

Supporting Information

Structure-based Discovery of New Maternal Embryonic Leucine Zipper Kinase Inhibitors

Shu Zhou^{a, §}, Guo-Bo Li^{b, §}, Lin Luo^a, Lei Zhong^c, Kai Chen^c, Hui Li^c, Xiao-juan Jiang^c, Qi Fu^c, Xin Long^a, Jin-ku Bao^{a, *}

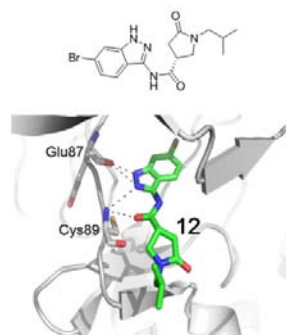
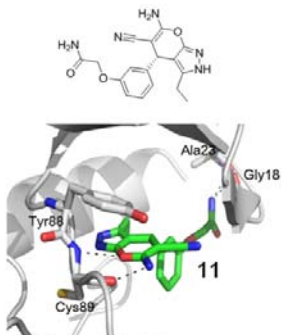
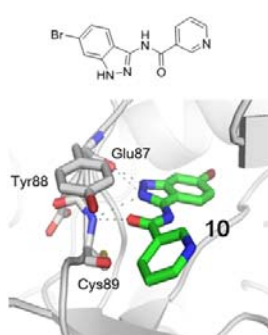
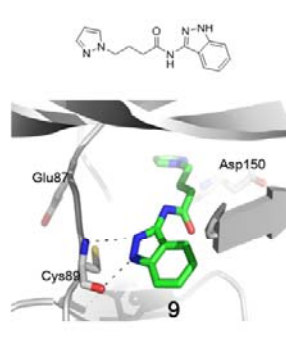
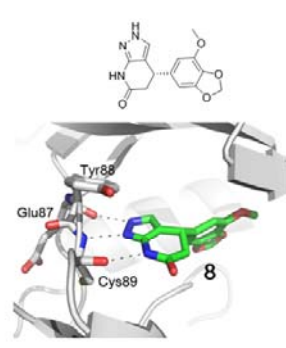
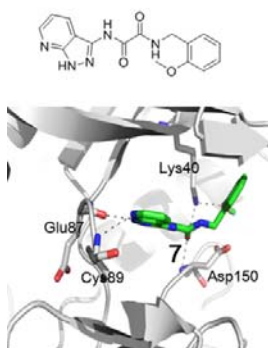
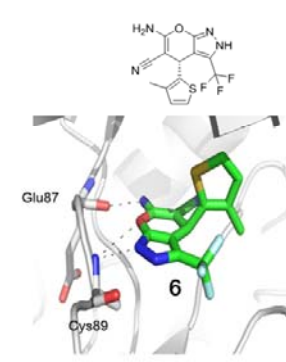
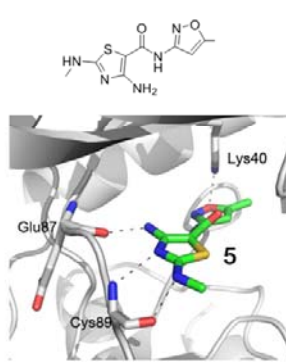
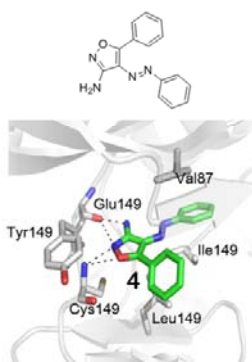
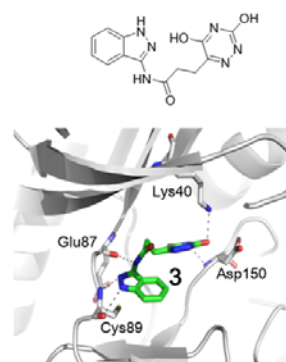
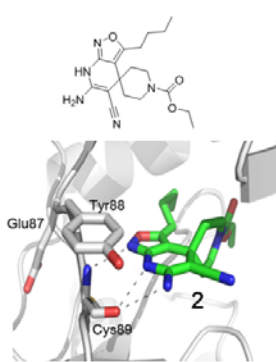
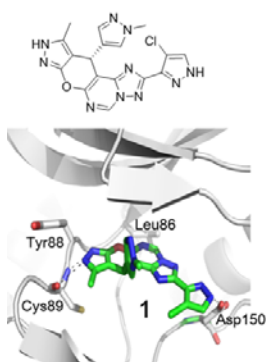
^a School of Life Sciences and Key Laboratory of Bio-resources and Eco-environment, Ministry of Education, State Key Laboratory of Biotherapy, Sichuan University, Chengdu, 610064, China

