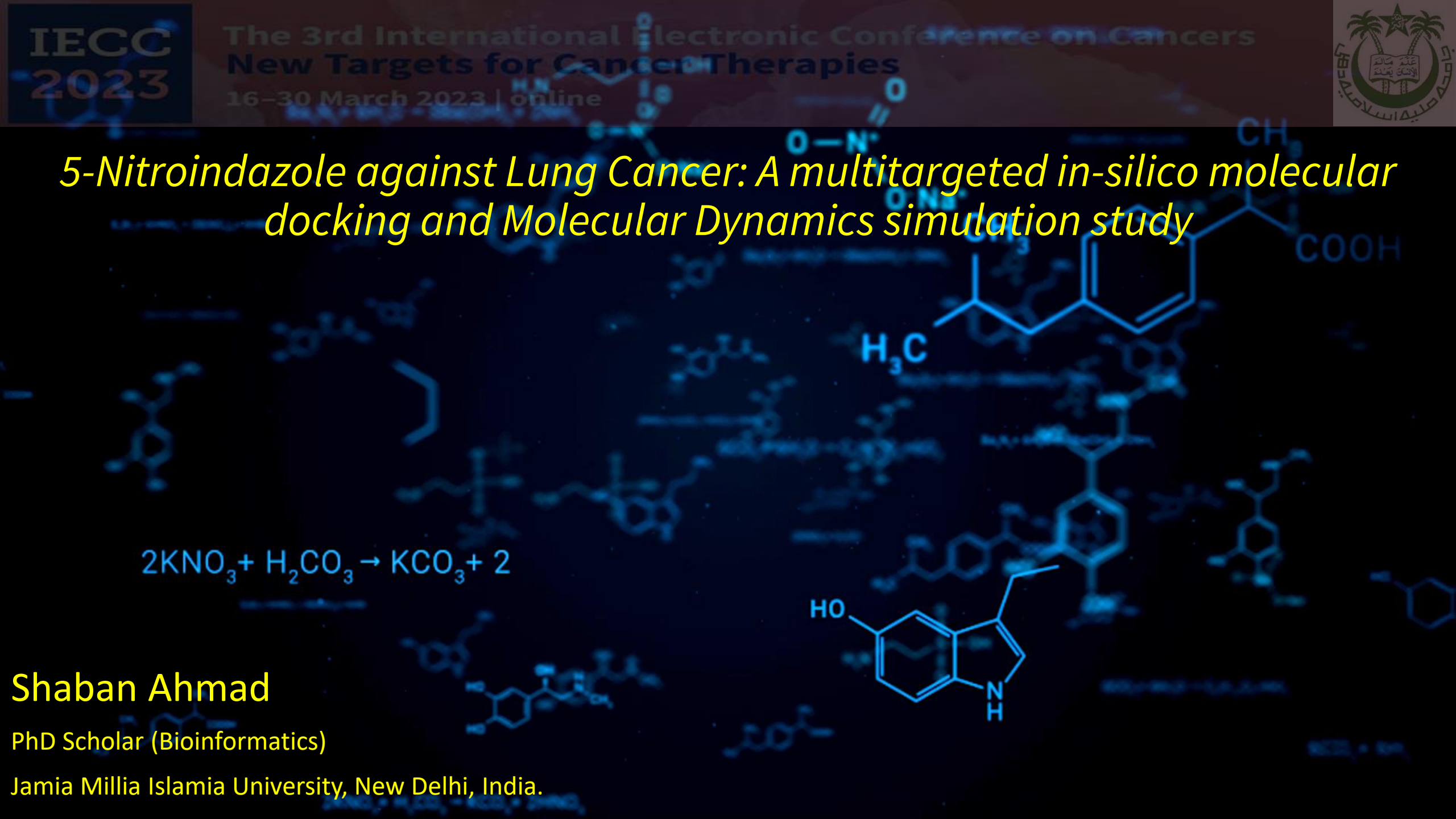
IECC 2023
The 3rd International Electronic Conference on Cancers
New Targets for Cancer Therapies
16–30 March 2023 | online

5-Nitroindazole against Lung Cancer: A multitargeted in-silico molecular docking and Molecular Dynamics simulation study



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Protein, ligand preparation and Screening

