

# The antiepileptic drug carbamazepine binds to a novel pocket on the Wnt receptor Frizzled-8

## Supporting Information

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### Content

List of screen compounds

Table S1

Size-exclusion chromatography of FZD\_CRD profiles

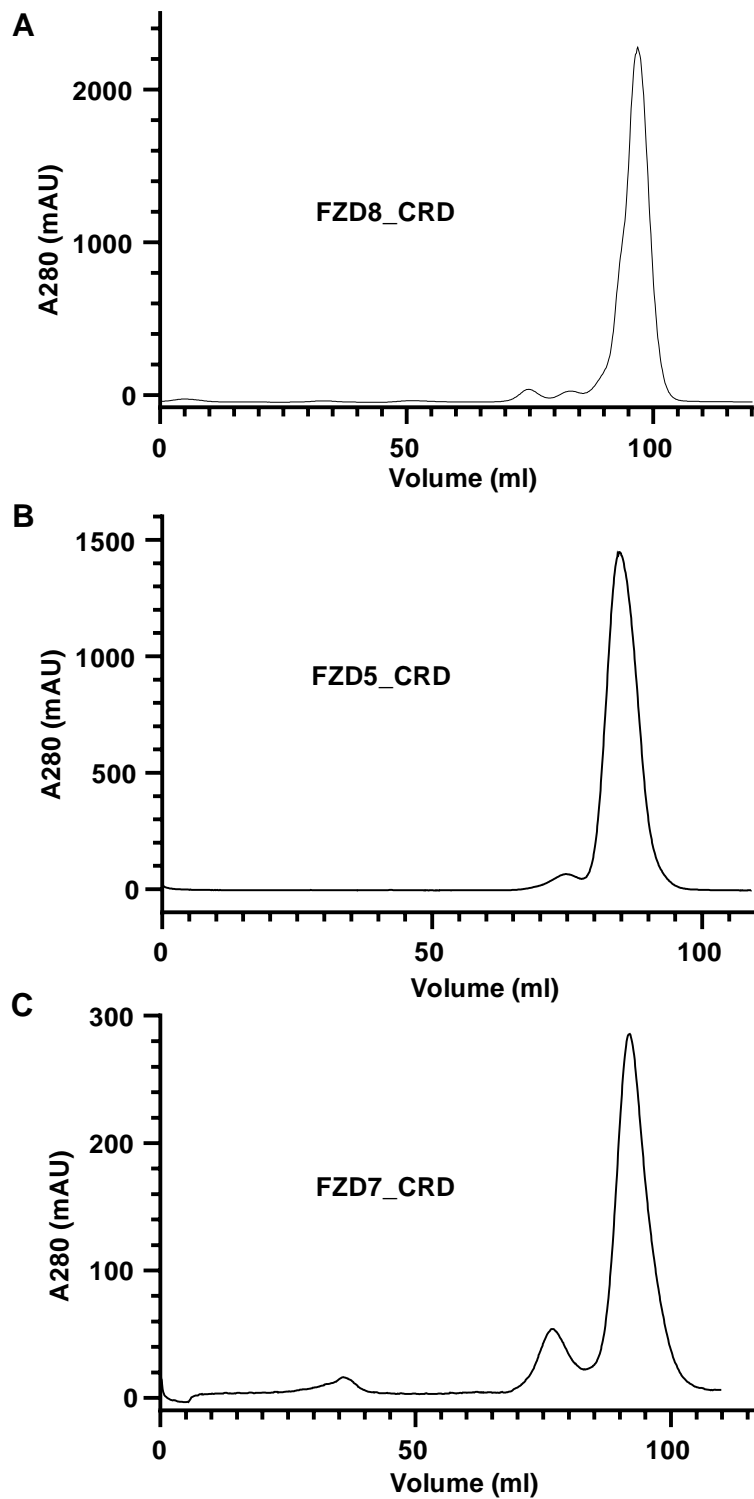
Fig.S1

Supplementary table S1 List of screen compounds			
#	Source	Chemical Name	SMILES
1	Maybridge RJC 02428	3,3'-Dicarboxy-4,4'-difurazan hydrate	<chem>c1(c(non1)C(=O)O)c2c(non2)C(=O)O.O</chem>
2	Maybridge RJF 01462	N1-phenyl-2-{2-[5-(3-nitrophenyl)-2H-1,2,3,4-tetraazol-2-yl]acetyl}hydrazine-1-carboxamide	<chem>c1ccc(cc1)NC(=O)NNC(=O)Cn2nc(nn2)c3cccc(c3)[N+](=O)[O-]</chem>
3	Maybridge SPB 03687	methyl 5-methyl-4-(1H-3-pyrazolyl)-3-isoxazolecarboxylate	<chem>CC1=C(C(=NN1)Cl)[N+](=O)[O-]</chem>
4	Maybridge SPB 00452	3-[4-(tert-butyl)phenyl]-1,2,4-oxadiazole-5-carbohydrazide	<chem>CC(C)(C)c1ccc(cc1)c2noc(n2)C(=O)NN</chem>
5	MaybridgeBTB 00676	N1-(4-methylphenyl)-2-[(2,4-dinitrophenyl)thio]acetamide	<chem>CC1=CC=C(C=C1)NC(=O)CSC2=C(C=C(C=C2)[N+](=O)[O-])[N+](=O)[O-]</chem>
6	Maybridge BTB 13947	1,3-dimethyl-8-nitro-2,3,6,7-tetrahydro-1H-purine-2,6-dione hydrate	<chem>CN1C2=C(C(=O)N(C1=O)C)NC(=N2)[N+](=O)[O-]</chem>
7	Maybridge BTB 10102	ethyl 5-hydroxy-6-nitro-4-oxo-8-propyl-4H-chromene-2-carboxylate	<chem>CCCC1=CC(=C(C2=C1OC(=CC2=O)C(=O)OCC)O)[N+](=O)[O-]</chem>
8	Maybridge RJF 01440	1-(4-chlorophenyl)-2-[5-(3-nitrophenyl)-2H-1,2,3,4-tetraazol-2-yl]ethan-1-one	<chem>C1=CC(=CC=C1)[N+](=O)[O-]C2=NN(N=N2)CC(=O)C3=CC=C(C=C3)Cl</chem>
