

补充材料

靶向 PD-L1 蛋白的计算机辅助药物筛选

林开东 ¹⁾ 林晓倩 ¹⁾²⁾ 林绪波 ¹⁾

1) (北京航空航天大学, 医学科学与工程学院/生物与医学工程学院, 北京市生物医学工程高精尖创新中心, 北京 100191)

2) (北京航空航天大学沈元学院, 北京 100191)

表 S1 数据来源及整理情况

Table S1. Data source and curation.

来源 (PMID/US Patent)	分类模型-阳性样本	分类模型-阴性样本	回归模型样本
34055224 ^[S1]	0	11	5
35450381 ^[S2]	15	6	15
33741334 ^[S3]	12	0	12
34116264 ^[S4]	35	1	37
35405572 ^[S5]	37	0	39
34610423 ^[S6]	19	0	28
35231577 ^[S7]	18	0	18
34481337 ^[S8]	8	0	5
34954618 ^[S9]	12	29	14
31734021 ^[S10]	17	4	26
32388281 ^[S11]	17	1	17
33272783 ^[S12]	20	0	24
33280898 ^[S13]	0	21	10
33770574 ^[S14]	33	0	33
34147746 ^[S15]	21	0	19
34839997 ^[S16]	21	0	17
35429911 ^[S17]	9	16	11
37207535 ^[S18]	26	0	25
31298541 ^[S19]	7	1	9
30964291 ^[S20]	14	11	20
32667799 ^[S21]	34	45	29
32936638 ^[S22]	11	25	31

33186040 ^[S23]	24	2	35
33264007 ^[S24]	8	0	8
34037385 ^[S25]	48	0	48
34056906 ^[S26]	21	0	21
34115499 ^[S27]	36	1	41
34313116 ^[S28]	16	0	9
34670084 ^[S29]	4	0	7
34761679 ^[S30]	13	0	13
33938739 ^[S31]	31	0	34
35188766 ^[S32]	11	2	14
37159395 ^[S33]	21	2	25
36579489 ^[S34]	17	6	34
33786726 ^[S35]	15	0	15
34199417 ^[S36]	17	0	17
35684392 ^[S37]	2	0	3
US10308644 ^[S38]	271	0	0
US10618916 ^[S39]	66	0	0
US10669271 ^[S40]	34	0	0
US10806785 ^[S41]	166	0	0
US10882833 ^[S42]	14	0	17
US10882844 ^[S43]	45	0	4
US10941129 ^[S44]	21	0	23
US10975049 ^[S45]	19	2	20
US11078192 ^[S46]	42	11	58
US11384048 ^[S47]	33	2	38
US11407749 ^[S48]	25	0	0
US11459339 ^[S49]	137	0	137
US11465981 ^[S50]	13	0	0
US11535615 ^[S51]	21	0	0
US9850225 ^[S52]	269	1	23
US9872852 ^[S53]	284	0	14
PubChem Bioassay 2316	0	1930	0
合计	2130	2130	1099

表 S2 候选化合物的药物相似性检验

Table S2. Drug similarity test for candidate compounds.

