Supporting Information

Potential Inhibitors of Fascin from A Database of Marine Natural Products: A Virtual Screening and Molecular Dynamics Study

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TABLE S1 Computational binding affinities of active and inactive ligands based on MM/GBSA in 5 replica MD simulations, Unit: Kcal/mol

Item	Ligand	1st MD	2nd MD	3rd MD	4th MD	5th MD	Average
Active	NP-G2-044	–41.18	–41.71	–41.11	–41.94	–41.32	–41.45
Inactive	NP-G2-112	–38.18	–38.88	–38.49	–38.46	–38.27	–38.45
Inactive	NP-G2-113	–35.95	–35.76	–35.66	–35.47	–35.15	–35.60

TABLE S2 ZINC IDs and the 2D structures of active and inactive ligands

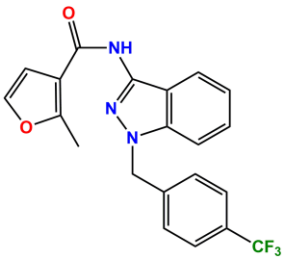
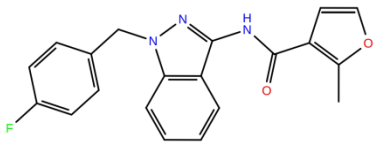
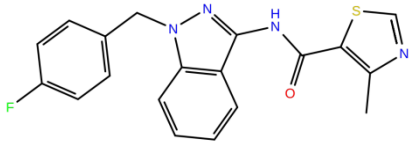
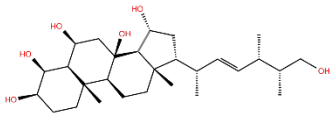
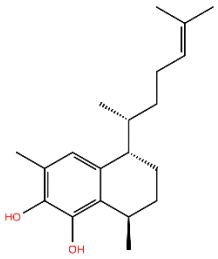
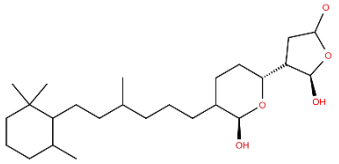
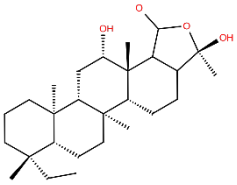
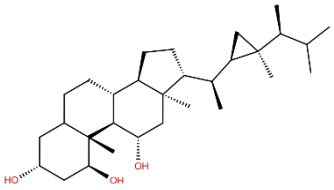
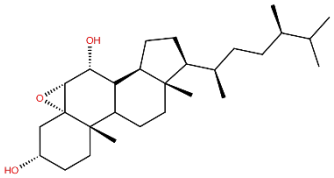
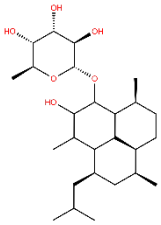
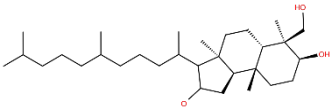
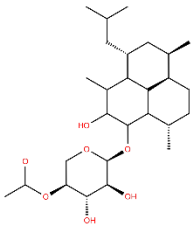
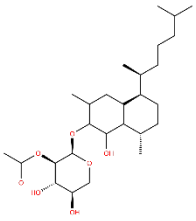
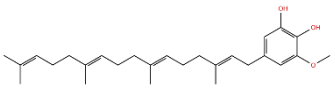
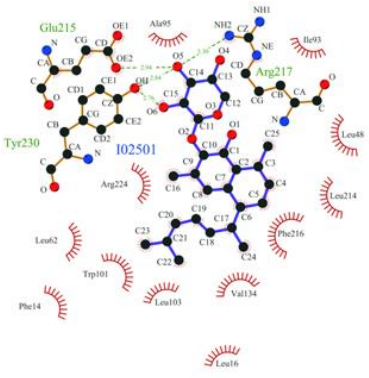
Compound/No.	Structure
NP-G2-044 $C_{21}H_{16}F_3N_3O_2$	
NP-G2-112 $C_{20}H_{16}FN_3O_2$	
NP-G2-113 $C_{19}H_{16}FN_4SO$	

TABLE S3 Binding affinities for small-molecule No. 20 to 30 in molecule docking. Unit: kcal/mol