9	Maybridge PHG 00900	2-({4-[(1,3-dioxo-2,3-dihydro-1H-benzo[de]isoquinolin-2-yl)methyl]cyclohexyl)methyl}-2,3-dihydro-1H-benzo[de]isoquinoline-1,3-dione hydrate	<chem>C1C2=CC=CC3=C2C(=CC=C3)CN1</chem>
10	Maybridge DFP 00242	2-[4-(tert-butyl)phenyl]-5-(3-nitrophenyl)-1,3,4-oxadiazole	<chem>CC(C)(C)C1=CC=C(C=C1)C2=NN=C(O2)C3=CC(=CC=C3)[N+](=O)[O-]</chem>
11	Maybridge SEW 05403	ethyl 5-amino-1-(4-amino-4H-1,2,4-triazol-3-yl)-1H-pyrazole-4-carboxylate	<chem>CCOC(=O)C1=C(N(N=C1)C2=NN=CN2)N</chem>
12	Maybridge SPB 03391	2-({5-[2,5-bis(2,2,2-trifluoroethoxy)phenyl]-1,3,4-oxadiazol-2-yl}thio)-1-(3-nitrophenyl)ethan-1-one	<chem>[O-][N+](=O)c1cccc(c1)C(=O)CSc1nnc(o1)-c1cc(OCC(F)(F)F)ccc1OCC(F)(F)F</chem>
13	Maybridge SPB 01232	N'-[3-(tert-butyl)-1H-pyrazol-5-yl]carbonyl-N,N-dimethylhydrazonoformamide	<chem>CN(C)\C=N\NC(=O)c1cc(n[nH]1)C(C)(C)C</chem>
14	Maybridge CD 04651	1-(4-nitrophenyl)-5-phenyl-1H-1,2,3-triazole-4-carboxamide	<chem>NC(=O)c1nnn(c1-c1cccc1)-c1ccc(cc1)[N+](=O)[O-]</chem>
15	Maybridge RJF 02111	N1-(2-chlorophenyl)-2-(2-[5-(3-(trifluoromethyl)phenyl)-2H-1,2,3,4-tetraazol-2-yl]acetyl)hydrazine-1-carbothioamide	<chem>FC(F)(F)c1cccc(c1)-c1nnn(CC(=O)NNC(=S)Nc2cccc2Cl)n1</chem>
16	Maybridge RDR 01375	N1-(3-fluorophenyl)-2-[5-(4-nitrophenyl)-2-furyl]methylenedihydrazine-1-carbothioamide	<chem>[O-][N+](=O)c1ccc(cc1)-c1ccc(\C=N\NC(=S)Nc2cccc(F)c2)o1</chem>
17	Maybridge RJC 03318	1,2-bis[2-(diaminomethylene)hydrazono]ethane dihydrochloride	<chem>Cl.Cl.N(\N=C\C=N\N=C(/N)N)=C(/N)N</chem>