候选化合物	MW	ALOGP	HBA	HBD	PSA	ROTB	AROM	QEPII
ZINC000012858649	261.712	2.9991	3	1	54.88	2	2	0.5044
ZINC000097015187	305.259	3.5328	3	1	65.78	2	2	0.5481
ZINC000015643758	289.338	3.7043	3	1	54.88	3	3	0.6199
ZINC000024776572	368.458	4.6964	4	1	60.45	5	3	0.8906
ZINC000133129569	390.461	3.9134	4	1	76.13	4	3	0.9036
ZINC000000423727	342.782	4.5643	4	1	64.36	4	3	0.8269
ZINC000097549003	441.553	4.7198	4	1	62.3	4	3	0.9156
ZINC000097549002	441.553	4.7198	4	1	62.3	4	3	0.9156
ZINC000020538424	395.484	4.5825	4	1	75.44	4	3	0.9079
ZINC000020538426	395.484	4.5825	4	1	75.44	4	3	0.9079
ZINC000065372236	384.432	2.7282	5	2	85.89	6	2	0.8467
ZINC000011916338	404.673	2.8567	5	1	89.02	3	2	0.7757
ZINC000004122995	389.411	4.4677	6	1	86.48	5	4	0.7634
ZINC000151357575	397.887	4.6248	3	1	62.3	3	3	0.8175
ZINC000952973088	341.396	2.7012	5	1	89.77	4	3	0.7081
ZINC000006781383	405.479	4.9362	5	1	73.34	5	4	0.7757
ZINC000426424415	363.439	1.4574	5	3	94.92	5	2	0.6773
ZINC000426424416	363.439	1.4574	5	3	94.92	5	2	0.6773
ZINC000057412202	325.799	4.5992	2	2	57.78	3	3	0.5389
ZINC000021721094	412.478	4.4997	5	1	85.59	4	5	0.5536
ZINC000012868656	288.35	4.3093	2	1	41.99	3	3	0.4734
ZINC000072427504	307.353	3.6514	3	3	78.01	3	3	0.6045
ZINC000047371782	356.389	3.4894	5	2	96.45	4	4	0.7722
ZINC000065455272	365.433	3.6953	5	2	76.39	7	3	0.9248
ZINC000058406518	310.279	3.0115	4	2	66.91	4	2	0.7374
ZINC000299781094	346.452	3.2516	4	1	60.45	6	2	0.7978
ZINC000299781068	346.452	3.2516	4	1	60.45	6	2	0.7978
ZINC000057412356	346.217	4.9442	2	2	57.78	3	3	0.5496
ZINC000038580264	261.712	3.0638	3	1	54.88	2	2	0.5047
ZINC000004881112	372.808	4.5729	5	1	73.59	5	3	0.9134
ZINC000000830435	363.329	4.5567	6	1	111.41	4	4	0.6974

ZINC000952968697	334.383	2.7102	5	1	85.59	4	3	0.7953
ZINC000005002017	348.402	4.4813	4	1	64.36	4	3	0.8316
ZINC000032932427	397.482	4.7804	4	1	72.7	3	4	0.7635
ZINC000000830413	364.317	3.9517	7	1	124.3	4	4	0.6007
ZINC000426443036	361.467	3.1391	4	1	63.69	5	2	0.8083
ZINC000175468610	393.468	4.6358	4	1	71.53	4	3	0.9048
ZINC000050344408	388.876	4.7412	4	1	60.45	7	3	0.9108
ZINC000004063088	380.86	4.9674	4	1	67.77	3	4	0.7499
ZINC000002056866	419.353	4.2669	8	1	154.3	5	4	0.5165
ZINC000003482123	226.279	2.9507	2	1	41.99	2	2	0.3708
ZINC000000830439	377.356	4.8651	6	1	111.41	4	4	0.7057
ZINC000170866712	363.458	2.7898	4	1	54.46	5	2	0.7839
ZINC000003908064	329.743	3.6509	5	1	77.25	4	3	0.8555
ZINC000952973550	356.455	2.5609	5	1	75.94	5	3	0.7419
ZINC000828150401	324.344	1.1365	5	1	94.7	3	3	0.6394
ZINC000170595786	352.438	2.9443	4	1	65.54	4	2	0.7566
ZINC000003909439	338.794	4.6543	3	1	55.13	2	3	0.6055
ZINC000019146880	287.319	2.4709	5	1	77.25	3	2	0.7003
ZINC000019146877	287.319	2.4709	5	1	77.25	3	2	0.7003
ZINC000064987401	362.433	3.7535	4	1	76.36	2	3	0.7755
ZINC000021874692	437.544	3.0454	4	2	96.33	4	2	0.8361
ZINC000021874694	437.544	3.0454	4	2	96.33	4	2	0.8361
ZINC000334155018	272.304	2.7675	4	1	64.36	3	2	0.6583
ZINC000952864005	325.372	3.1542	5	1	85.84	4	3	0.7908
ZINC000003908573	328.755	4.2613	4	2	75.36	3	3	0.7935
ZINC000013121834	327.771	3.9964	3	3	78.01	3	3	0.6177
ZINC000021723762	380.81	4.7495	3	1	59.29	3	4	0.7093
ZINC000002911784	474.59	4.2906	7	1	83.48	5	4	0.6198
ZINC000225535926	344.418	3.9961	4	1	58.12	4	3	0.8136
ZINC000057413133	355.369	3.7937	4	2	76.24	5	3	0.8789
ZINC000019770413	283.287	3.1987	5	1	81.16	3	3	0.7705
ZINC000253473522	374.44	4.5587	4	1	60.45	6	3	0.8708
ZINC000253473523	374.44	4.5587	4	1	60.45	6	3	0.8708
ZINC000005573911	351.406	3.9333	5	1	77.25	6	3	0.9040

