH4	5N55	5ZGE	6HF5	6LJ5	6TT8	7AYJ
1DD6	2WRS	4RL0	5JMX	5N58	5ZH1	6IBS	6MDU	6TTA	7CHV
1HLK	2YZ3	4RL2	5K48	5N5G	5ZJ1	6IBV	6NY7	6U0Z	7CJL
1JJE	3IOF	4TYT	5LCA	5NDB	5ZJ8	6J8R	6O3R	6U2Z	
1JJT	3IOG	4U4I	5LCF	5NHZ	6D1B	6JN6	6O5T	6V1M	
1VGN	3VQZ	5ACW	5LCH	5NIO	6D1C	6K4T	6OGO	6V1P	
1X8I	3WXC	5ACX	5LE1	5O2E	6D1D	6K4X	6R73	6V3Q	
2AIO	4C1C	5AZ5Z	5LM6	5W8W	6D1G	6KW1	6R78	6TMB	
2DOO	4C1D	5B15	5M5D	5WCM	6DD0	6KXO	6RPN	6V5M	
2FU7	4C1H	5DPX	5MM9	5XP6	6DLA	6KZL	6RZR	6V72	
2GFJ	4EYL	5EV8	5MXQ	5XP9	6DR8	6LIP	6S0H	6Y6J	
2GFK	4F6Z	5EVB	5MXR	5Y5B	6EFJ	6LIZ	6TGI	6YRP	
2HB9	4HL2	5EWA	5N0H	5Y6D	6EUM	6LJ0	6TM9	6ZGM	
2N2E	4NQ5	5FGB	5N4S	5Y6E	6EWE	6LJ1	6TMB	6ZYN	

Table 3S: List of the Protein-ligand complexes used in Molecular dynamics simulations

S.No	Protein-Ligand Complexes
High Throughput Virtual Screening Approach	
1	NDM-1 with *N*-Methyl mycosporine Ser
2	VIM-2 with Anguibactin
3	IMP-1 with Sydowiol B
Pharmacophore-based Screening Approach	
4	NDM-1 with Makaluvic Acid B
5	VIM-2 with Makaluvic acid B
6	IMP-1 with Makaluvic acid C

Table S4: Docking score of top-scoring FDA-approved drugs against NDM-1, VIM-2 & IMP-1

PDB ID: 4EXS (NDM-1)			
S.No	PubChem ID	Compound name	Glide gscore (kcal/mol)
1	150610	Ertapenem	−9.407
2	56843746	Ceftolozane	−8.973
3	71339	Biapenem	−8.587
4	9809656	Tomopenem	−8.351
5	5481173	Ceftazidime	−8.152
PDB ID: 5O7N (VIM-2)			
1	9809656	Tomopenem	−12.737
2	216262	Lenapenem	−12.319
3	76902493	Tanibor bactam	−11.109
4	104838	Imipenem	−11.104
5	72015	Panipenem	−10.120
PDB ID: 6C6I (IMP-1)			
1	216262	Lenapenem	−10.075
2	104838	Imipenem	−9.953
3	9809656	Tomopenem	−9.177
4	76902493	Taniborbactam	−8.533
5	9852981	Ceftaroline	−8.461

Table S5: IC50 values for the co-crystallized ligands used as actives for validation of the hits

Ligand	PDB ID	IC50(nM)		Ligand	PDB ID	IC50(nM)
BYS	1JJE	3.7		JTY	5MXR	6.20E+03
BDS	1JJT	9		H32	5LM6	7700
8P0	5Y6E	13.7		DZ5	5JMX	8200
R38	5N4S	55		6UW	5LE1	1.06E+04
CF8	6F2N	200		WL3	5ACX	1.40E+04
OK3	5FQB	300		L13	2HB9	1.50E+04
BY5	6EUM	300		6TJ	5LCF	1.78E+04
8SH	5MM9	3.80E+02		6TU	5LCH	2.03E+04
BEZ	5N4T	1.06E+03		X8Z	4C1H	2.58E+04
R59	5N4T	1.06E+03		VII	2GFK	3.00E+04
8XW	5NI0	1.80E+03		B06	5LCA	3.28E+04
C0W	6EWE	3100		VI	2GFJ	1.50E+05
8XZ	5NHZ	4.70E+03		8SH	5MM9	3.80E+02