No.	Zinc Number	Molecule weight	Chemical Structure	Binding affinity
No. 20	ZINC000044387005	480.68		-33.35
No. 21	ZINC000033977462	302.45		-30.68
No. 22	ZINC000003874163	416.55		-28.33

No. 23	ZINC000038299972	430.62		-31.74
No. 24	ZINC000137551534	458.72		-36.54
No. 25	ZINC000255258130	428.65		-36.88
No. 26	ZINC000140370169	446.58		-29.75
No. 27	No data	No data		-33.27
No. 28	ZINC000044431210	474.59		-32.83
No. 29	ZINC000006041800	476.60		-32.97
No. 30	ZINC000040873606	412.61		-37.87



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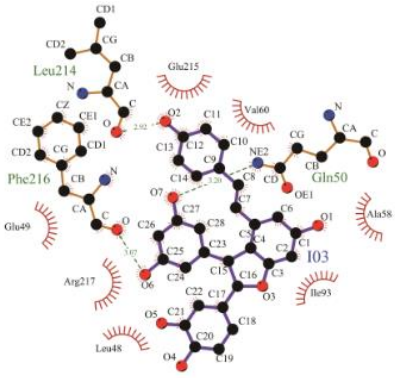

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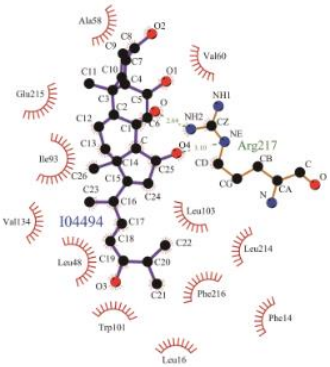

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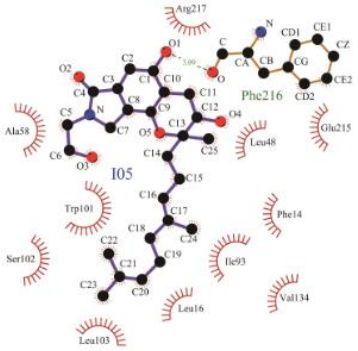

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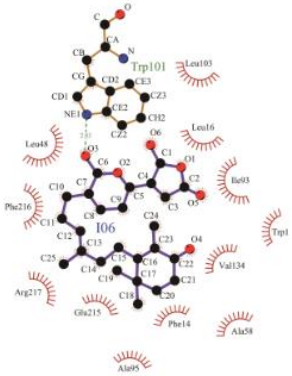

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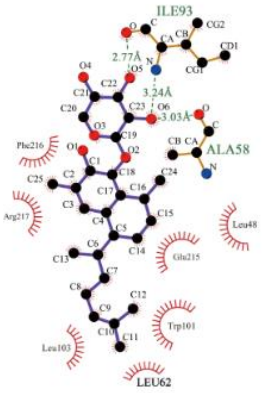

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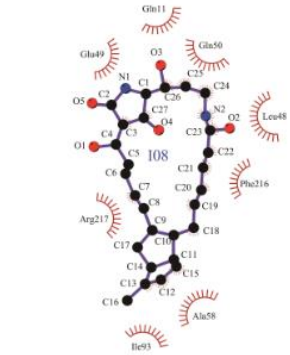

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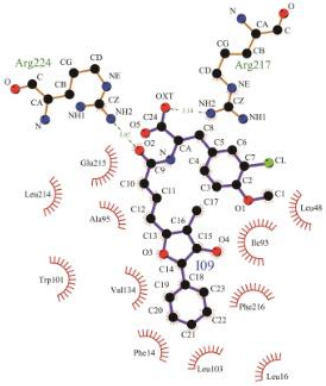

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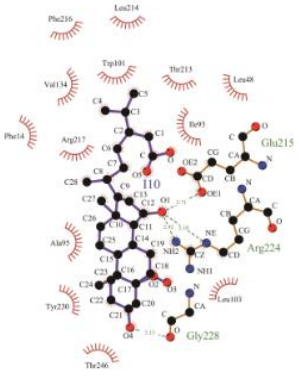


Inhibitor No.10

Figure representation

- Inhibitor bond
- Fascin residue bond
- Hydrogen bond and its leng
- Fascin residue involved in hydrophobic contact
- Corresponding atom involved in hydrophobic contact