ZINC000065469976	328.412	3.0489	4	2	59.59	7	2	0.7615
ZINC000072427490	335.407	4.2683	3	3	78.01	3	3	0.6231
ZINC000096344675	351.406	2.7728	3	3	87.3	4	2	0.5985

注: MW, ALOGP, HBA, HBD, PSA, ROTB和AROM分别代表化合物的分子质量、脂水表面分配系数、氢键受体、氢键受体、极表面积、可旋转化学键数和芳香环数等结构性质。

Note: MW, ALOGP, HBA, HBD, PSA, ROTB and AROM respectively represent the molecular weight, lipid water surface partition coefficient, hydrogen bond receptor, hydrogen bond receptor, polar surface area, rotatable chemical bond number and aromatic ring number of the compound.

表 S3 候选化合物的 ADMET 检验

Table S3. ADMET test for candidate compounds.

候选化合物	HIA	VD	CYP2C9-sub	$T_{1/2}$	hERG
ZINC000065455272	0.004	1.674	0.562	0.646	0.757
ZINC000097549003	0.004	0.69	0.852	0.047	0.013
ZINC000097549002	0.004	0.69	0.852	0.047	0.013
ZINC000004881112	0.004	0.478	0.873	0.081	0.207
ZINC000050344408	0.002	0.663	0.772	0.053	0.231
ZINC000020538424	0.003	0.713	0.829	0.043	0.03
ZINC000020538426	0.003	0.713	0.829	0.043	0.03
ZINC000175468610	0.003	0.395	0.79	0.048	0.083
ZINC000005573911	0.003	0.709	0.763	0.56	0.022
ZINC000133129569	0.006	0.393	0.745	0.037	0.034
ZINC000024776572	0.003	0.28	0.869	0.127	0.117
ZINC000057413133	0.005	0.647	0.913	0.119	0.161
ZINC000253473522	0.003	1.418	0.413	0.091	0.863
ZINC000253473523	0.003	1.411	0.45	0.094	0.667
ZINC000003908064	0.004	0.646	0.773	0.156	0.095
ZINC000065372236	0.002	1.01	0.476	0.718	0.331
ZINC000021874692	0.005	1.121	0.554	0.075	0.008
ZINC000021874694	0.013	0.858	0.82	0.427	0.009
ZINC000005002017	0.003	3.913	0.736	0.191	0.024
ZINC000000423727	0.004	0.502	0.832	0.09	0.169
ZINC000151357575	0.004	0.752	0.848	0.073	0.046
ZINC000225535926	0.005	1.747	0.441	0.258	0.624
ZINC000426443036	0.003	0.955	0.156	0.491	0.038
ZINC000299781094	0.003	0.919	0.134	0.331	0.131

