

SUPPLEMENT

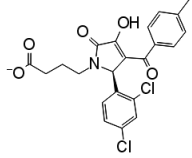
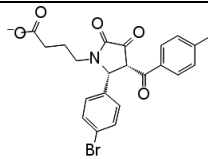
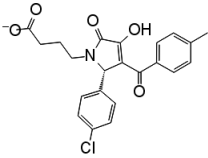
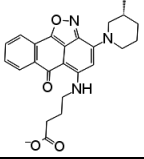
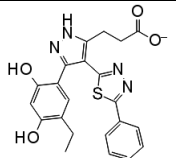
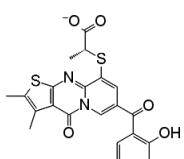
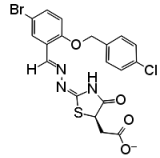
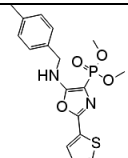
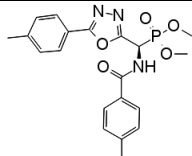
Discovery and Design of Novel Small Molecule GSK-3 Inhibitors Targeting the Substrate Binding Site

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Contents

Tables S1-S4

Compound	Zinc Number	Structure	Glide Score (Kcal/mol)
1-1	ZINC 08438527		-7.86
1-2	ZINC 17124459		-7.78
1.3	ZINC 19923071		-7.53
1-4	ZINC02457285		-7.38
1-5	ZINC09509071		-7.38
1-6	ZINC03426092		-7.29
1-7	ZINC09763113		7.19
1-8	ZINC16752220		-4.73
1-9	ZINC26842591		-4.55

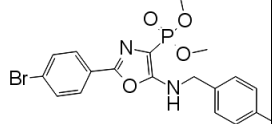
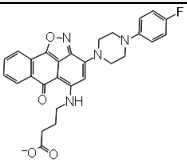
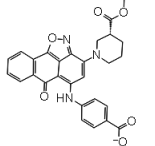
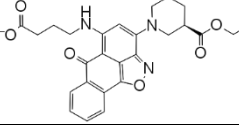
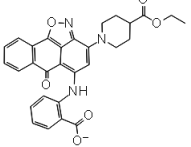
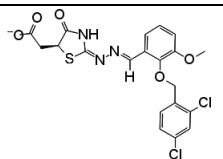
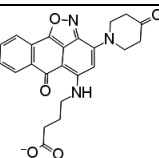
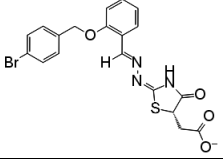
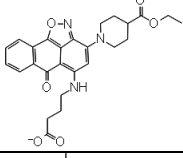
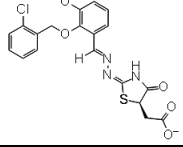
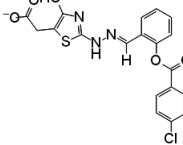
<i>1-10</i>	ZINC08915175		-4.01
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Table S1: 1st cycle hits. Identified hits are listed along with their Glide score

Name	Zinc Number	Structure	Glide Score (Kcal/mol)	Related analogue to
2-1	ZINC03742058		-12.38	1-4
2-2	ZINC09780556		-11.87	1-4
2-3	ZINC04128291		-11.87	1-4
2-4	ZINC09780536		-11.704	1-4
2-5	ZINC08722310		-11.44	1-4
2-6	ZINC02457300		-11.13	1-4
2-7	ZINC09763193		-10.2	1-6
2-8	ZINC04128340		-7.58	1-4
2-9	ZINC08722309		-7.77	1-7
2-10	ZINC16115790		-7.32	1-7