PDB collection, preparation

Filling gaps, side chains, loops, het states

Optimisation

Minimised with OPLS4

Drug Bank Library collected and prepared

Ligand library

Molecular Docking

Screened with HTVS, SP, followed by XP algorithms

Sampled with MM\GBSA

Characterisation

ADMET Analysis

Interaction Pattern Analysis

5-Nitroindazole fingerprinting

Reporting 5-Nitroindazole as multitargeted inhibitor against Lung Cancer

RMSF

RMSD

SID

MD Simulation Analysis

100 ns in water

NVT ensemble

Optimisation, prediction and validations

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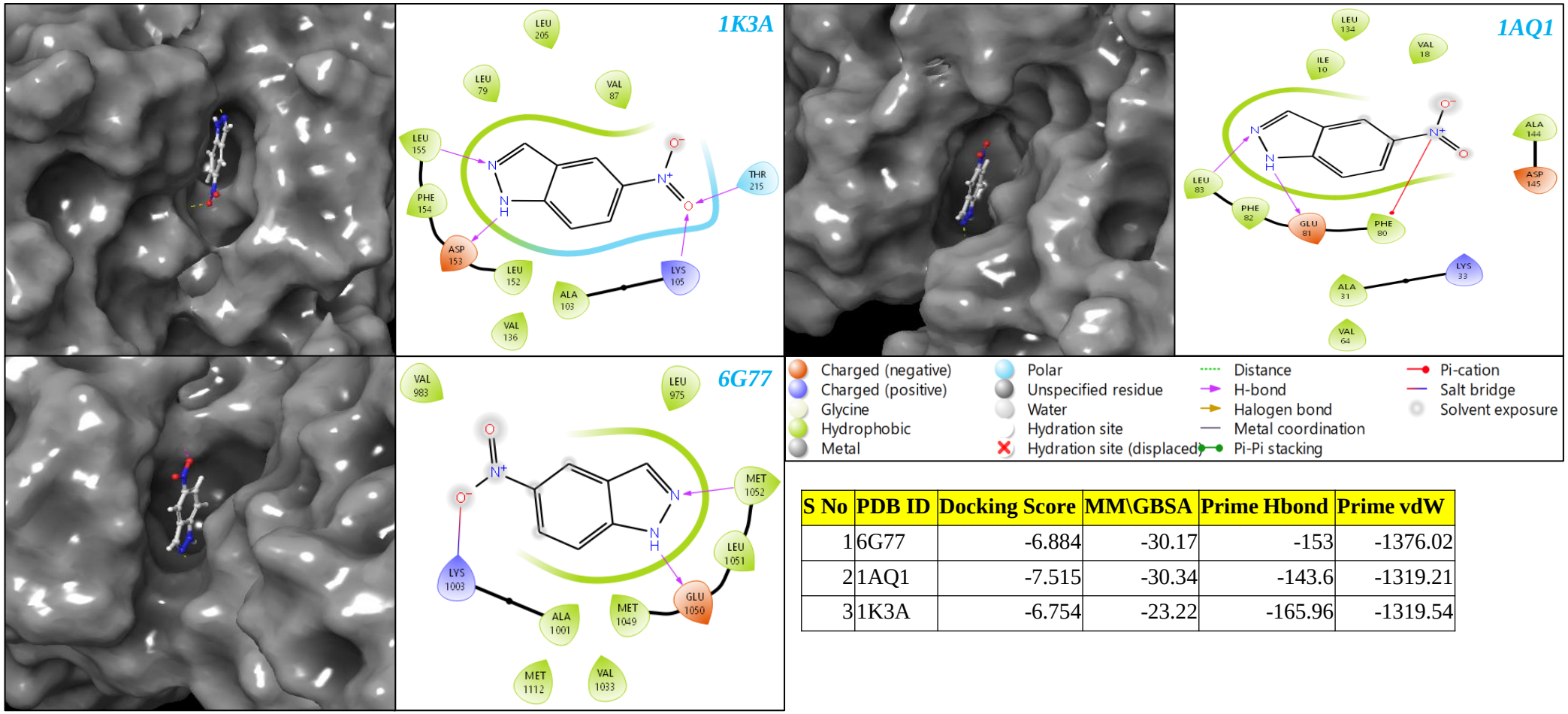
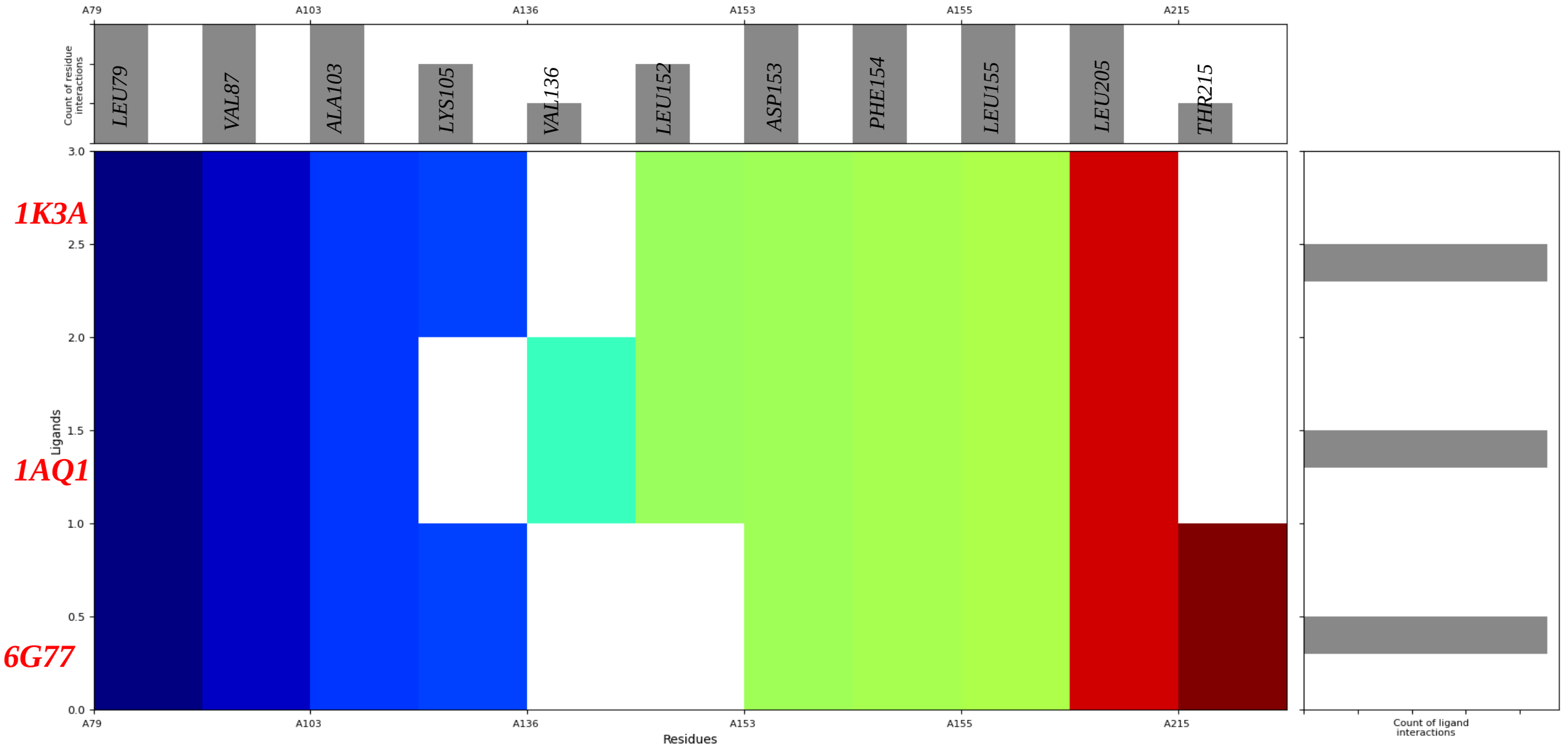