ZINC000299781068	0.003	0.733	0.101	0.388	0.35
ZINC000952968697	0.007	1.946	0.227	0.464	0.124
ZINC000003908573	0.004	0.258	0.837	0.129	0.04
ZINC000952864005	0.004	1.3	0.429	0.521	0.019
ZINC000170866712	0.002	1.441	0.429	0.042	0.051
ZINC000006781383	0.004	0.599	0.898	0.077	0.08
ZINC000011916338	0.043	0.539	0.497	0.208	0.141
ZINC000064987401	0.006	1.894	0.898	0.263	0.029
ZINC000047371782	0.008	1.992	0.92	0.317	0.089
ZINC000019770413	0.004	1.62	0.342	0.584	0.175
ZINC000032932427	0.007	0.857	0.35	0.303	0.602
ZINC000004122995	0.005	0.898	0.892	0.233	0.217
ZINC000065469976	0.004	2.154	0.583	0.811	0.529
ZINC000170595786	0.006	1.767	0.233	0.27	0.302
ZINC000004063088	0.004	1.578	0.78	0.092	0.045
ZINC000952973550	0.008	1.862	0.542	0.551	0.057
ZINC000058406518	0.004	1.27	0.892	0.21	0.13
ZINC000021723762	0.005	0.836	0.793	0.106	0.177
ZINC000952973088	0.013	1.649	0.444	0.299	0.007
ZINC000000830439	0.006	1.161	0.774	0.132	0.624
ZINC000019146880	0.003	0.775	0.2	0.52	0.024
ZINC000019146877	0.003	0.775	0.2	0.52	0.024

注：HIA代表人体肠道吸收性，其数值小于0.3代表化合物可被良好吸收，大于0.7代表化合物不可被良好吸收；VD是描述化合物体内分布的重要参数，其数值介于0.04至20之间代表化合物可在体内均匀分配；CYP2C9-sub代表化合物可作为CYP2C9底物被代谢的概率； $T_{1/2}$ 描述化合物体内清除率和分配体积，其数值小于0.3代表化合物可被良好排泄至体外，大于0.7代表化合物不可被良好排泄至体外；hERG代表化合物阻断心脏电压门控钾通道产生的心脏毒性，其数值小于0.3代表化合物不会显著产生心脏毒性，大于0.7代表化合物会显著产生心脏毒性^[S54]。

Note: HIA represents human intestinal absorption, with a value less than 0.3 indicating that the compound can be well absorbed, and a value greater than 0.7 indicating that the compound cannot be well absorbed; VD is an important parameter that describes the distribution of compounds in the body, with values between 0.04 and 20 indicating that compounds can be evenly distributed in the body; CYP2C9-sub represents the probability that a compound can be metabolized as a CYP2C9 substrate; $T_{1/2}$ describes the clearance rate and distribution volume of a compound in vivo. Values below 0.3 indicate that the compound can be well excreted into the body, while values above 0.7 indicate that the compound cannot be well excreted into the body; hERG represents the cardiotoxicity caused by the compound blocking the cardiac voltage gated potassium channel. A value less than 0.3 indicates that the compound will not significantly produce cardiotoxicity, while a value greater than 0.7 indicates that the compound will significantly produce cardiotoxicity^[S54].

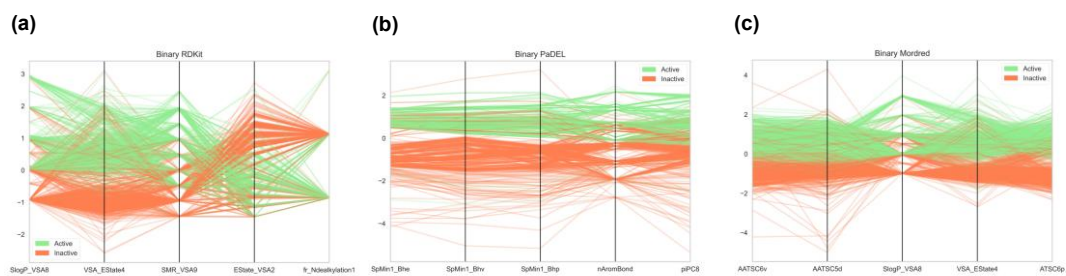


图 S1 高权重描述符特征在两类样本间的分布差异

(a) RDKit; (b) PaDEL; (c) Mordred

Fig. S1. Distribution differences of high weight descriptor features between active **and** inactive compounds:(a) RDKit; (b) PaDEL; (c) Mordred.

