

# Drug repurposing in the battle against *P. aeruginosa* MvfR using Docking, Virtual Screening, Molecular Dynamics, and Free Energy Calculations

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**Table S1.** Cross-docking scores obtained with the six scoring functions tested.

		Vina											
		4JVC	4JVD	4JVI	6B8A	6Q7U	6Q7V	6Q7W	6TPR	6Z07	6Z17	6Z5K	6YZ3
4JVD	NNQ	-7.20	-7.20	-7.10	-7.30	-7.70	-7.30	-7.50	-7.70	-7.50	-7.50	-7.50	-7.60
4JVI	QZN	-7.50	-9.80	-7.80	-7.90	-9.90	-7.80	-8.00	-7.60	-7.30	-7.50	-7.60	-7.80
6B8A	M64	-9.00	-9.10	-9.00	-9.90	-9.40	-8.70	-9.20	-9.30	-8.10	-7.80	-7.80	-8.10
6Q7U	HLH	-6.70	-7.00	-7.20	-7.00	-8.00	-7.00	-7.30	-7.60	-7.70	-7.80	-7.40	-8.10
6Q7V	HLK	-8.10	-8.20	-7.90	-8.50	-8.90	-8.60	-8.00	-8.30	-7.50	-7.50	-7.90	-7.60
6Q7W	HLQ	-7.60	-7.60	-8.10	-8.10	-8.60	-7.60	-7.50	-8.10	-7.20	-7.30	-7.60	-7.40
6TPR	NV5	-9.20	-9.30	-9.70	-10.40	-9.90	-8.60	-9.40	-9.80	-7.10	-7.20	-7.60	-7.90
6Z07	Q4E	-4.30	-7.50	-7.70	-9.50	-7.20	-8.60	-7.80	-9.50	-7.60	-7.70	-7.90	-8.20
6Z17	Q4W	-4.40	-7.40	-7.90	-8.60	-6.70	-7.90	-7.60	-10.00	-7.50	-7.50	-7.90	-8.20
6Z5K	QAE	-4.80	-7.00	-7.50	-9.60	-7.10	-8.50	-7.70	-9.20	-7.20	-7.20	-7.40	-7.80
6YZ3	Q25	-4.50	-7.50	-8.00	-9.70	-7.20	-8.00	-7.70	-9.80	-7.20	-7.60	-7.60	-8.00
		LeDock											
		4JVC	4JVD	4JVI	6B8A	6Q7U	6Q7V	6Q7W	6TPR	6Z07	6Z17	6Z5K	6YZ3
4JVD	NNQ	-5.08	-5.06	-5.15	-5.49	-5.32	-4.91	-5.23	-5.11	-5.64	-5.83	-6.04	-6.13
4JVI	QZN	-6.27	-6.19	-6.44	-6.92	-6.25	-5.97	-6.75	-5.66	-5.81	-5.97	-6.68	-6.76