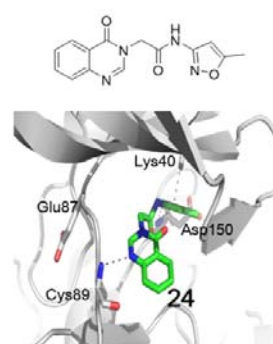
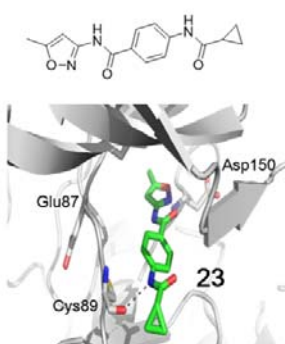
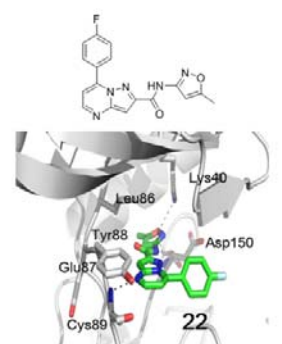
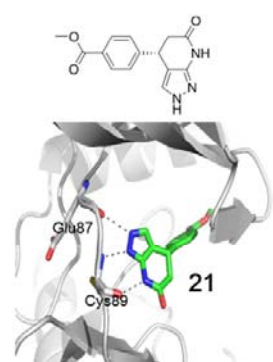
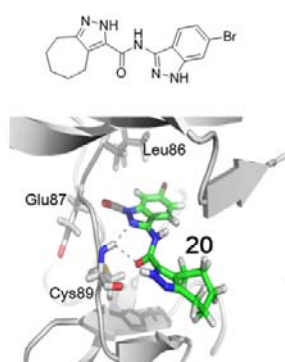
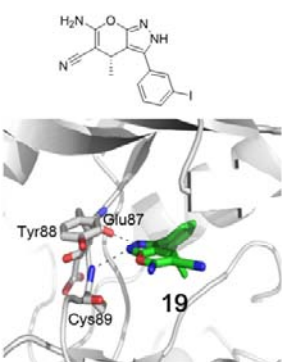
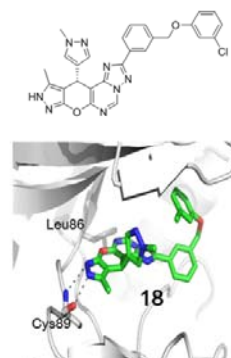
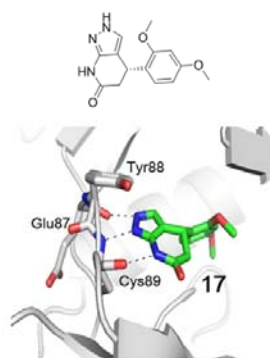
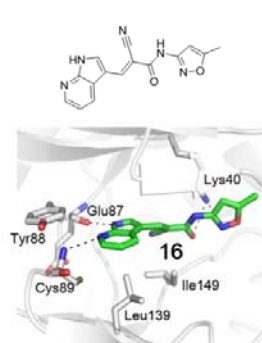
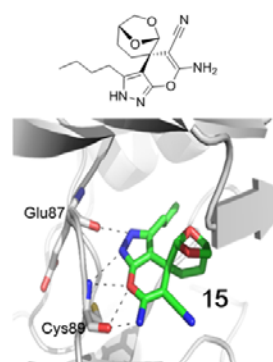
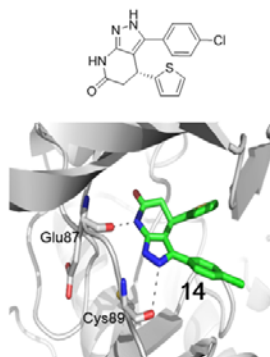
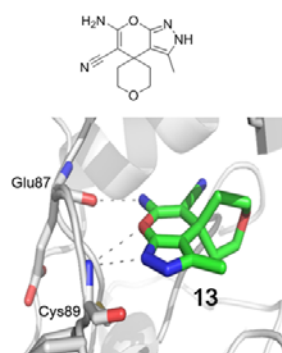
^bKey Laboratory of Drug Targeting and Drug Delivery System of Ministry of Education, West China School of Pharmacy, Sichuan University, Sichuan 610041, China.

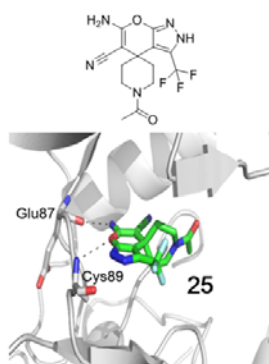
^c Laboratory of Biotherapy and Cancer Center, West China Hospital, West China Medical School, Sichuan University, Chengdu 610041, China.

