Electronic Supplementary Information

Integration of Pharmacophore Mapping and Molecular Docking in Sequential Virtual Screening: toward the Discovery of Novel JAK2 Inhibitors

Ting-Ting Yao,[a,b,+] Jiang-Feng Xie[+,a], Xing-Guo Liu,[c] Jing-Li Cheng,[b] Cheng-Yuan Zhu,[a] Jin-Hao Zhao,[a,b,*] Xiao-Wu Dong[a,*]

[a]ZJU-ENS Joint Laboratory of Medicinal Chemistry, Zhejiang Province Key Laboratory of Anti-Cancer Drug Research, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, 310058, P. R. China

[b]Institute of Pesticide and Environmental Toxicology, Ministry of Agriculture Key Laboratory of Agricultural Entomology, Zhejiang University, Hangzhou 310029, P. R. China

[c]School of Chemical Engineering and Light Industry, Guangdong University of Technology, Guangzhou, 510006, P.R. China

[*]Correspondence and requests for materials should be addressed to Jin-Hao Zhao (email: jinhaozhao@zju.edu.cn) and Xiao-Wu Dong (email: dongxw@zju.edu.cn).

[+] These authors contributed equally to this work.

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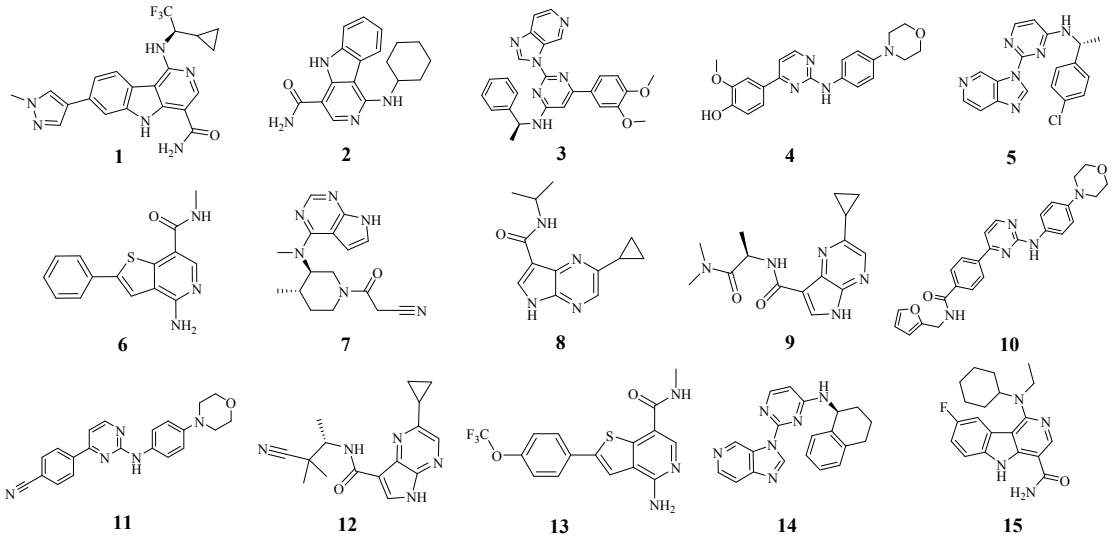


Figure S1. Chemical structures of all 15 training set molecules used for HypoGen pharmacophore generation.