<b>6B8A</b>	<b>M64</b>	-8.40	-6.90	-7.26	-7.87	-8.30	-8.07	-7.36	-7.80	-5.97	-6.44	-6.91	-6.97
<b>6Q7U</b>	<b>HLH</b>	-4.76	-4.77	-4.95	-5.24	-4.98	-4.73	-5.15	-4.98	-5.31	-5.94	-5.97	-6.03
<b>6Q7V</b>	<b>HLK</b>	-5.69	-6.37	-5.78	-6.23	-6.15	-5.88	-6.23	-5.97	-5.42	-6.05	-6.30	-6.27
<b>6Q7W</b>	<b>HLQ</b>	-6.19	-6.17	-6.29	-6.44	-6.59	-6.14	-6.04	-5.89	-5.22	-5.44	-5.95	-6.12
<b>6TPR</b>	<b>NV5</b>	-6.98	-7.70	-6.39	-7.64	-7.38	-7.20	-8.03	-7.18	-5.05	-5.66	-6.10	-6.23
<b>6Z07</b>	<b>Q4E</b>	-3.31	-4.78	-6.01	-7.64	-4.58	-6.58	-6.02	-6.45	-5.40	-5.63	-6.14	-6.05
<b>6Z17</b>	<b>Q4W</b>	-3.32	-5.23	-6.33	-8.38	-4.74	-6.04	-6.67	-6.96	-5.75	-6.00	-6.58	-6.26
<b>6Z5K</b>	<b>QAE</b>	-3.30	-5.29	-6.40	-7.60	-4.8	-5.73	-6.16	-6.89	-5.39	-5.77	-6.25	-6.09
<b>6YZ3</b>	<b>Q25</b>	-3.28	-5.18	-6.56	-7.58	-4.77	-5.74	-5.94	-6.70	-5.33	-5.56	-6.13	-6.07
<b>CHEMPLP</b>													
		<b>4JVC</b>	<b>4JVD</b>	<b>4JVI</b>	<b>6B8A</b>	<b>6Q7U</b>	<b>6Q7V</b>	<b>6Q7W</b>	<b>6TPR</b>	<b>6Z07</b>	<b>6Z17</b>	<b>6Z5K</b>	<b>6YZ3</b>
<b>4JVD</b>	<b>NNQ</b>	62.09	61.31	63.41	67.70	65.77	66.06	67.95	67.98	53.17	58.96	68.64	72.91
<b>4JVI</b>	<b>QZN</b>	71.07	68.84	67.23	75.11	72.53	69.56	74.36	67.83	58.28	57.54	69.46	72.89
<b>6B8A</b>	<b>M64</b>	85.59	78.33	84.79	89.29	86.21	79.93	83.48	81.86	68.13	66.34	76.52	80.6
<b>6Q7U</b>	<b>HLH</b>	54.28	53.30	54.45	59.92	64.38	60.58	60.26	59.95	56.46	54.85	70.67	68.83
<b>6Q7V</b>	<b>HLK</b>	58.78	57.29	57.26	59.59	58.36	61.11	63.43	55.03	61.67	60.89	70.69	72.26
<b>6Q7W</b>	<b>HLQ</b>	67.57	66.06	65.66	69.42	67.04	63.14	69.53	63.51	57.50	60.05	71.86	74.33
<b>6TPR</b>	<b>NV5</b>	73.76	82.01	81.87	95.86	86.80	79.95	84.02	84.78	54.41	59.58	70.63	77.16
<b>6Z07</b>	<b>Q4E</b>	36.35	63.76	72.26	81.83	58.04	61.02	66.39	84.52	61.42	63.58	75.00	80.88
<b>6Z17</b>	<b>Q4W</b>	36.04	69.41	70.72	78.30	56.09	56.09	63.31	80.02	59.86	60.55	75.17	78.93
<b>6Z5K</b>	<b>QAE</b>	42.04	64.79	71.27	85.47	59.02	57.86	64.94	82.87	59.63	61.10	74.84	77.03
<b>6YZ3</b>	<b>Q25</b>	41.35	64.08	72.96	91.05	56.69	60.03	65.94	85.25	59.44	62.19	73.16	77.13
<b>GoldScore</b>													
		<b>4JVC</b>	<b>4JVD</b>	<b>4JVI</b>	<b>6B8A</b>	<b>6Q7U</b>	<b>6Q7V</b>	<b>6Q7W</b>	<b>6TPR</b>	<b>6Z07</b>	<b>6Z17</b>	<b>6Z5K</b>	<b>6YZ3</b>
<b>4JVD</b>	<b>NNQ</b>	56.25	54.80	55.82	55.77	52.66	47.76	54.4	54.92	52.60	57.29	56.43	60.30
<b>4JVI</b>	<b>QZN</b>	56.75	61.98	62.01	64.44	52.14	51.71	58.95	53.00	51.04	51.49	58.48	60.53