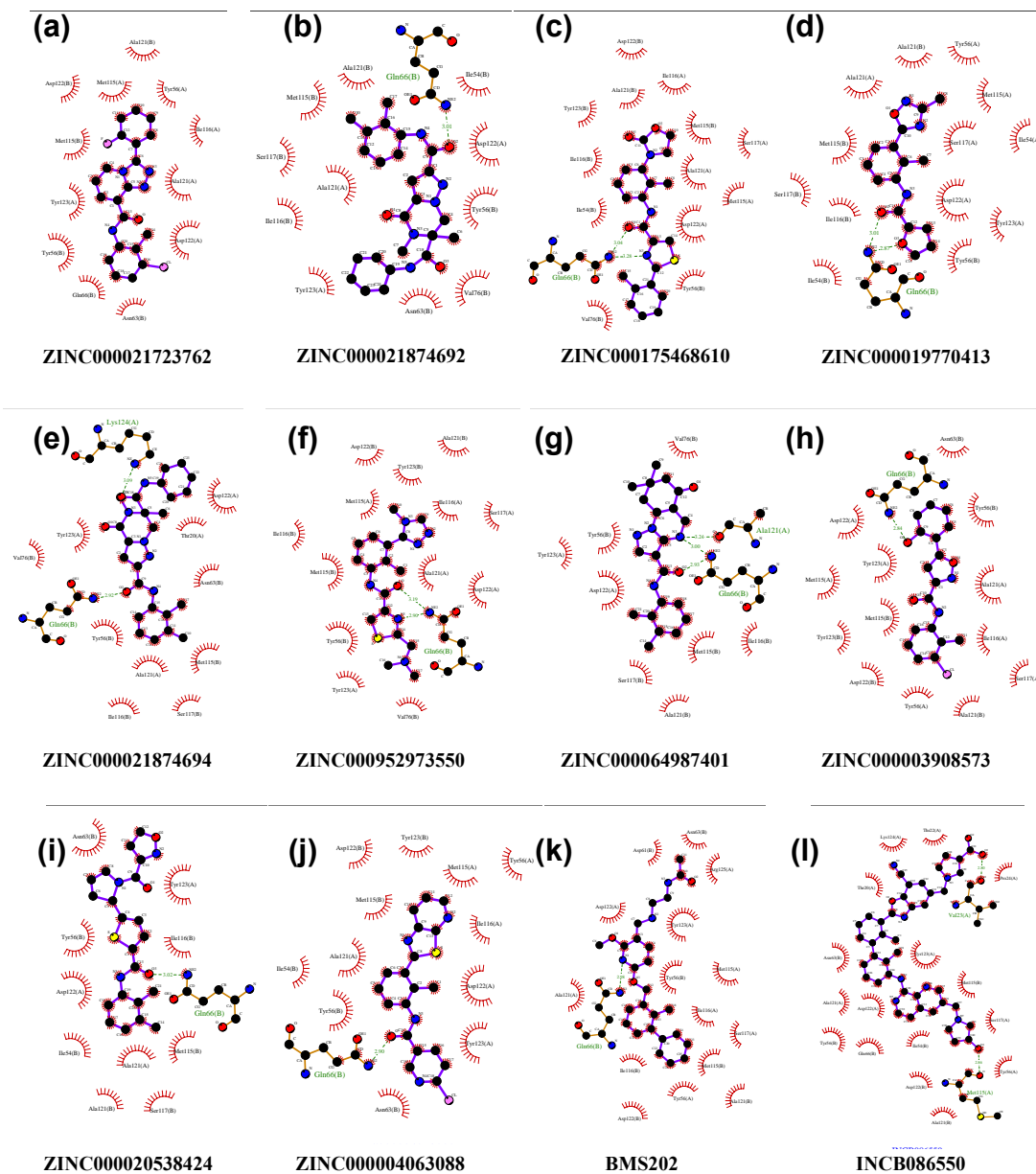


图 S2 配体与 PD-L1 结合相互作用 (a) ZINC000021723762; (b) ZINC000021874692; (c) ZINC000175468610; (d) ZINC000019770413; (e) ZINC000021874694; (f) ZINC000952973550; (g) ZINC000064987401; (h) ZINC000003908573; (i) ZINC000020538424; (j) ZINC000004063088; (k) BMS202; (l) INCB086550. 碳、氧、氮、硫和卤素原子分别以黑、红、蓝、黄和粉着色, 红色扇状图形代表参与疏水性相互作用的氨基酸残基, 绿色虚线代表氢键相互作用

Fig. S2. Ligand binding interaction with PD-L1: (a) ZINC000021723762; (b) ZINC000021874692; (c) ZINC000175468610; (d) ZINC000019770413; (e) ZINC000021874694; (f) ZINC000952973550; (g) ZINC000064987401; (h) ZINC000003908573; (i) ZINC000020538424; (j) ZINC000004063088; (k) BMS202; (l) INCB086550.