* Correspondence: baojinku@scu.edu.cn

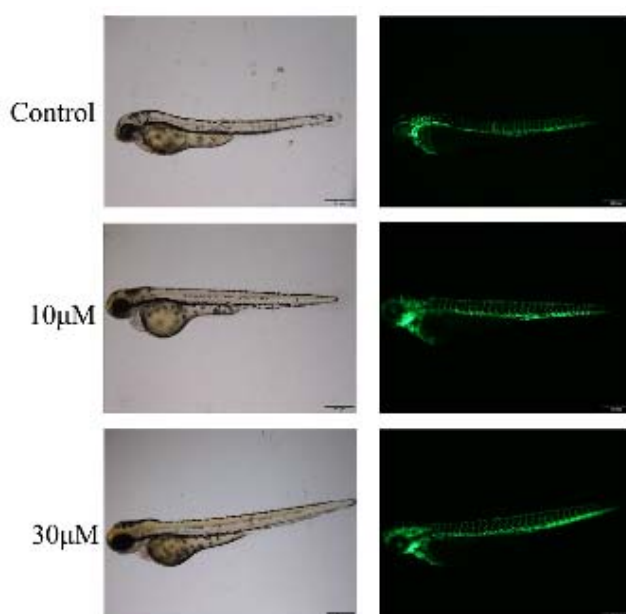
§ These authors contributed equally to this work.







Supplementary Figure S1. Binding modes of compound 1-25 in the active site of MELK.



Supplementary Figure S2. 72hpf zebrafish embryos treated with blank control, 10 and 30 μM compound 16.

Supplementary Table S1. Anti-viability activity of compound 4 and compound 16 against various cancer cells at 10 μ M. NI, no inhibition.

Cancer type	Cell line	4 inh%@10 μ M	16 inh%@10 μ M
Liver cancer	HepG2	1.66%	NI
Non-small cell lung cancer, NSCLC	A549	5.04%	8.75%
Non-small cell lung cancer, NSCLC	PC-9	4.34%	NI
Non-small cell lung cancer, NSCLC	HCC827	NI	NI
Non-small cell lung cancer, NSCLC	H1975	NI	10.38%
Melanoma	CHL-1	NI	4.29%
Melanoma	A375	1.65%	NI
Melanoma(<i>Mus</i>)	B16	4.87%	NI
Breast cancer	MCF-7	4.82%	16.10%
Breast cancer	MDA-MB-435	NI	NI
Cervical cancer	HeLa	12.11%	2.91%
Chronic myelogenous leukemia, CML	K562	NI	NI
Gastric cancer	HGC-27	5.89%	NI
Colorectal adenocarcinoma	HT29	NI	5.68%
Fibrosarcoma	HT1080	4.49%	8.34%
Ovarian cancer	SKOV3	NI	0.96%

Supplementary Table S2. The 12 used anticancer drugs and their targets

Compound	The main targets
Perifosine	AKT
Afatinib	EGFR , HER2
Apatinib	VEGFR2
Tivantinib	c-Met
Purvalanol B	CDK
Brigatinib	ALK
Sunitinib	PDGFR α/β , VEGFR1/2/3, KIT, FLT3, RET
Ruxolitinib	JAK
Regorafenib	KIT, PDGFR β , RAF, RET, VEGFR1/2/3
Dabrafenib	BRAF
Amlexanox	IKK
Trametinib	MEK

Supplementary Table S3. The effects of the 16 and 12 anti-cancer drugs combinations.

Cell Q value Compound	A549	MDA-MB-231	MDA-MB-435	H1975	HepG2	HCT116
Perifosine	0.996	0.940	0.665	0.639	1.126	1.092
Afatinib	1.097	0.881	0.929	0.983	1.134	0.972
Apatinib	1.047	0.865	0.625	0.263	0.896	0.823
Tivantinib	1.058	0.871	0.981	1.057	1.003	0.879
Purvalanol B	0.115	1.080	-0.508	0.739	0.684	1.138
Brigatinib	1.004	-0.039	1.135	1.003	0.971	1.012
Sunitinib	0.864	1.022	1.028	0.618	0.983	0.978
Ruxolitinib	0.012	0.968	0.455	0.607	1.115	0.056
Regorafenib	1.016	0.768	0.528	0.474	0.824	0.916
Dabrafenib	0.990	0.790	0.348	0.988	1.089	1.091
Amlexanox	0.368	0.639	0.215	0.237	0.894	0.649
Trametinib	0.950	1.128	1.120	0.797	1.004	0.968