S No	PDB ID	Docking Score	MM\GBSA	Prime Hbond	Prime vdW
1	6G77	-6.884	-30.17	-153	-1376.02
2	1AQ1	-7.515	-30.34	-143.6	-1319.21
3	1K3A	-6.754	-23.22	-165.96	-1319.54

Descriptors	Standard Values	Nitroindazole	Descriptors	Standard Values	Nitroindazole
#stars	0 – 5	0	QPlogS	−6.5 – 0.5	-1.73
#amine	0 – 1	0	CIQPlogS	−6.5 – 0.5	-2.244
#amidine	0	0	QPlogHERG	concern below −5	-3.457
#acid	0 – 1	0	QPPCaco	<25 poor, >500 great	264.335
#amide	0 – 1	0	QPlogBB	−3.0 – 1.2	-0.773
#rotor	0 – 15	1	QPPMDCK	<25 poor, >500 great	117.427
#rtvFG	0 – 2	0	QPlogKp	−8.0 – −1.0	-3.883
CNS	−2 (inactive), +2 (active)	-1	IP(eV)	7.9 – 10.5	9.544
mol MW	130.0 – 725.0	163.135	EA(eV)	−0.9 – 1.7	1.223
dipole	1.0 – 12.5	6.586	#metab	1 – 8	1
SASA	300.0 – 1000.0	336.065	QPlogKhsa	−1.5 – 1.5	-0.375
FOSA	0.0 – 750.0	0	HumanOralAbsorption	N/A	3
FISA	7.0 – 330.0	165.954	PercentHumanOralAbsorption	>80% is high, <25% is poor	77.139
PISA	0.0 – 450.0	170.11	SAfluorine	0.0 – 100.0	0
WPSA	0.0 – 175.0	0	SAamideO	0.0 – 35.0	0
volume	500.0 – 2000.0	520.507	PSA	7.0 – 200.0	75.765
donorHB	0.0 – 6.0	1	#NandO	2 – 15	5
accptHB	2.0 – 20.0	2	RuleOfFive	maximum is 4	0
dip^2/V	0.0 – 0.13	0.083336	RuleOfThree	maximum is 3	0
ACxDN^.5/SA	0.0 – 0.05	0.0059512	#ringatoms	N/A	9
glob	0.75 – 0.95	0.931165	#in34	N/A	0
QPpolrz	13.0 – 70.0	15.659	#in56	N/A	9
QPlogPC16	4.0 – 18.0	5.814	#noncon	N/A	0
QPlogPoct	8.0 – 35.0	8.667	#nonHatm	N/A	12
QPlogPw	4.0 – 45.0	6.028	Jm	N/A	0.577
QPlogPo/w	−2.0 – 6.5	1.168			