Carbon, oxygen, nitrogen, sulfur, and halogen atoms are colored in black, red, blue, yellow, and pink, respectively. The red fan-shaped pattern represents amino acid residues involved in hydrophobic interactions, and the green dashed line represents hydrogen bonding interactions.

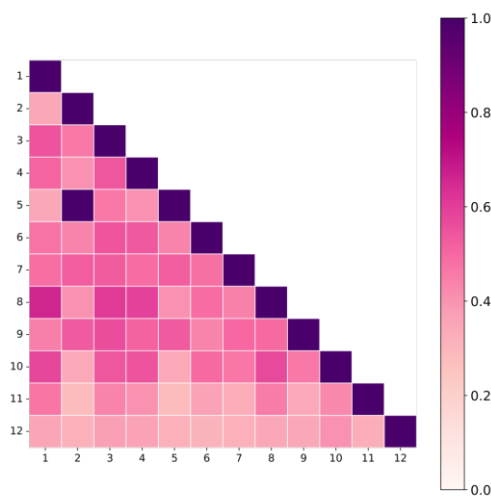


图 S3 10 种候选化合物及 2 种对照化合物间的结构相似性

Fig. S3. Structural similarity between 10 candidate compounds and 2 control compounds.

参考文献

- [S1] Butera R, Ważyńska M, Magiera-Mularz K, Plewka J, Musielak B, Surmiak E, Sala D, Kitel R, de Bruyn M, Nijman H W, Elsinga P H, Holak T A, Dänling A 2021 *ACS Med. Chem. Lett.* **12** 768
- [S2] Lu L, Qi Z, Wang T, Zhang X, Zhang K, Wang K, Cheng Y, Xiao Y, Li Z, Jiang S 2022 *ACS Med. Chem. Lett.* **13** 586
- [S3] Cao H, Cheng B, Liu T, Chen J 2021 *Biochem. Pharmacol.* **188** 114522
- [S4] Dai X, Wang K, Chen H, Huang X, Feng Z 2021 *Bioorg. Chem.* **114** 105034
- [S5] Gao Y, Wang H, Shen L, Xu H, Deng M, Cheng M, Wang J 2022 *Bioorg. Chem.* **123** 105769
- [S6] Huang X, Chen H, Dai X, Xu M, Wang K, Feng Z 2021 *Bioorg. Med. Chem. Lett.* **52** 128403
- [S7] Meng Y, Chu C, Niu X, Cheng L, Wu D, Liu L, Zhang S, Li T, Hou Y, Liu Y, Qin M 2022 *Bioorg. Med. Chem. Lett.* **63** 128647
- [S8] Fang L, Tian J, Zhang K, Zhang X, Liu Y, Cheng Z, Zhou J, Zhang H 2021 *Bioorg. Med. Chem.* **46** 116370
- [S9] Zhang M, Liu J, Wang Y, Wang P, Morris-Natschke S, Lee K H 2022 *Bioorg. Med. Chem.* **54** 116579
- [S10] Qin M, Cao Q, Wu X, Liu C, Zheng S, Xie H, Tian Y, Xie J, Zhao Y, Hou Y, Zhang X, Xu B, Zhang H, Wang X 2020 *Eur. J. Med. Chem.* **186** 111856
- [S11] Cheng B, Ren Y, Cao H, Chen J 2020 *Eur. J. Med. Chem.* **199** 112377
- [S12] Yang Y, Wang K, Chen H, Feng Z 2021 *Eur. J. Med. Chem.* **211** 113001
- [S13] Yang X, Cheng B, Xiao Y, Xue M, Liu T, Cao H, Chen J 2021 *Eur. J. Med. Chem.* **213** 113058
- [S14] Chen H, Wang K, Yang Y, Huang X, Dai X, Feng Z 2021 *Eur. J. Med. Chem.* **217** 113377
- [S15] Wu Y, Zhang Y, Guo Y, Pan Z, Zhong S, Jin X, Zhuang W, Chen S, Gao J, Huang W, Dong X, Che J 2021 *Eur. J. Med. Chem.* **223** 113637
- [S16] Wang Y, Kun H, Gao Y, Yuan D, Ling L, Liu J, Wu S, Chen R, Li H, Xiong Y, Liu H, Ma J 2022 *Eur. J. Med. Chem.* **229** 113998
- [S17] Le Biannic R, Magnez R, Klupsch F, Leleu-Chavain N, Thiroux B, Tardy M, El Bouazzati H,