6B8A	M64	73.57	69.82	72.26	76.77	68.40	70.76	70.04	71.56	56.73	53.93	61.64	64.94
6Q7U	HLH	49.42	46.56	51.66	50.59	47.06	48.62	51.15	49.83	58.39	63.61	54.59	59.26
6Q7V	HLK	50.25	51.81	49.37	54.93	48.17	49.27	49.56	45.58	53.51	51.64	59.25	58.64
6Q7W	HLQ	46.03	49.32	44.24	49.13	50.31	48.63	47.11	55.24	54.88	53.77	61.76	60.73
6TPR	NV5	70.97	65.11	68.86	79.12	65.91	74.45	70.11	75.15	51.76	60.15	57.56	57.14
6Z07	Q4E	30.07	54.87	58.81	73.51	52.89	52.89	51.19	73.58	53.88	56.44	59.80	59.98
6Z17	Q4W	28.74	54.99	59.96	73.43	53.37	49.71	51.38	73.69	57.26	55.68	62.71	65.23
6Z5K	QAE	31.29	54.09	57.26	73.50	57.35	48.69	52.16	71.04	54.14	59.88	65.56	61.80
6YZ3	Q25	31.66	53.9	58.95	73.63	58.10	50.78	52.37	73.24	51.61	49.26	60.29	59.16
ChemScore													
		4JVC	4JVD	4JVI	6B8A	6Q7U	6Q7V	6Q7W	6TPR	6Z07	6Z17	6Z5K	6YZ3
4JVD	NNQ	33.67	33.54	34.44	34.66	30.05	33.80	36.57	33.97	24.18	27.72	33.92	34.75
4JVI	QZN	33.99	30.98	36.02	34.35	30.59	30.91	34.80	32.23	23.80	27.61	34.04	35.11
6B8A	M64	34.64	32.89	35.30	37.39	34.51	32.07	31.16	35.78	28.6	30.63	32.92	34.96
6Q7U	HLH	29.57	29.41	31.17	30.39	23.63	30.81	31.53	28.99	25.73	27.43	31.97	33.19
6Q7V	HLK	24.65	24.41	25.53	25.05	27.92	25.15	25.01	24.16	27.12	29.12	33.57	35.35
6Q7W	HLQ	27.58	28.04	28.56	29.00	25.37	27.32	27.65	28.22	26.18	30.07	32.54	33.83
6TPR	NV5	33.99	32.60	33.47	39.59	31.97	37.08	35.67	34.11	27.03	28.48	34.48	34.93
6Z07	Q4E	19.50	33.85	31.70	34.33	30.65	25.07	27.92	34.92	27.33	29.17	32.61	34.73
6Z17	Q4W	20.95	35.89	34.53	33.72	32.01	25.31	28.67	35.41	26.57	30.82	34.53	35.3
6Z5K	QAE	20.66	33.52	31.58	36.00	30.36	24.43	27.38	35.69	25.56	30.32	32.65	35.02
6YZ3	Q25	20.19	34.03	32.27	38.53	30.08	24.38	27.82	36.48	26.90	29.09	32.64	34.24
ASP													
		4JVC	4JVD	4JVI	6B8A	6Q7U	6Q7V	6Q7W	6TPR	6Z07	6Z17	6Z5K	6YZ3
4JVD	NNQ	27.04	27.14	26.91	29.53	27.6	27.13	27.15	27.45	29.94	28.46	31.59	32.81

<b>4JVI</b>	<b>QZN</b>	30.50	30.58	33.77	33.12	31.33	29.84	29.97	31.21	29.84	28.09	31.89	33.85
<b>6B8A</b>	<b>M64</b>	41.90	40.71	41.85	47.36	46.78	39.24	38.05	40.65	30.92	30.51	33.43	34.95
<b>6Q7U</b>	<b>HLH</b>	24.30	23.72	24.83	26.19	29.67	24.07	23.78	24.98	30.56	29.10	32.40	33.46
<b>6Q7V</b>	<b>HLK</b>	27.09	27.85	28.40	28.50	24.37	28.7	28.24	26.47	29.77	29.44	31.88	33.34
<b>6Q7W</b>	<b>HLQ</b>	31.27	32.32	31.09	32.44	30.45	31.22	32.78	31.26	28.59	28.07	30.52	32.60
<b>6TPR</b>	<b>NV5</b>	32.54	34.13	37.49	35.94	38.22	33.15	33.42	36.23	30.45	28.59	32.46	33.47
<b>6Z07</b>	<b>Q4E</b>	11.47	27.48	31.00	40.65	24.87	29.32	32.23	34.43	30.43	29.19	32.96	33.93
<b>6Z17</b>	<b>Q4W</b>	11.51	27.55	30.49	41.03	24.84	27.37	31.22	33.07	31.89	30.01	33.33	33.95
<b>6Z5K</b>	<b>QAE</b>	11.42	27.63	31.43	43.13	24.77	28.34	31.96	35.80	30.02	29.08	33.11	33.41
<b>6YZ3</b>	<b>Q25</b>	11.48	27.69	31.57	42.74	25.40	28.92	32.12	35.23	29.73	28.86	32.88	34.22

**Table S2.** Summary of the MD simulations results on the replicas performed for the top 5 Mvfr-FDA complexes. Average protein RMSD values (Å), average ligand RMSD (Å), Average Mvfr-ligand complex SASA (Å<sup>2</sup>), Percentage of SASA for the buried ligand, average number of ligand hydrogen bonds.