18	Maybridge KM 08121	2-[(3-nitro-2-pyridyl)thio]acetic acid	C1=CC(=C(N=C1)SCC(=O)O)[N+](=O)[O-]
19	Maybridge RJC 00833	5-(acetyloxy)-3-[4-(acetyloxy)phenyl]-4-oxo-4H-chromen-7-yl acetate	CC(=O)OC1=CC=C(C=C1)C2=COC3=C(C2=O)C(=CC(=C3)OC(=O)C)OC(=O)C
20	Maybridge KM 08783	ethyl N-[(2,4-dioxo-1-[[6-(trifluoromethyl)-2-pyridyl]amino]-1,2,3,4-tetrahydropyrimidin-5-yl)carbonyl]carbamate	CCOC(=O)NC(=O)c1cn(c(=O)[nH]c1=O)Nc2cccc(n2)C(F)(F)F
21	Maybridge RJC 02908	2-(carboxymethyl)-1,3-dioxoisindoline-5-carboxylic acid	C1=CC2=C(C=C1C(=O)O)C(=O)N(C2=O)CC(=O)O
22	Maybridge BTB 02820	3-(3-nitrophenyl)-5-(4-nitrophenyl)-1,2,4-oxadiazole	C1=CC(=CC(=C1)[N+](=O)[O-])C2=NOC(=N2)C(Cl)(Cl)Cl
23	Maybridge RJF 00729	[(imino[[3-(2-thienyl)-1H-pyrazol-5-yl]amino)methyl]amino]methanimidamide hydrochloride	c1cc(sc1)c2cc(n[nH]2)/N=C(\N)/N=C(N)N.Cl
24	Maybridge BTB 01724	N1-(3-methoxypropyl)-2-[[4-methylphenyl]sulfonyl]hydrazine-1-carbothioamide	Cc1ccc(cc1)S(=O)(=O)NNC(=S)NCCCOC
25	Maybridge SEW 01414	5-(4-chlorophenyl)-1,3-oxazole-4-carbohydrazide	NNC(=O)c1ncoc1c2ccc(Cl)cc2
26	Maybridge KM 09668	2-(2,1,3-benzoxadiazol-5-ylcarbonyl)-N-methylhydrazine-1-carbothioamide	CNC(=S)NNC(=O)c1ccc2nocc2c1
27	Maybridge DP 01130	N1-methyl-2-[1-(3-nitrophenyl)ethylidene]hydrazine-1-carbothioamide	CC(=NNC(=S)NC)C1=CC(=CC=C1)[N+](=O)[O-]
28	Maybridge DFP 00343	N1-[[2-(3-nitrobenzoyl)hydrazino]carbothioyl]-2-chlorobenzamide	[O-][N+](=O)c1cccc(c1)C(=O)NNC(=S)NC(=O)c1cccc1Cl
29	Maybridge BTB 06968	N-(2-[5-[4-(tert-butyl)phenyl]-1,3,4-oxadiazol-2-yl]phenyl)-N'-phenylurea	CC(C)(C)c1ccc(cc1)c2nnc(o2)c3cccc3NC(=O)Nc4cccc4
30	Maybridge KM 00434	N-benzoyl-N'-[4-[2-(4-bromophenyl)diaz-1-enyl]-3-cyclopropyl-1H-pyrazol-5-yl]thiourea	c1ccc(cc1)C(=O)NC(=S)Nc2c(c(n[nH]2)C3CC3)/N=N/c4ccc(cc4)Br
31	Maybridge SPB 03710	methyl 4-(1-hydroxyiminoethyl)-5-methylisoxazole-3-carboxylate	CC1=C(C(=NO1)C(=O)OC)/C(=N/O)/C
32	Maybridge KM 06646	N2-(3-phenyl-1H-pyrazol-5-yl)-2,3-dihydro-1,4-benzodioxine-2-carboxamide	c1ccc(cc1)c2cc(n[nH]2)NC(=O)C3OCc4cccc4O3
33	Maybridge SEW 04296	2-[[4-cyano-2-nitrophenyl]thio]ethyl N-[4-(trifluoromethoxy)phenyl]carbamate	c1cc(ccc1NC(=O)OCCSc2ccc(cc2[N+](=O)[O-])C#N)OC(F)(F)F