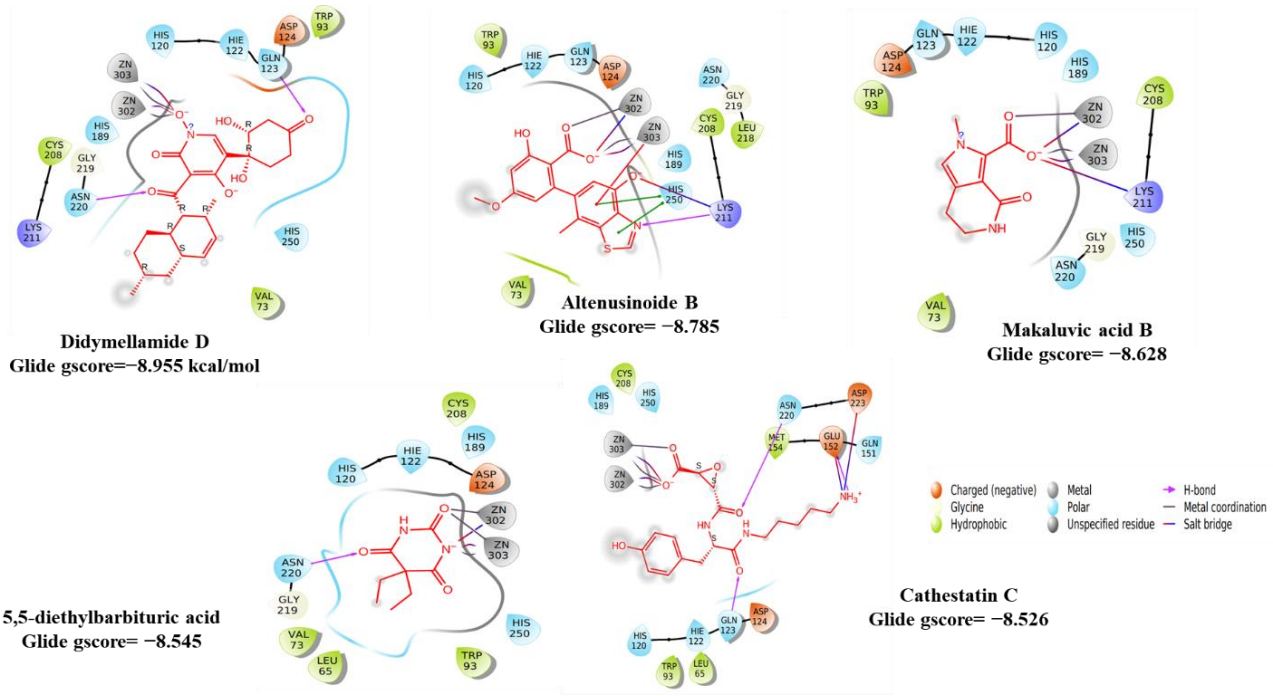

Figure 1S: Ligand interaction Diagram for top-scoring ligands from CMNPD docked with NDM-1 based on pharmacophore-based feature generated from co-crystallized ligands