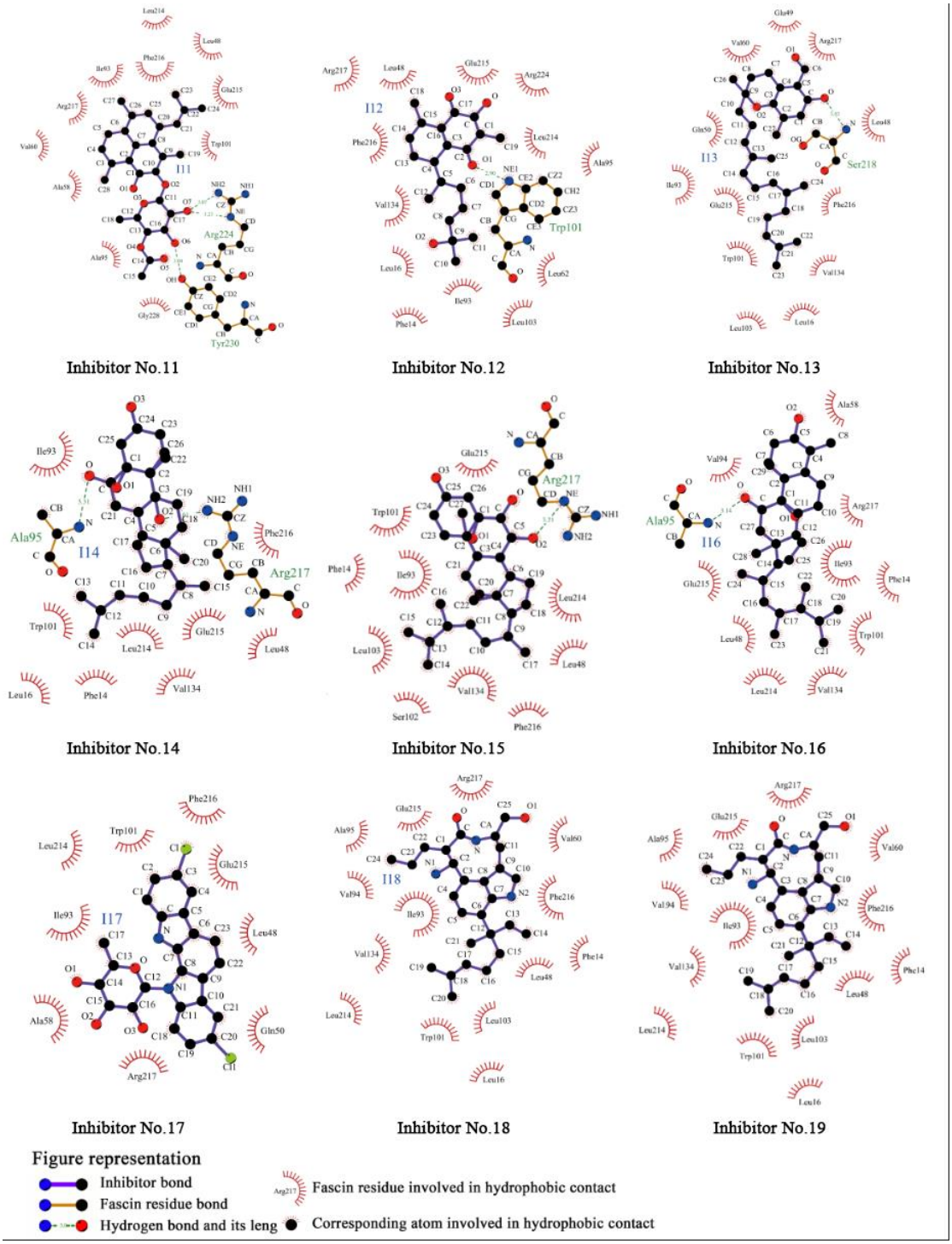
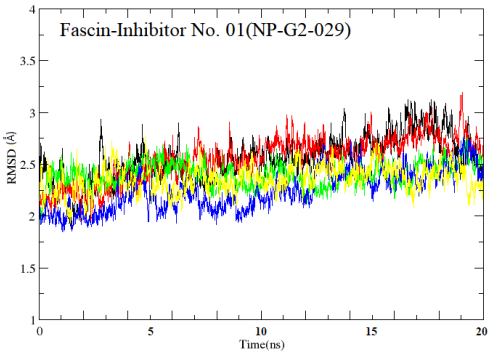
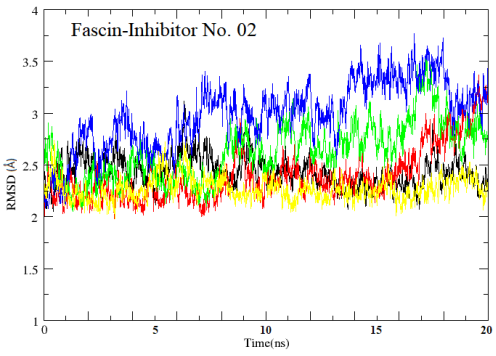