- Dezitter X, Renault N, Vergoten G, Bailly C, Quesnel B, Thuru X, Millet R 2022 *Eur. J. Med. Chem.* **236** 114343
- [S18] Cai S, Wang K, Qi Z, Ye K, Zhou X, Jiang S, Zhang K, Zhang X, Wang T 2023 *Eur. J. Med. Chem.* **256** 115468
- [S19] Qin M, Cao Q, Zheng S, Tian Y, Zhang H, Xie J, Xie H, Liu Y, Zhao Y, Gong P 2019 *J. Med. Chem.* **62** 4703
- [S20] Basu S, Yang J, Xu B, Magiera-Mularz K, Skalniak L, Musielak B, Kholodovych V, Holak T A, Hu L 2019 *J. Med. Chem.* **62** 7250
- [S21] Cheng B, Ren Y, Niu X, Wang W, Wang S, Tu Y, Liu S, Wang J, Yang D, Liao G, Chen J 2020 *J. Med. Chem.* **63** 8338
- [S22] Konieczny M, Musielak B, Kocik J, Skalniak L, Sala D, Czub M, Magiera-Mularz K, Rodriguez I, Myrcha M, Stec M, Siedlar M, Holak T A, Plewka J 2020 *J. Med. Chem.* **63** 11271
- [S23] Guo J, Luo L, Wang Z, Hu N, Wang W, Xie F, Liang E, Yan X, Xiao J, Li S 2020 *J. Med. Chem.* **63** 13825
- [S24] Cheng B, Wang W, Niu X, Ren Y, Liu T, Cao H, Wang S, Tu Y, Chen J, Liu S, Yang X, Chen J 2020 *J. Med. Chem.* **63** 15946
- [S25] Qin M, Meng Y, Yang H, Liu L, Zhang H, Wang S, Liu C, Wu X, Wu D, Tian Y, Hou Y, Zhao Y, Liu Y, Xu C, Wang L 2021 *J. Med. Chem.* **64** 5519
- [S26] Wang T, Cai S, Wang M, Zhang W, Zhang K, Chen D, Li Z, Jiang S 2021 *J. Med. Chem.* **64** 7390
- [S27] OuYang Y, Gao J, Zhao L, Lu J, Zhong H, Tang H, Jin S, Yue L, Li Y, Guo W, Xu Q, Lai Y 2021 *J. Med. Chem.* **64** 7646
- [S28] Liu L, Yao Z, Wang S, Xie T, Wu G, Zhang H, Zhang P, Wu Y, Yuan H, Sun H 2021 *J. Med. Chem.* **64** 8391
- [S29] Muszak D, Surmiak E, Plewka J, Magiera-Mularz K, Kocik-Krol J, Musielak B, Sala D, Kitel R, Stec M, Weglarczyk K, Siedlar M, Dömling A, Skalniak L, Holak T A 2021 *J. Med. Chem.* **64** 11614
- [S30] Russomanno P, Assoni G, Amato J, D'Amore V M, Scaglia R, Brancaccio D, Pedrini M, Polcaro G, La Pietra V, Orlando P, Falzoni M, Cerofolini L, Giuntini S, Fragai M, Pagano B, Donati G, Novellino E, Quintavalle C, Condorelli G, Sabbatino F, Seneci P, Arosio D, Pepe S, Marinelli L 2021 *J. Med. Chem.* **64** 16020
- [S31] Song Z, Liu B, Peng X, Gu W, Sun Y, Xing L, Xu Y, Geng M, Ai J, Zhang A 2021 *J. Med. Chem.* **64** 16687
- [S32] Wang T, Cai S, Cheng Y, Zhang W, Wang M, Sun H, Guo B, Li Z, Xiao Y, Jiang S 2022 *J. Med. Chem.* **65** 3879
- [S33] Sun C, Yin M, Cheng Y, Kuang Z, Liu X, Wang G, Wang X, Yuan K, Min W, Dong J, Hou Y, Hu L, Zhang G, Pei W, Wang L, Sun Y, Yu X, Xiao Y, Deng H, Yang P 2023 *J. Med. Chem.* **66** 2064
- [S34] Jing T, Zhang Z, Kang Z, Mo J, Yue X, Lin Z, Fu X, Liu C, Ma H, Zhang X, Hu W 2023 *J. Med. Chem.* **66** 6811
- [S35] Zhu P, Zhang J, Yang Y, Wang L, Zhou J, Zhang H 2022 *Mol. Divers.* **26** 245
- [S36] Zhang H, Xia Y, Yu C, Du H, Liu J, Li H, Huang S, Zhu Q, Xu Y, Zou Y 2021 *Molecules* **26** 3347
- [S37] Shaabani S, Gadina L, Surmiak E, Wang Z, Zhang B, Butera R, Zarganes-Tzitzikas T, Rodriguez I, Kocik-Krol J, Magiera-Mularz K, Skalniak L, Dömling A, Holak T A 2022 *Molecules* **27** 3454
- [S38] Wu L, Li J, Yao W 2019 *US Patent* 103 086 44 B2
- [S39] Wu L, Xiao K, Yao W 2020 *US Patent* 106 189 16 B2
- [S40] Wu L, Li J, Yao W 2020 *US Patent* 106 692 71 B2