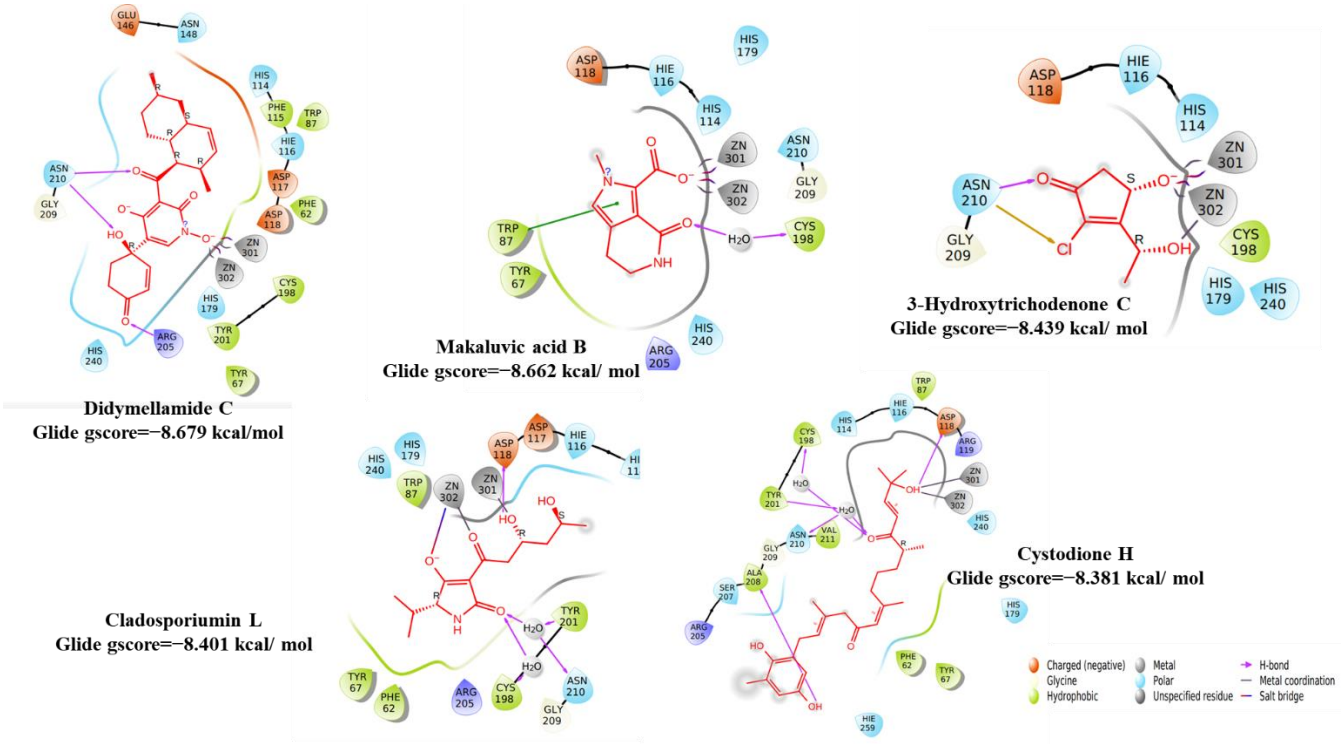

Figure 2S: Ligand interaction Diagram for top-scoring ligands from CMNPD docked with VIM-2 based on pharmacophore-based feature generated with co-crystallized ligands

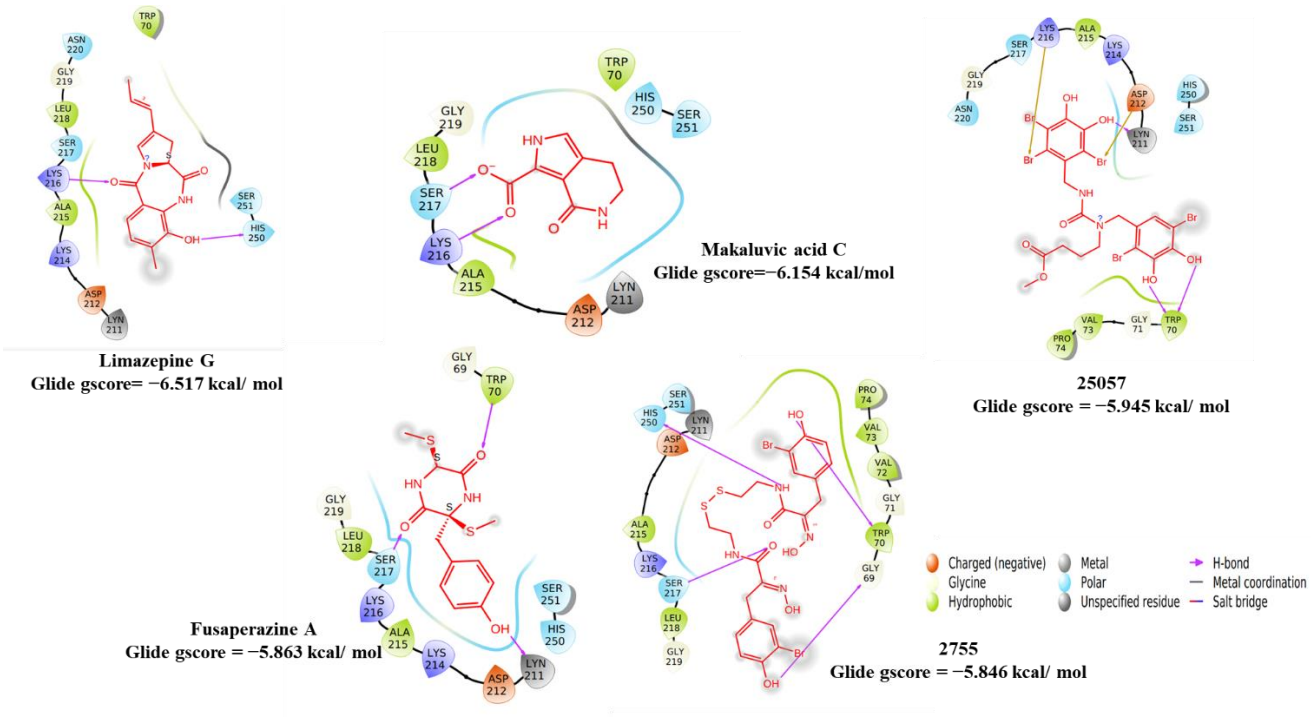

Figure S3: Ligand interaction Diagram for top-scoring ligands from CMNPD docked with IMP-1 based on pharmacophore-based feature generated from co-crystallized ligands