FIGURE S1 Interactions between Fascin and small-molecules No.2 to 19. (No.1 is the inhibitor NP-G2-029). Plotted by LIGPLOT Software (C. et al., 1995).


Fascin-Inhibitor No. 01(NP-G2-029)
RMSD (Å)
Time(ns)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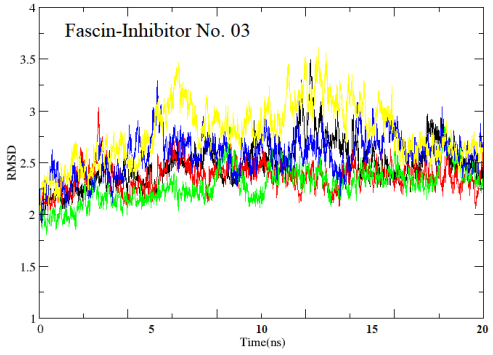
Time(ns)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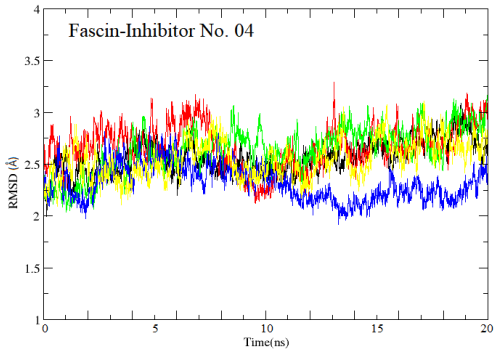
RMSD
Time(ns)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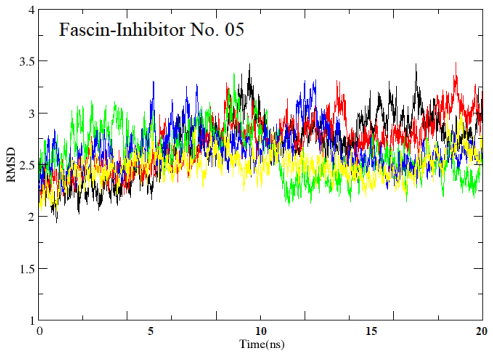
Time(ns)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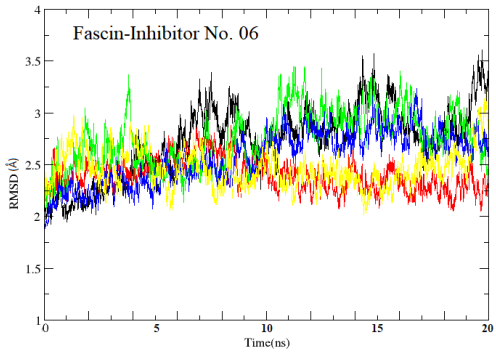
RMSD