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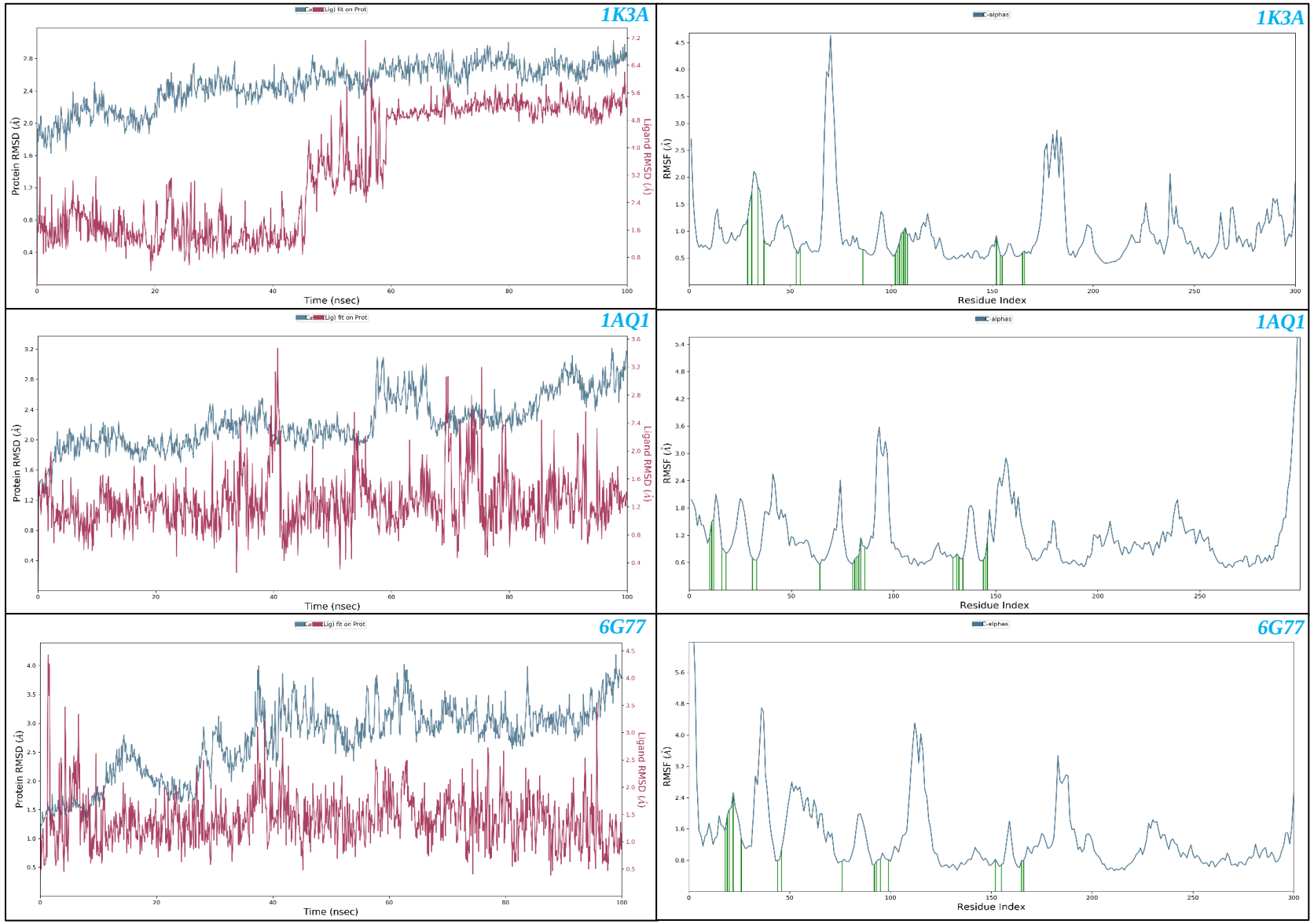
1K3A
Protein RMSD (Å)
Ligand RMSD (Å)
Time (nsec)
1K3A
RMSF (Å)
Residue Index
1AQ1
Protein RMSD (Å)
Ligand RMSD (Å)
Time (nsec)
1AQ1
RMSF (Å)
Residue Index
6G77
Protein RMSD (Å)
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Time (nsec)
6G77
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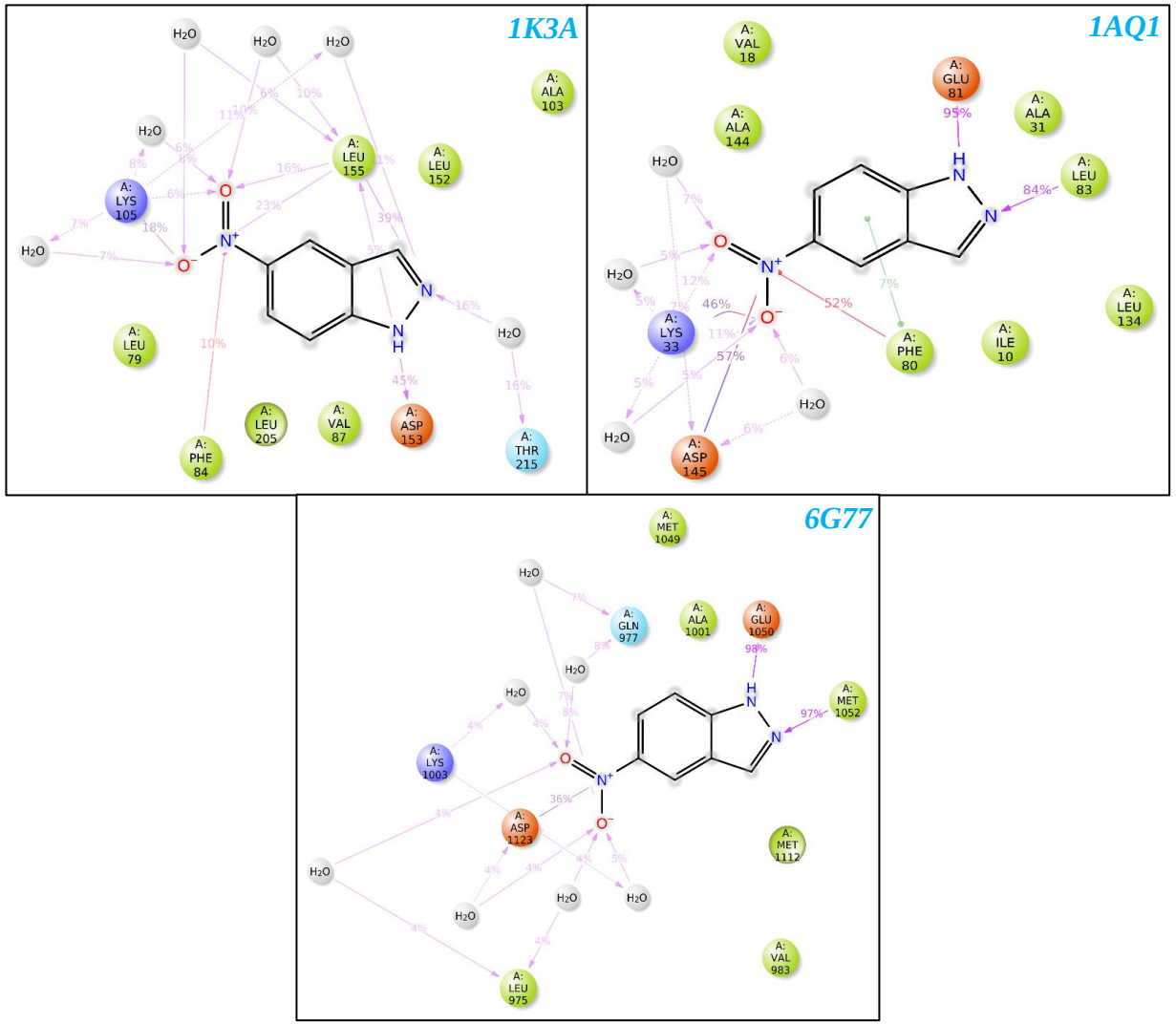
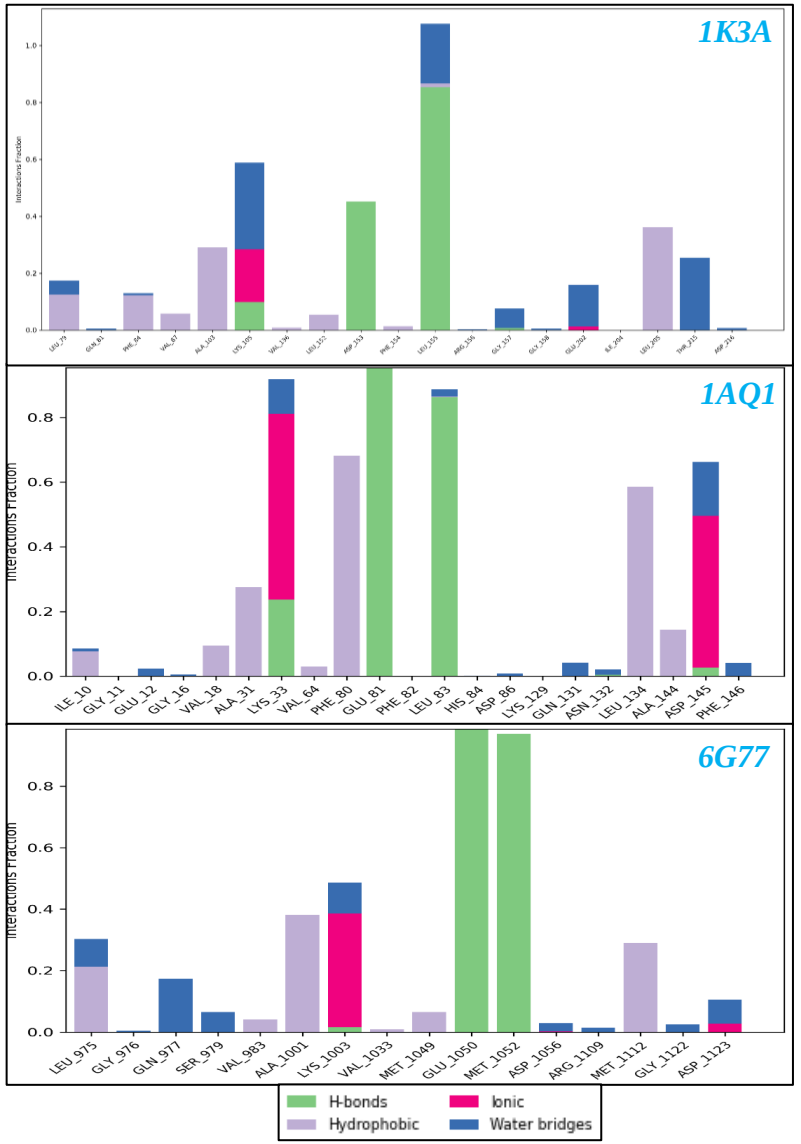
Residue Index





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Conclusion

The food and drug administration has approved almost 100 drugs against SCLC and NSCLC, which are being used actively. However, this is unfortunate; even after so much expenditure, the world frequently faces the drug resistance problem and needs a new drug.

This study includes multisampling algorithms based on screening, ADMET analysis, interaction pattern analysis and MD simulation for 100ns in the SPC water medium has produced a promising results.

In this study, we have identified 5-Nitroindazole as a multitargeted inhibitor against lung cancer, validated with computational methods, and proven as a prominent candidate.

The identified compound 5-Nitroindazole has less chance to develop resistance, or it might take a more extended period. It can be experimentally validated and used for the welfare of humankind.

This study also set an example of how to proceed with multitargeted drug designing or repurposing to cure any prevalent disease and developing resistance.