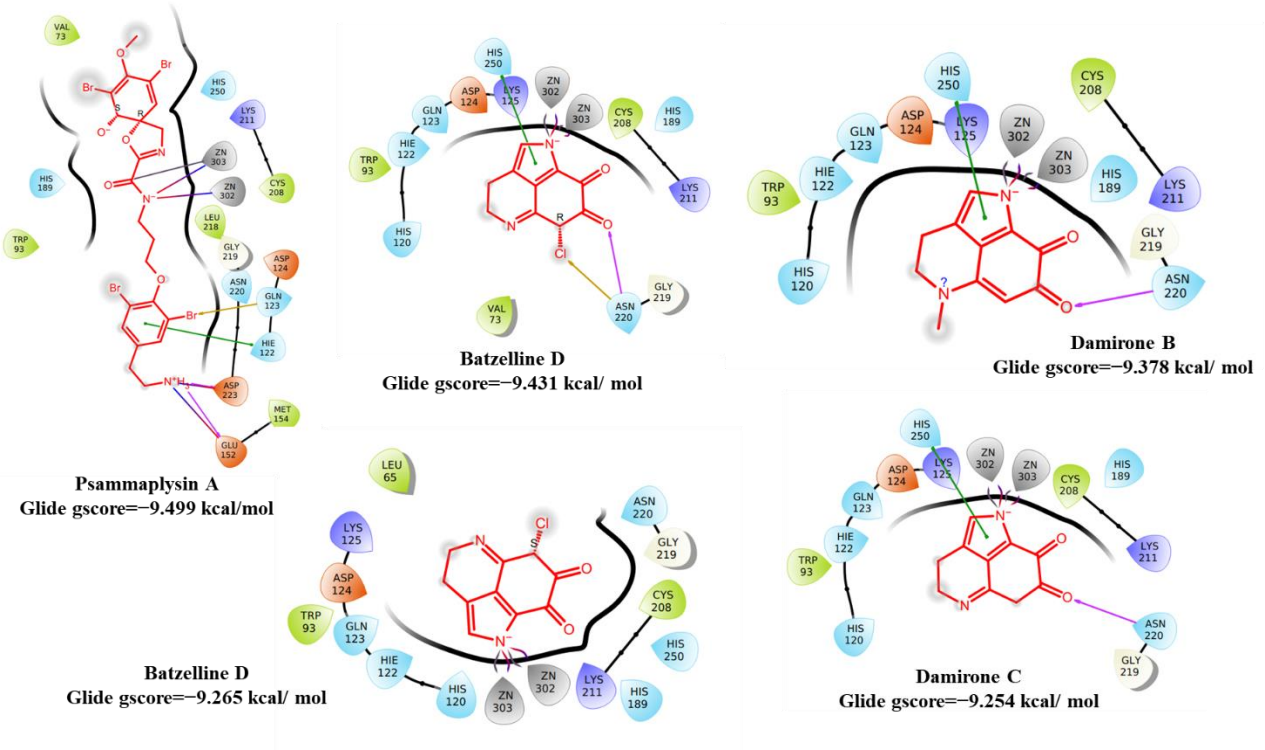

Figure S4: Ligand interaction Diagram for top-scoring ligands from CMNPD docked with NDM-1 based on pharmacophore-based feature generated from FDA-approved drugs