Time(ns)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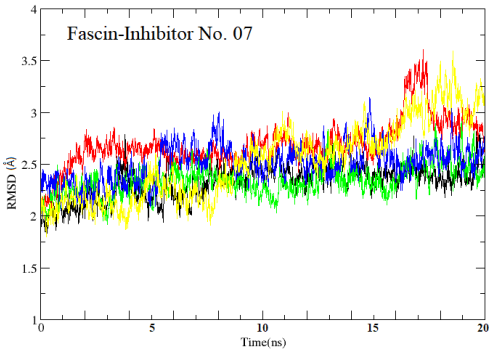
RMSD (Å)
Time(ns)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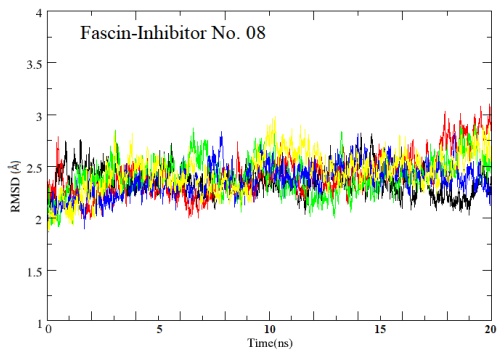
RMSD (Å)
Time(ns)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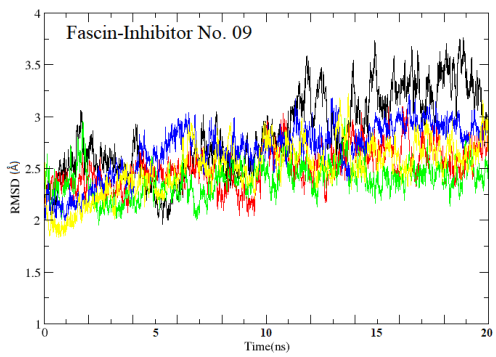
Time(ns)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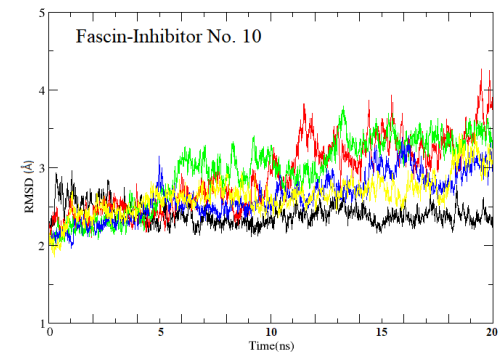
Time(ns)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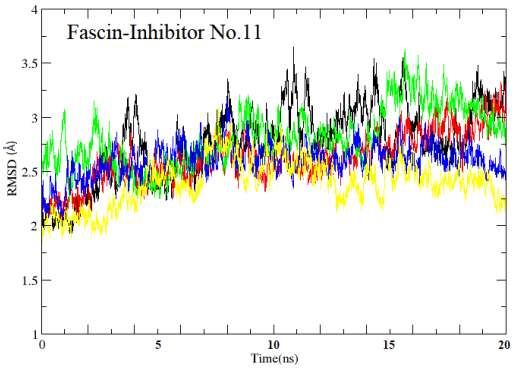
Time(ns)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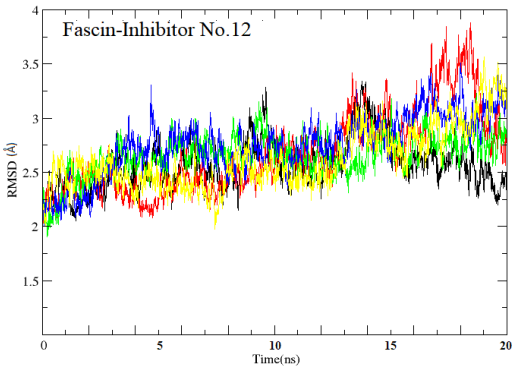
RMSD (Å)
Time(ns)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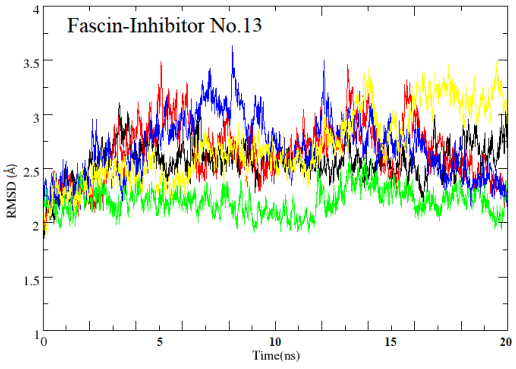