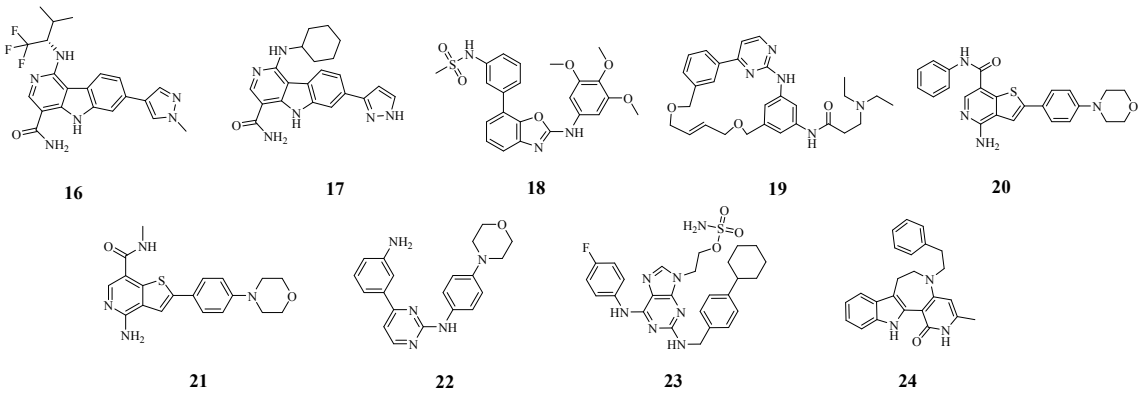


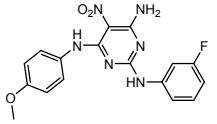
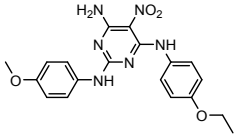
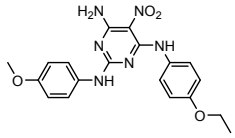
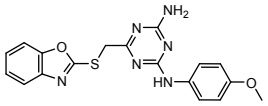
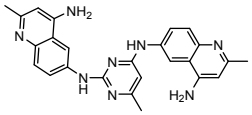
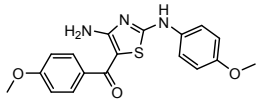
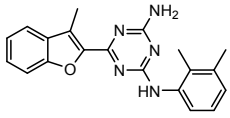
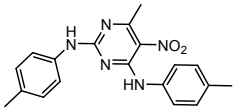
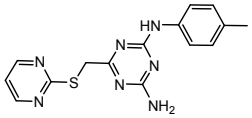
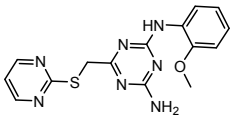
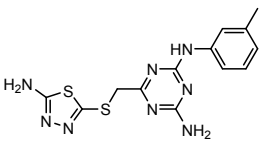
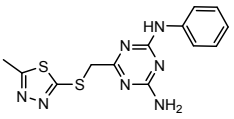
Figure S2. Chemical structures of all 9 test set molecules used for HypoGen pharmacophore validation.

Table S1. Information of statistical significance and predictive power presented in cost values for top 10 hypothesis

No.	Total cost	delta Cost	R.m.s deviation	Correlation	Features
1	73.20	73.08	1.25	0.94	HBD, HBD, HY, HY, EV, EV, EV, EV
2	74.31	71.97	1.36	0.92	HBD, HBD, HY, HY, EV, EV, EV, EV
3	76.28	70.00	1.46	0.91	HBD, HBD, HY, HY, EV, EV, EV, EV
4	88.76	57.53	1.93	0.85	HBA, HY, HY
5	91.44	54.84	2.00	0.84	HBA, HY, HY, EV, EV, EV
6	93.75	52.53	2.13	0.81	HBA, HBA, HBD, HY
7	94.44	51.84	2.15	0.81	HBA, HBD, HBD, HY, EV
8	94.49	51.79	2.11	0.82	HBA, HBA, HBD, EV
9	94.56	51.72	2.14	0.81	HBD, HBD, HY, HY, EV
10	95.51	50.77	2.17	0.80	HBD, HBD, HY, HY, EV

delta Cost=null cost - total cost; Fixed cost=59.69 bits; Null cost=146.29; Configuration=15.02 bits; HBA=Hydrogen Bond Acceptor; HBD=Hydrogen Bond Donor; HY= Hyrophobic; EV= Excluded Volume.

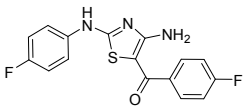
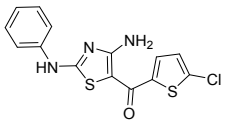
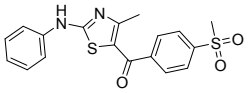
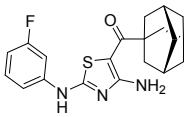
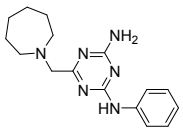
Table S2. The corresponding Specs ID, structure, docking score and FitValue generated by pharmacophore of the virtual screening hits*

NO.	ID in Specs	Structure	LigScore1_Dreiding	FitValue
A1	AO-022/43349386		4.42	7.84
A2	AO-022/43349135		4.00	7.78
A3	AJ-292/42284769		9.00	7.76
A4	AO-022/43452642		4.27	7.50
A5	AN-584/43416482		4.23	7.46
A6	AM-807/12426021		4.10	7.34
A7	AO-022/43356671		4.21	7.01
A8	AG-670/36572045		4.17	6.98
A9	AJ-292/42284768		3.99	6.46
A10	AJ-292/42490236		4.03	5.77
A11	AJ-292/42226268		4.61	5.74
A12	AJ-292/42284691		4.12	5.57

* The purity of all compounds purchased from Specs is higher than 95% according to the purity

statements.

Table S3. The corresponding Specs ID, structure and similarity to the query structures (A5, A6, A9) of the virtual screening hits*

NO.	ID in Specs	Structure	Similarity to query structure (A5, A6, A9)
B1	AK-777/09836064		0.63
B2	AM-807/12427247		0.44
B3	AR-434/43295104		0.37
B4	AM-807/14956082		0.31
B5	AJ-292/42284682		0.31

* The purity of all compounds purchased from Specs is higher than 95% according to the purity statements.