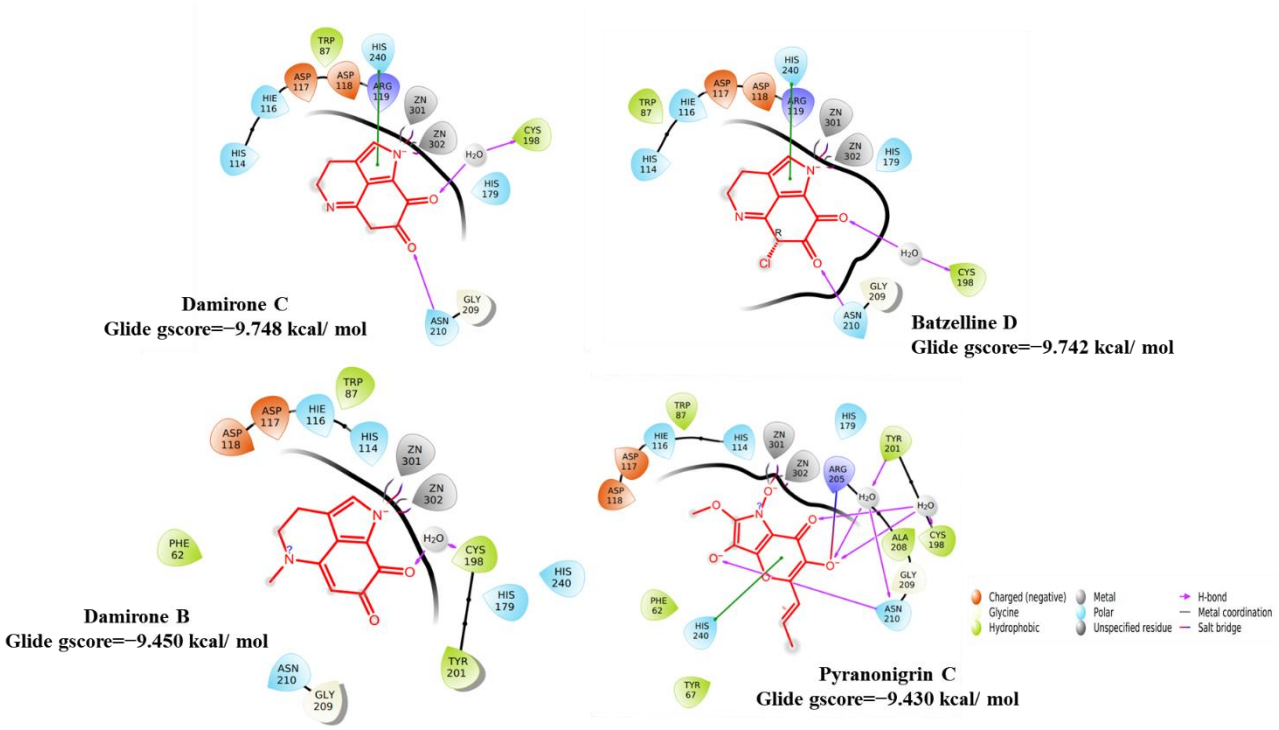

Figure S5: Ligand interaction Diagram for top-scoring ligands from CMNPD docked with VIM-2 based on pharmacophore-based feature generated from FDA-approved drugs