RMSD (Å)
Time(ns)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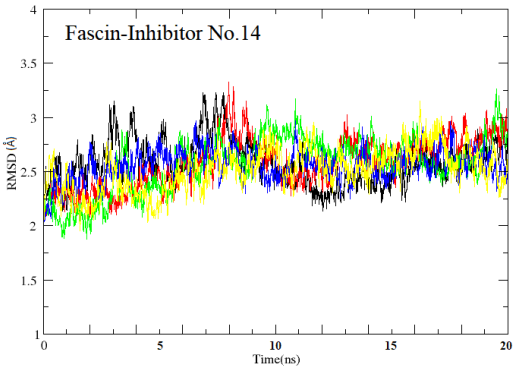
RMSD (Å)
Time(ns)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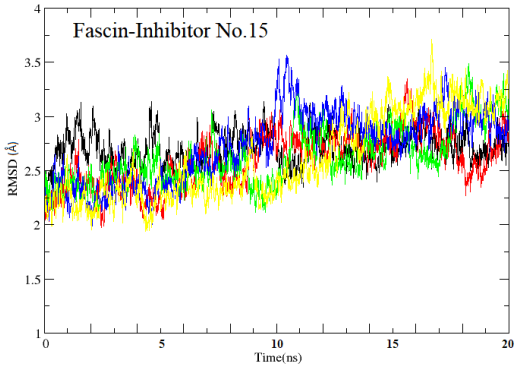
RMSD (Å)
Time(ns)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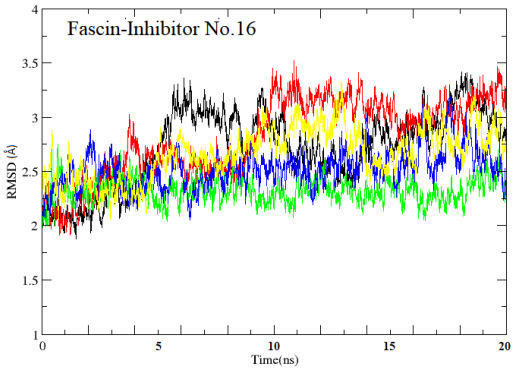
RMSD (Å)
Time(ns)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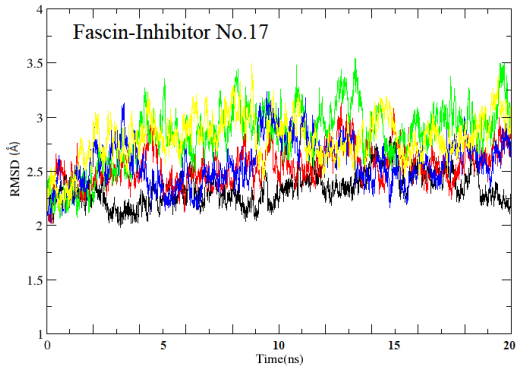
Time(ns)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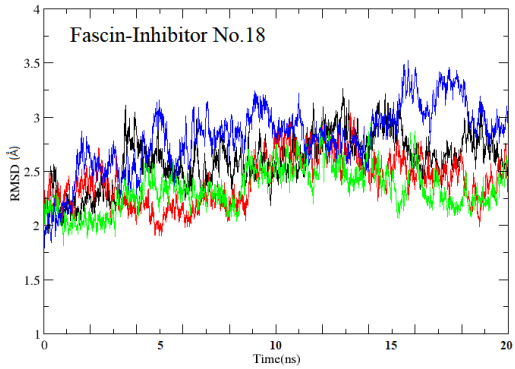
RMSD (Å)
Time(ns)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RMSD (Å)
Time(ns)