- [S41] Lu L, Zhu W, Qian D-Q, Xiao K 2020 *US Patent* 108 067 85 B2
- [S42] Feng Z, Chen X, Yang Y, Zhou C, Lai F, Ji M, Jin X, Xue N, Zheng Y, Chen H, Li L 2021 *US Patent* 108 828 33 B2
- [S43] Yeung K-S, Grant-Young K A, Sun L-Q, Langley D R, Laurent D R S, Scola P M 2021 *US Patent* 108 828 44 B2
- [S44] Feng Z, Chen X, Yang Y, Lai F, Ji M, Zhang L, Zheng Y, Xue N, Wang K, Li L 2021 *US Patent* 109 411 29 B2
- [S45] Feng Z, Chen X, Yang Y, Zheng Y, Lai F, Ji M, Zhou C, Zhang L, Wang K, Xue N, Li L 2021 *US Patent* 109 750 49 B2
- [S46] Wang Y, Xu Z, Wu T, He M, Zhang N 2021 *US Patent* 110 781 92 B2
- [S47] Wang Y, Zhang N, Wu T, He M 2022 *US Patent* 113 840 48 B2
- [S48] Wu L, Shen B, Li J, Li Z, Liu K, Zhang F, Yao W 2022 *US Patent* 114 077 49 B2
- [S49] Yang F, Zhang Y, Ying H, Yu H, Chen Z, Xu Y 2022 *US Patent* 114 593 39 B2
- [S50] Wu L, Yu Z, Zhang F, Yao W 2022 *US Patent* 114 659 81 B2
- [S51] Lajkiewicz N, Wu L, Yao W 2022 *US Patent* 115 356 15 B2
- [S52] Chupak L S, Ding M, Martin S W, Zheng X, Hewawasam P, Connolly T P, Xu N, Yeung K-S, Zhu J, Langley D R, Scola P M 2017 *US Patent* 985 022 5 B2
- [S53] Chupak L S, Zheng X 2016 *US Patent* 987 285 2 B2
- [S54] Xiong G, Wu Z, Yi J, Fu L, Yang Z, Hsieh C, Yin M, Zeng X, Wu C, Lu A, Chen X, Hou T, Cao D 2021 *Nucleic Acids Res.* **49** W5