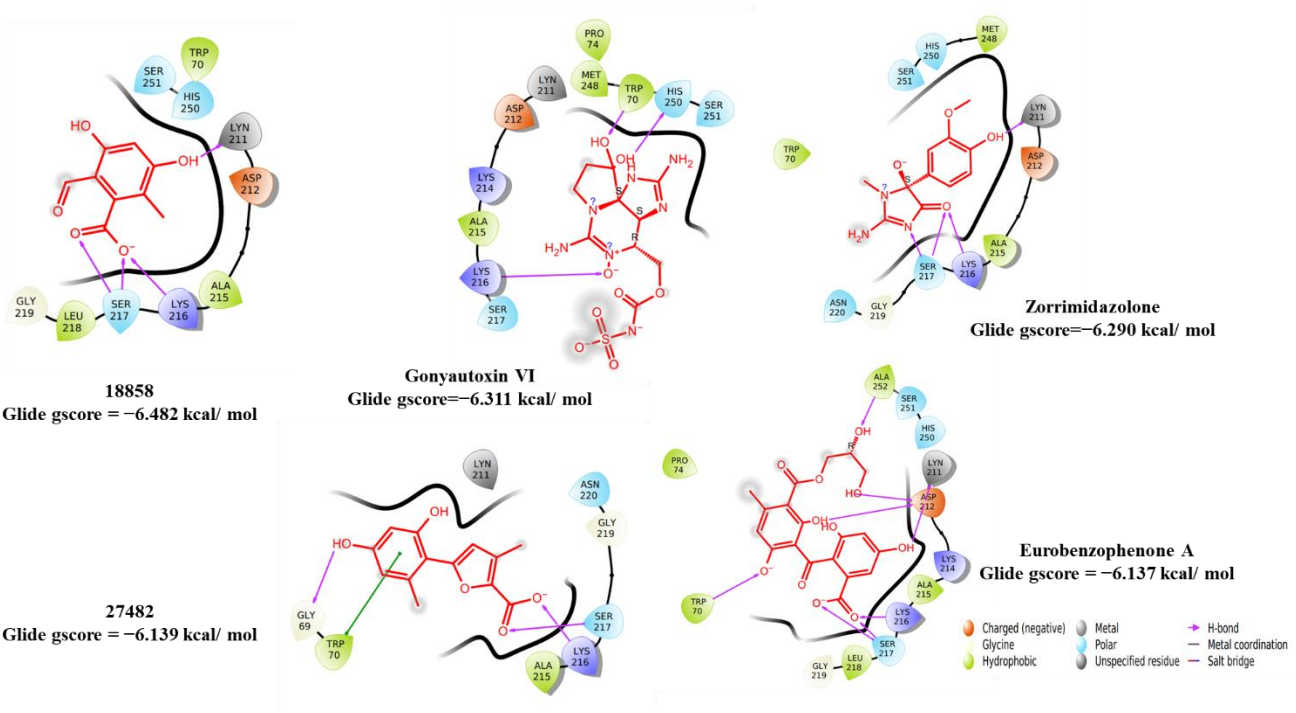

Figure S6: Ligand interaction Diagram for top-scoring ligands from CMNPD docked with IMP-1 based on pharmacophore-based feature generated from FDA-approved drugs