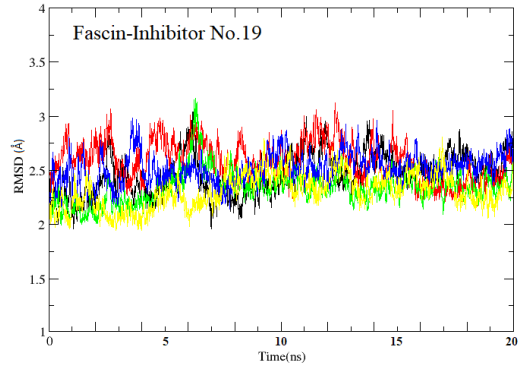
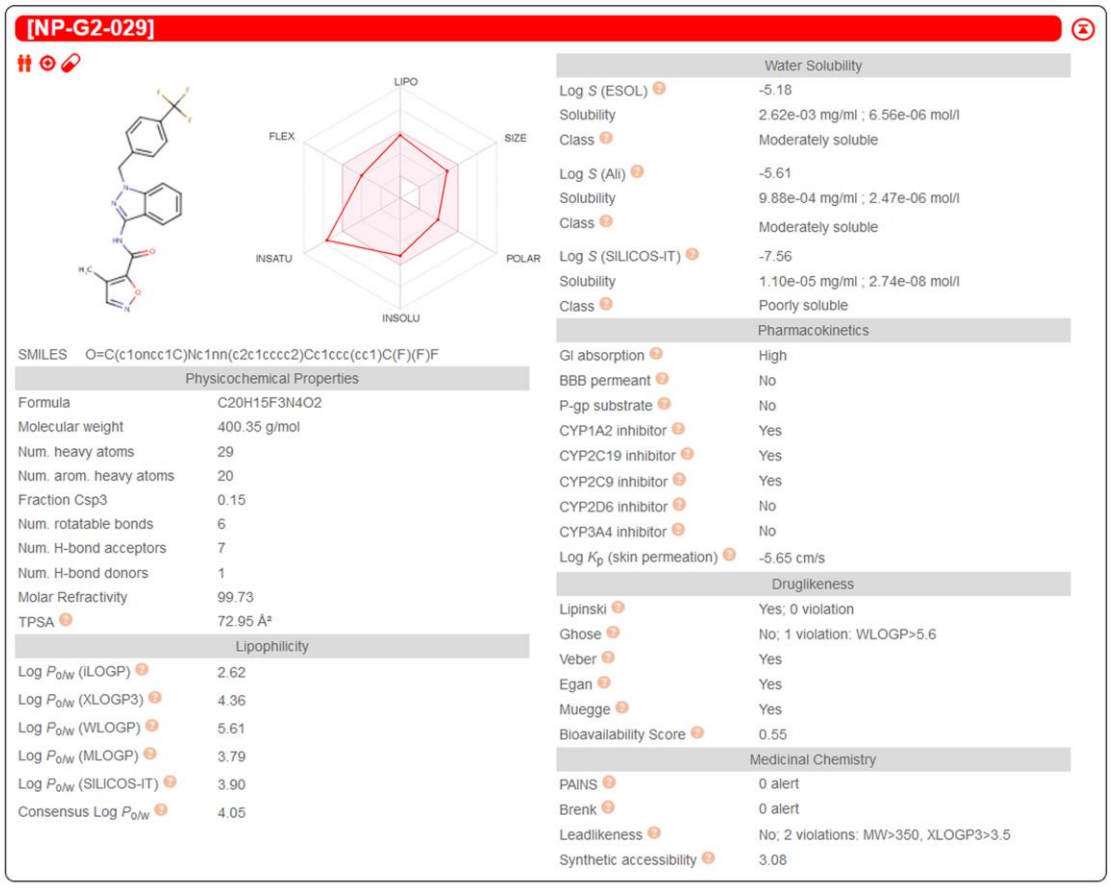