34	Maybridge KM 00777	1-methyl-5-nitro-1H-pyrazole-4-carboxylic acid	CN1C(=C(C=N1)C(=O)O)[N+](=O)[O-]
35	Maybridge BTB 14347	3-phenyl-1H-pyrazole-5-carbohydrazide	C1=CC=C(C=C1)C2=NNC(=C2)C(=O)NN
36	Maybridge BTB 05815	N'-hydroxy-N-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]iminofornamide	C(=Nc1nnc(s1)C(F)(F)F)NO
37	Maybridge KM 08488	N-(3,5-dichlorophenyl)-N'-[3-(2-furyl)-1H-pyrazol-5-yl]urea	C1=COC(=C1)C2=CC(=NN2)NC(=O)NC3=CC(=CC(=C3)Cl)Cl
38	Maybridge BTB 12967	3,4-dihydroxycyclobutane-1,2-dione dioxime	C1(C(C(=C1NO)N=O)O)O
39	Maybridge JFD 03059	ethyl 4-amino-5-oxo-6-[2-(2-thienyl)vinyl]-4,5-dihydro-1,2,4-triazine-3-carboxylate	CCOC(=O)C1=NN=C(C(=O)N1N)C=CC2=CC=CS2
40	Maybridge SPB 07258	4,6-di[[5-[4-(tert-butyl)phenyl]-4H-1,2,4-triazol-3-yl]thio]-2-(methylthio)pyrimidine	CSc1nc(Sc2nnc([nH]2)-c2ccc(cc2)C(C)(C)C)cc(Sc2nnc([nH]2)-c2ccc(cc2)C(C)(C)C)n1
41	Maybridge SPB 02525	1-(3-nitrophenyl)-2-[[5-(3-thienylmethyl)-1,3,4-oxadiazol-2-yl]thio]ethan-1-one	c1cc(cc1)[N+](=O)[O-]C(=O)CSc2nnc(o2)Cc3ccsc3
42	Maybridge BTB 05482	1-methyl-2-[2-nitro-4-(trifluoromethyl)anilino]ethyl 5-nitro-2-furoate	CC(CNC1=C(C=C(C=C1)C(F)(F)F)[N+](=O)[O-])OC(=O)C2=CC(=O2)[N+](=O)[O-]
43	Maybridge KM 08486	N-(3,5-dichlorophenyl)-N'-(3-phenyl-1H-pyrazol-5-yl)urea	c1ccc(cc1)c2cc(n[nH]2)NC(=O)Nc3cc(cc3)Cl)Cl
44	Maybridge SPB 03409	3,4-dimethyl-6,7-dihydroisoxazolo[3,4-d]pyridazin-7-one	CC1=C2C(=NNC(=O)C2=NO1)C
45	Maybridge SPB 00154	2-[[5-[4-(tert-butyl)phenyl]phenyl]-4H-1,2,4-triazol-3-yl]thio]-1-(4-chloro-3-nitrophenyl)ethan-1-one	CC(C)(C)c1ccc(cc1)c2[nH]c(nn2)SCC(=O)c3ccc(c3)[N+](=O)[O-]Cl
46	Maybridge BTB 01129	ethyl 3-(4-hydroxy-3-nitrophenyl)propanoate	CCOC(=O)CCC1=CC(=C(C=C1)O)[N+](=O)[O-]
47	Maybridge SPB 00508	3-phenyl-1,2,4-oxadiazole-5-carbohydrazide	C1=CC=C(C=C1)C2=NOC(=N2)C(=O)NN
48	Maybridge SPB 03421	5-[3-methyl-5-(4-methyl-1,2,3-thiadiazol-5-yl)isoxazol-4-yl]-3-(5-nitro-2-furyl)-1,2,4-oxadiazole	CC1=C(SN=N1)C2=C(C(=NO2)C)C3=NC(=NO3)C4=CC(=O4)[N+](=O)[O-]
49	Maybridge SPB 01577	ethyl 3-[(2-chlorophenoxy)methyl]-1,2,4-oxadiazole-5-carboxylate	CCOC(=O)C1=NC(=NO1)COC2=CC=CC=C2Cl