ID	Average Protein RMSd (Å)	Average Ligand RMSD	SASA (Å <sup>2</sup> )	Percentage of Potential Ligand SASA Buried (%)	Average number H bonds	ΔGbind (kcal/mol)	Main Contributors (kcal/mol)
Venetoclax	2.3 ± 0.2	2.7 ± 0.4	344.8 ± 27.0	70.4 ± 0.02	0.5 ± 0.6	-70.1 ± 0.3	TYR258 (-4.9), ILE186 (-4.3), ILE236 (-2.9)
	2.7 ± 0.2	2.9 ± 0.4	307.8 ± 42.3	72.2 ± 0.04	0.4 ± 0.6	-64.1 ± 0.3	TYR258 (-3.6), ILE186 (-3.3), ILE236 (-2.5)
	2.2 ± 0.2	2.9 ± 0.2	352.8 ± 33.2	68.5 ± 0.03	0.4 ± 0.5	-66.2 ± 0.2	TYR258 (-4.6), ILE186 (-3.2), ILE236 (-3.1)
Indocyanine Green	2.2 ± 0.2	2.3 ± 0.2	298.9 ± 28.3	72.3 ± 0.03	1.1 ± 0.8	-58.6 ± 0.3	ILE186 (-4.2), ILE236 (-3.1), TYR258 (-3.1)
	2.2 ± 0.2	2.4 ± 0.2	283.5 ± 32.0	73.6 ± 0.03	1.0 ± 0.7	-59.2 ± 0.3	ILE186 (-4.1), ILE236 (-3.3), TYR258 (-3.2)
	2.6 ± 0.4	2.3 ± 0.3	279.4 ± 32.9	74.1 ± 0.03	0.8 ± 0.6	-55.3 ± 0.3	ILE186 (-3.3), ILE236 (-3.1), TYR258 (-3.0)
Nilotinib	2.0 ± 0.2	1.7 ± 0.4	105.2 ± 23.2	86.8 ± 0.03	0.1 ± 0.3	-48.1 ± 0.2	ILE186 (-2.4), LEU208 (-2.1), ILE236 (-3.4)
	2.2 ± 0.2	0.9 ± 0.1	71.6 ± 18.6	91.0 ± 0.02	0.3 ± 0.4	-53.3 ± 0.2	ILE186 (-2.7), LEU208 (-1.7), ILE236 (-3.8)
	2.7 ± 0.5	1.0 ± 0.2	84.7 ± 23.2	89.3 ± 0.03	0.1 ± 0.3	-50.7 ± 0.2	ILE186 (-2.6), LEU208 (-1.5), ILE236 (-3.7)
Cabozantinib	2.3 ± 0.3	1.6 ± 0.4	135.3 ± 40.5	82.3 ± 0.1	0.03 ± 0.2	-44.6 ± 0.2	ILE236 (-3.2), ILE186 (-2.4), LEU208 (-2.3)
	2.3 ± 0.3	1.2 ± 0.2	147.4 ± 46.3	80.7 ± 0.1	0.3 ± 0.4	-43.1 ± 0.2	ILE236 (-3.2), ILE186 (-2.5), LEU208 (-2.4)
	2.3 ± 0.2	1.4 ± 0.1	104.6 ± 25.0	86.4 ± 0.03	0.02 ± 0.1	-47.9 ± 0.2	ILE236 (-3.4), ILE186 (-1.4), LEU208 (-2.1)
Montelukast	2.2 ± 0.2	2.2 ± 0.4	228.8 ± 35.6	73.8 ± 0.04	0.04 ± 0.2	-43.2 ± 0.2	ILE236 (-2.8), LEU207 (-2.4), ILE263 (-2.0)
	2.2 ± 0.2	2.6 ± 0.4	231.9 ± 48.4	73.3 ± 0.1	0.2 ± 0.4	-44.9 ± 0.3	ILE236 (-3.1), LEU207 (-2.3), ILE263 (-2.2)
	2.2 ± 0.2	2.5 ± 0.4	261.2 ± 38.4	70.2 ± 0.04	0.2 ± 0.4	-41.0 ± 0.2	ILE236 (-2.9), LEU207 (-2.7), ILE263 (-2.0)