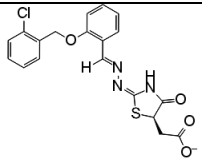
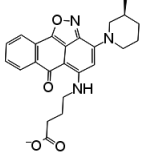
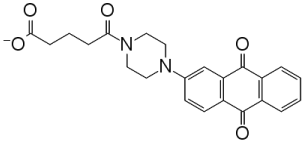
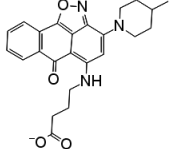
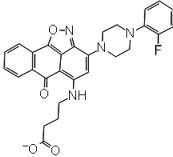
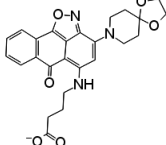
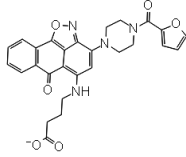
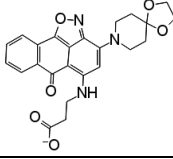
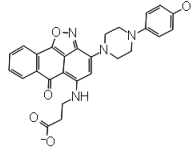
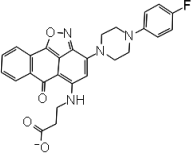
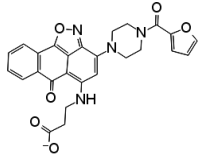
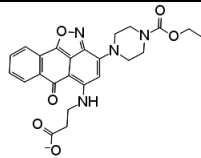
2-11	ZINC15857451		-7.13	<i>1-7</i>
2-12	ZINC02457283			<i>1-4</i>

Table S2: 2nd cycle hits. Hits were identified by searching analogues with 90% similarity to compounds *1-4*, *1-6*, and *1-7*. Hits are sorted by score values.

Name	Zinc Number	Structure	Glide Score (Kcal/Mol)
3-1	ZINC04535276		-12.907
3-2	ZINC02457282		-11.894
3-3	ZINC03742056		-12.5739
3-4	ZINC02457288		-12.53
3-5	ZINC03742059		-13.649
3-6	ZINC02457314		-11.464
3-7	ZINC20108011		-15.535
3-8	ZINC02494295		-12.218
3-9	ZINC02494297		-14.534
3-10	ZINC03958636		-12.353

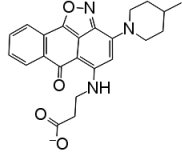
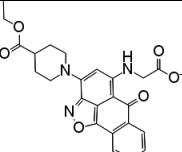
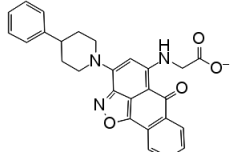
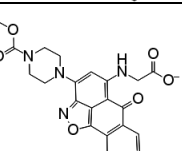
3-11	ZINC02457319		-12.721
3-12	ZINC58012534		-11.08
3-13	ZINC03742061		-12.14
3-14	ZINC58012537		-11.272

Table S3: 3rd cycle hits. The search identified molecules bearing anthracene/piperazine/ cyclohexane substructures and filtered by docking into the GSK-3 substrate binding site.

Table S4: GSK-3 ATP competitive inhibitor used in PCA analysis

ChEMBL #	Name
CHEMBL102714	SB-216763
CHEMBL322970	SB-415286
CHEMBL1080901	CHIR-99021
CHEMBL259850	AR-A014418
CHEMBL1969664	AZD1080
CHEMBL2178570	AZD4818
CHEMBL405759	TWS119
CHEMBL209849	Indirubin-3-Acetoxime
CHEMBL126077	indirubin-3'-monoxime
CHEMBL336961	1-Azakenpaullone
CHEMBL50894	Alsterpaullone
CHEMBL7463	GF-109203
CHEMBL296586	Kenpaullone
CHEMBL259638	Cazupaullone
CHEMBL409450	6Bio
CHEMBL3747661	VP2.51
CHEMBL362558	LY-2090314
CHEMBL300138	LY317615
CHEMBL2177167	Pyrazine analogue
CHEMBL2182002	Pyrazine analogue
CHEMBL2386102	Melemiede
CHEMBL2163772	dihydroxy-1-aza-9-oxafluorene
CHEMBL319244	Cafeic acid
CHEMBL388978	Staurosporine
CHEMBL50498	Meridianin A
CHEMBL584304	XD-4241
CHEMBL4073799	Dibromocantherelline
CHEMBL75680	Aloisine A
CHEMBL3621636	Hymenidin