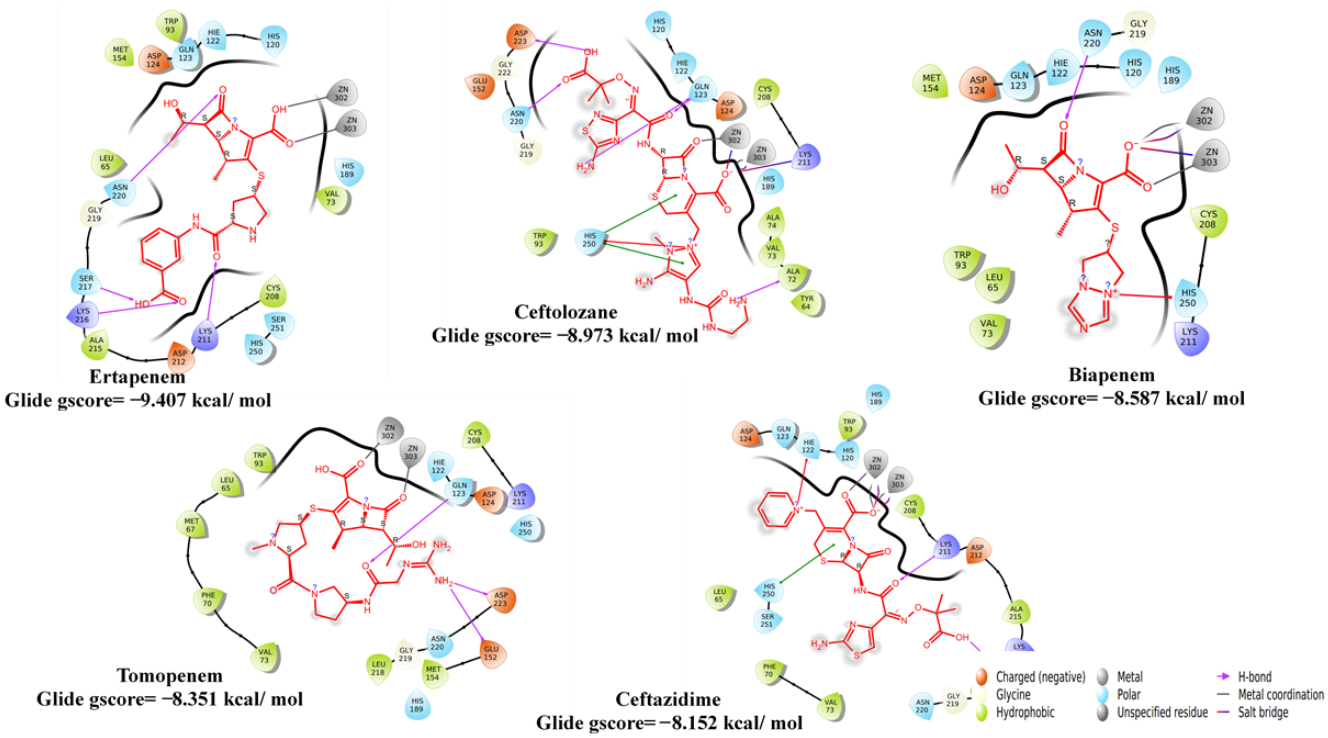

Figure S7: Ligand interaction Diagram of FDA-approved drugs with NDM-1

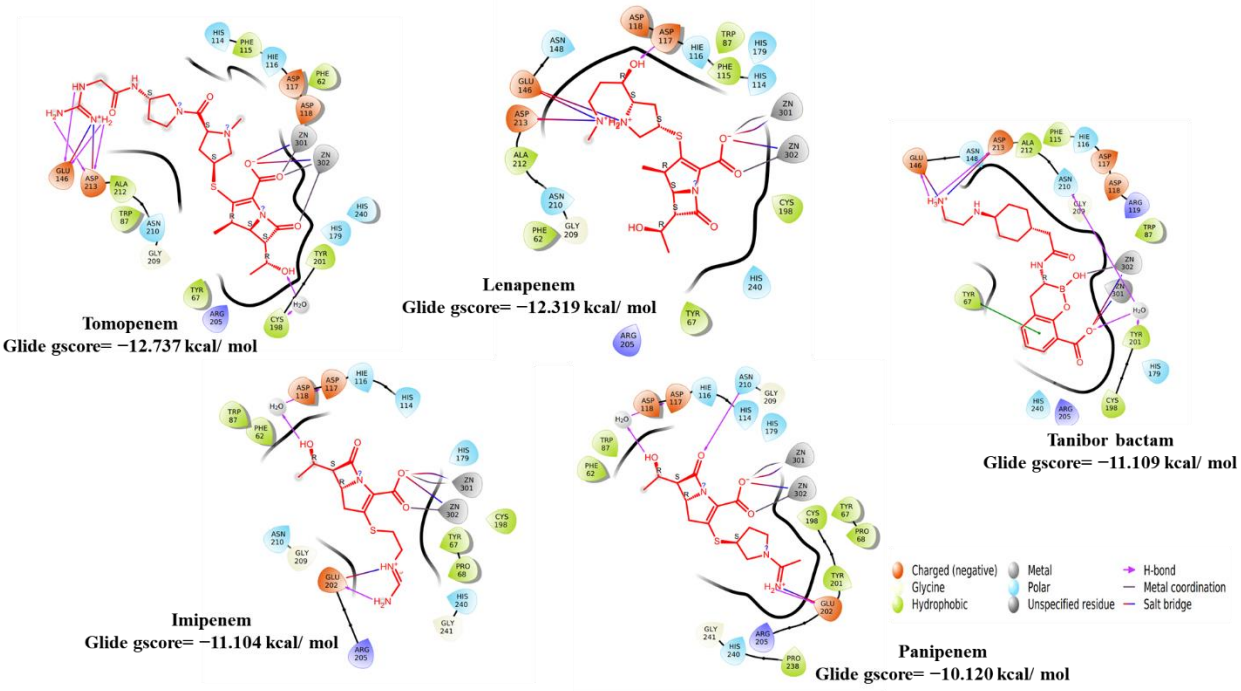

Figure S8: Ligand interaction Diagram of FDA-approved drugs with VIM-2

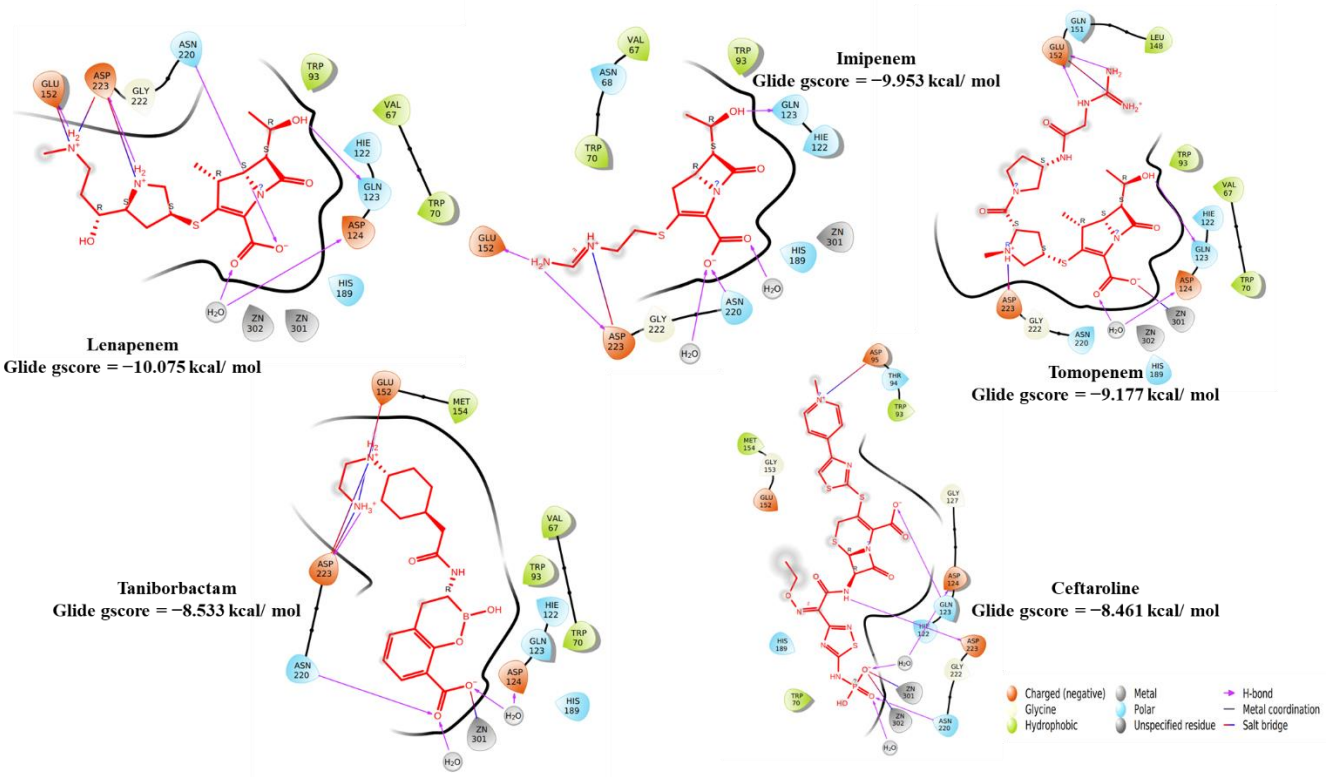