Fascin-Inhibitor No.19
RMSD (Å)
Time(ns)

FIGURE S2 RMSD files for each complex of Fascin with inhibitor No. 01-19. Fine color lines stand for 5 replicates of conventional MD simulation. RMSD calculated by using the CPPTRAJ module in AMBER 20 (Case et al., 2020).



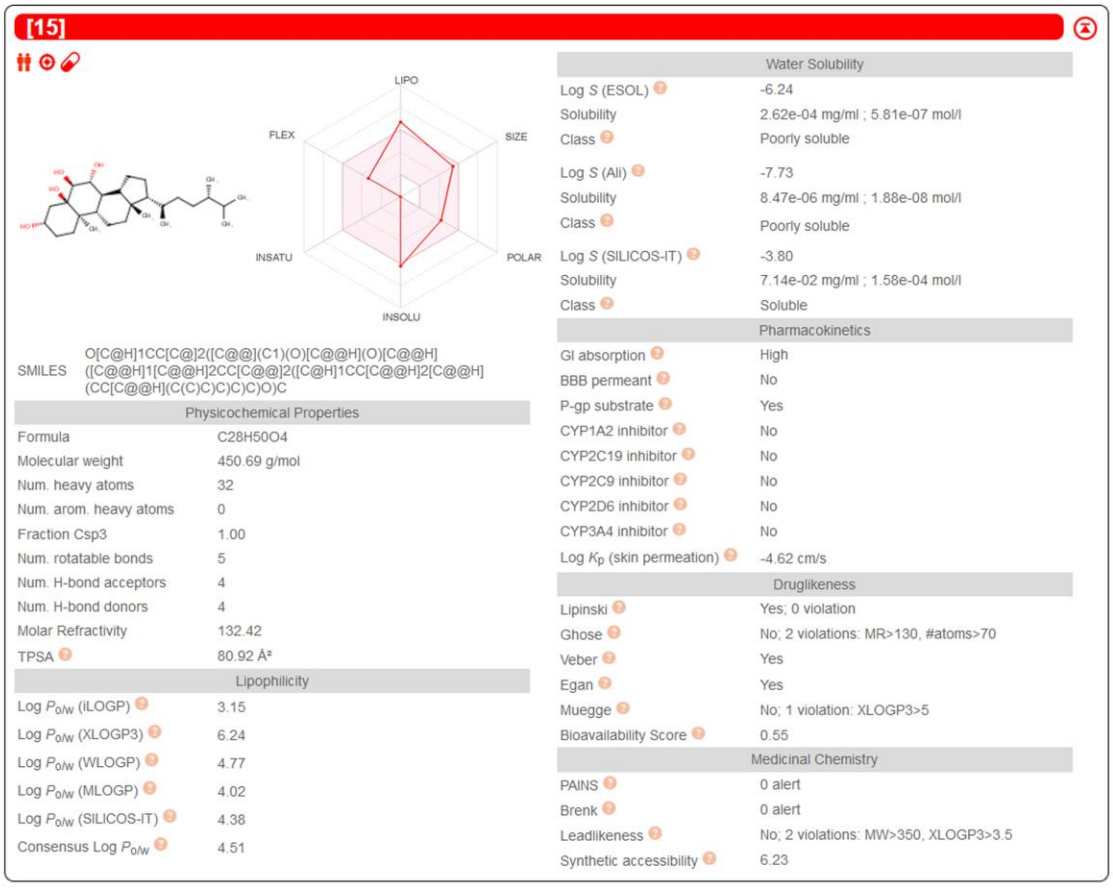


FIGURE S3 Toxicity data for potential inhibitor No. 07, 15, 18. Evaluation processed by ProTox-II server (Banerjee et al., 2018).

TABLE S4 Toxicity evaluation data collection. Evaluation processed by ProTox-II server (Banerjee et al., 2018).

ITEM		NP-G2-029		I07		I15		I018	
Classification	**Target**	**Prediction**	**Probability**	**Prediction**	**Probability**	**Prediction**	**Probability**	**Prediction**	**Probability**
Organ toxicity	Hepatotoxicity	Active	0.52	Inactive	0.91	Inactive	0.84	Inactive	0.72
Toxicity end points	Carcinogenicity	Active	0.58	Inactive	0.65	Inactive	0.58	Inactive	0.63
Toxicity end points	Immunotoxicity	Inactive	0.99	Active	0.99	Active	0.99	Active	0.99
Toxicity end points	Mutagenicity	Active	0.6	Inactive	0.82	Active	0.64	Inactive	0.68
Toxicity end points	Cytotoxicity	Inactive	0.75	Inactive	0.82	Inactive	0.98	Inactive	0.73
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor	Inactive	0.62	Inactive	0.86	Inactive	0.99	Inactive	0.79
Tox21-Nuclear receptor signalling pathways	Androgen Receptor	Inactive	0.97	Inactive	0.97	Inactive	0.95	Inactive	0.93
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain	Inactive	0.96	Inactive	0.93	Inactive	0.95	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Aromatase	Inactive	0.84	Inactive	0.59	Inactive	0.94	Inactive	0.9
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	Inactive	0.82	Inactive	0.79	Inactive	0.74	Inactive	0.89
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	Inactive	0.91	Inactive	0.92	Inactive	0.86	Inactive	0.96
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	Inactive	0.91	Inactive	0.95	Inactive	0.99	Inactive	0.91
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element	Inactive	0.94	Inactive	0.85	Inactive	0.84	Inactive	0.92
Tox21-Stress response pathways	Heat shock factor response element	Inactive	0.94	Inactive	0.85	Inactive	0.84	Inactive	0.92
Tox21-Stress response pathways	Mitochondrial Membrane Potential	Inactive	0.62	Inactive	0.54	Active	0.52	Inactive	0.8
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	Inactive	0.86	Inactive	0.64	Inactive	0.78	Inactive	0.82
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	Inactive	0.85	Inactive	0.92	Inactive	0.91	Inactive	0.88

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