Targeting *Pseudomonas aeruginosa* MvfR in the battle against biofilm formation: A multi-level computational approach

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Supporting Information

Table S1. RMSD of the re-docking for the other targets and their respective crystallographic ligand.

		Redocking RMSD (Å)						
PDB Code	Ligand	Vina	LeDock	CHEMPLP	GoldScore	ChemScore	ASP	Average per target
4JVD	NNQ	6.67	3.51	2.16	3.20	1.18	2.68	3.23
4JVI	QZN	1.59	3.07	1.33	2.93	3.18	1.85	2.33
6B8A	M64	0.34	0.58	0.46	0.63	3.48	1.92	1.24
6Q7U	HLH	7.26	5.80	3.71	3.14	2.64	2.11	4.11
6Q7V	HLK	5.77	6.16	3.49	5.73	3.76	1.77	4.98
6Q7W	HLQ	3.54	4.50	1.99	5.15	3.17	1.71	3.34
6TPR	NV5	9.15	5.23	1.54	1.16	4.59	1.35	3.84
6Z07	Q4E	1.22	1.41	0.92	0.87	1.31	1.32	1.18
6Z17	Q4W	1.18	7.25	1.59	4.08	2.32	1.96	3.06
6Z5K	QAE	1.43	4.46	1.17	8.13	3.95	1.60	3.46
6YZ3	Q25	1.11	7.67	1.25	0.99	3.46	1.56	2.67
Average by SF		3.57	4.51	1.78	3.27	3.00	1.81	

Table S2. Average protein RMSD values (Å), average ligand RMSD (Å), Average MvfR-ligand complex SASA (Å^2), Percentage of SASA for the buried ligand, average number of ligand hydrogen bonds obtained from the MD simulations of MvfR-ligand complexes. ΔG binding energy determined using MM/GBSA and per-residue decomposition, calculated for the last 90 ns of the simulation for all the replicas.

	Average RMSd (Å)	Ligand RMSD (Å)	SASA (Å^2)	SASA (%)	average H bonds	ΔGbind (kcal/mol)	Main Contributors (kcal/mol)
CMLDID2589	2.3 ± 0.2	1.5 ± 0.6	118.9 ± 38.6	83.4 ± 0.1	0.5 ± 0.6	-49.4 ± 0.2	ILE236 (-3.7 ± 0.5), Tyr258 (-2.4 ± 0.8), Leu208 (-2.3 ± 0.5)
	2.1 ± 0.2	1.4 ± 0.2	114.4 ± 29.4	84.3 ± 0.04	0.4 ± 0.5	-48.3 ± 0.2	ILE236 (-3.7 ± 0.5); TYR258 (-2.7 ± 0.6); ILE186 (-2.4 ± 0.5)
	2.3 ± 0.2	1.5 ± 0.3	99.4 ± 28.7	86.2 ± 0.04	0.2 ± 0.4	-47.8 ± 0.2	ILE236 (-3.5 ± 0.5); TYR258 (-2.5 ± 0.6); ILE186(-2.0 ± 0.6)
CMLDID25998	2.1 ± 0.2	1.6 ± 0.3	119.2 ± 23.0	82.6 ± 0.03	0.6 ± 0.6	-47.0 ± 0.2	ILE186 (-2.1 ± 0.4), Val211 (-2.0 ± 0.5), LEU208 (-1.8 ± 0.5)
	2.2 ± 0.2	1.7 ± 0.3	136.1 ± 27.3	80.1 ± 0.04	0.6 ± 0.6	-46.6 ± 0.2	ILE236 (-3.4 ± 0.5); ILE186 (-2.2 ± 0.4); LEU208 (-1.9 ± 0.5)
	2.1 ± 0.2	2.1 ± 0.3	166.7 ± 30.9	75.4 ± 0.1	0.7 ± 0.7	-42.5 ± 0.2	ILE236 (-3.8 ± 0.5); ILE186 (-2.1 ± 0.6); LEU208 (-2.0 ± 0.5)
AB-00022705	2.0 ± 0.2	1.1 ± 0.3	65.0 ± 18.5	90.5 ± 0.03	0.1 ± 0.1	-46.0 ± 0.1	ILE236 (-3.7 ± 0.4); ILE186 (-2.0 ± 0.5); LEU208 (-1.9 ± 0.5)
	2.0 ± 0.2	0.9 ± 0.3	67.5 ± 20.3	90.1 ± 0.03	0.1 ± 0.3	-47.7 ± 0.2	ILE236 (-3.6 ± 0.5); ILE186 (-2.1 ± 0.5); LEU208 (-2.1 ± 0.7)
	2.1 ± 0.2	1.0 ± 0.3	73.2 ± 21.6	89.4 ± 0.03	0.1 ± 0.1	-46.0 ± 0.2	ILE236 (-3.6 ± 0.4); ILE186 (-2.1 ± 0.5); LEU208 (-2.1 ± 0.6)

Table S3. Alanine scanning results. Influence of the substitution by alanine of some of the most important residues for binding. The results represent the difference between the predicted free energy before and after the substitution of each residue for alanine.

	CMLDID2589 (kcal/mol)	CMLDID25998 (kcal/mol)	AB-00022705 (kcal/mol)	CMLDID1670 (kcal/mol)
ILE186	1.8 ± 0.8	1.8 ± 0.6	1.9 ± 0.6	1.1 ± 0.7
GLN194	4.3 ± 0.7	2.8 ± 0.7	0.6 ± 0.5	2.7 ± 0.8
SER196	0.0 ± 0.5	1.9 ± 0.2	0.0 ± 0.2	0.5 ± 0.8
LEU197	0.3 ± 0.2	0.6 ± 0.5	0.6 ± 0.3	1.5 ± 0.6
TYR258	3.6 ± 0.8	2.5 ± 0.9	2.0 ± 0.7	0.5 ± 0.7

Table S4. Entropy contribution (TΔS)

	MM-GBSA (kcal/mol)	Entropy Contribution (kcal/mol)	Total Binding Free Energy (kcal/mol)
CMNPD14033	-51.9	-32.9	-19.0
CMLDID2589	-49.4	-35.0	-14.4
CMNPD21979	-47.5	-38.3	-9.2
STOCK1N-82736	-47.3	-36.1	-11.1
CMLDID25998	-48.0	-34.2	-13.7
AB-00022705	-46.0	-33.9	-12.1
CMLDID1670	-45.8	-34.7	-11.1
CMNPD20212	-45.2	-34.7	-10.5
STOCK1N-80709	-42.4	-36.2	-6.2
CMNPD18560	-43.2	-36.7	-6.4
CMLDID13602	-43.1	-35.7	-7.5
STOCK1N-83846	-40.5	-36.8	-3.7
AB-00049404	-40.7	-35.4	-5.4
STOCK1N-80896	-38.8	-34.5	-4.3
AB-00049441	-40.4	-35.8	-4.6
CMNPD4732	-39.5	-36.3	-3.2
M64 (reference)	-39.0	-34.2	-4.8
STOCK1N-05087	-38.8	-36.2	-2.6
AB-00023101	-38.3	-37.1	-1.2
AB-00069267	-36.6	-32.8	-3.8
NNQ	-36.4	-32.4	-4.0
CMLDID26149	-33.8	-33.1	-0.7