Figure S9: Ligand interaction Diagram of FDA-approved drugs with IMP-1

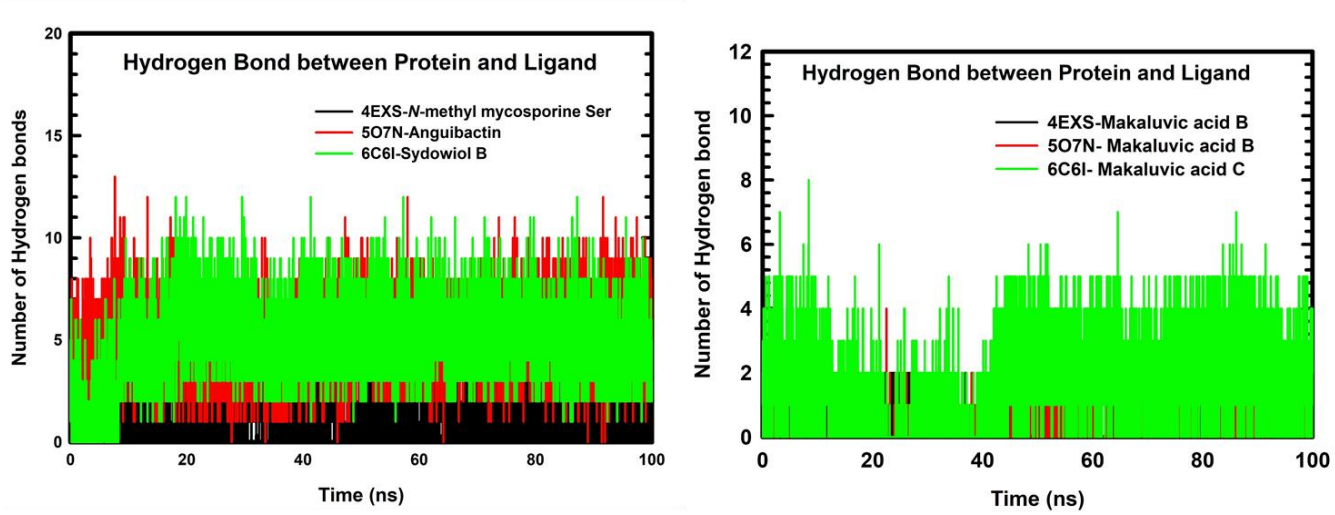

Figure S10: Number of hydrogen bond formed between protein and ligand throughout the simulation at the maximum distance of 2.8Å and the minimum donor angle of 120°