50	Maybridge XAX 00121	N-[5-(4-fluorobenzyl)-1,3,4-thiadiazol-2-yl]-N'-hydroxyiminofornamide	C1=CC(=CC=C1CC2=NN=C(S2)N=CNO)F
51	Maybridge JFD 01245	4-nitrobenzaldehyde 1-(4-methyl-6-oxo-1,6-dihydropyrimidin-2-yl)hydrazone	CC1=CC(=O)N=C(N1)NN=CC2=CC=C(C=C2)[N+](=O)[O-]
52	Maybridge JFD 00150	5-[[4-oxo-2-phenyl-4H-chromen-7-yl]oxy]pentanenitrile	C1=CC=C(C=C1)C2=CC(=O)C3=C(O2)C=C(C=C3)OCCCC#N
53	Maybridge SPB 02682	3-(2-methyl-1,3-thiazol-4-yl)-1,2,4-oxadiazole-5-carbohydrazide	Cc1nc(cs1)c2nc(on2)C(=O)NN
54	Maybridge SPB 01712	ethyl 3-[[[4-chlorophenyl]sulfonyl]methyl]-1,2,4-oxadiazole-5-carboxylate	CCOC(=O)c1nc(no1)CS(=O)(=O)c2ccc(cc2)Cl
55	Maybridge RJC 01297	5-amino-1-phenyl-1H-pyrazole-4-carboxylic acid	C1=CC=C(C=C1)N2C(=C(C=N2)C(=O)O)N
56	Maybridge RH 00806	4,5-dichloro-6-nitro-2,3-dihydropyridazin-3-one	C1(C(C(=NNC1=O)[N+](=O)[O-])Cl)Cl
57	Maybridge KM 09203	N-phenyl-N'-(3-phenyl-1H-pyrazol-5-yl)urea	c1ccc(cc1)c2cc(n[nH]2)NC(=O)Nc3ccccc3
58	Maybridge RJC 03531	3-(1-[1,1'-biphenyl]-4-yl-1H-1,2,3,4-tetraazol-5-yl)quinolin-4(1H)-one	O=C/1c5ccccc5N\C=C\1c4nncn4c2ccc(cc2)c3ccccc3
59	Fluka 387721	Ellagic acid	C1=C2C3=C(C(=C1O)O)OC(=O)C4=CC(=C(C(=C43)OC2=O)O)O
60	Aldrich 465119	Baicalein (5,6,7-Trihydroxyflavone)	C1=CC=C(C=C1)C2=CC(=O)C3=C(C(=C(C=C3O2)O)O)O
61	Sigma BP902	Dinoprostone	CCCCC(C=CC1C(CC(=O)C1CC=CCCC(=O)O)O)O
62	Sigma O4139	orlistat	CCCCCCCCCCC(CC1C(C(=O)O1)CCCCC)OC(=O)C(CC(C)C)NC=O
63	Sigma SML 1114	IWP-4	O=C(CSC(N1C2=CC=CC=C2OC)=NC3=C(SCC3)C1=O)NC4=NC5=C(C=C(C)C=C5)S4
64	Sigma I0536	IWP-2	O=C(CSC(N1C2=CC=CC=C2)=NC3=C(SCC3)C1=O)NC4=NC5=C(C=C(C)C=C5)S4
65	Sigma 07039	(R)-(+)- $\alpha$ -Lipoic acid	C1CSS[C@@H]1CCCCC(=O)O
66	Cayman CAY14765	Sulprostone	CS(=O)(=O)NC(=O)CCCC=CCC1C(C(C1=O)O)C=CC(COC2=CC=CC=C2)O
67	Sigma C1386	curcumin	COC1=C(C=CC(=C1)C=CC(=O)CC(=O)C=CC2=CC(=C(C=C2)O)OC)O
68	Sigma R2625	Retinoic acid	CC1=C(C(CCC1)(C)C)C=CC(=CC=CC(=CC(=O)O)C)C
69	Cayman CAY16727	Tideglusib	C1=CC=C(C=C1)CN2C(=O)N(SC2=O)C3=CC=CC4=CC=CC=C43
70	Cayman CAY71750	Troglitazone	CC1=C(C(=C2CCC(OC2=C1C)(C)COC3=CC=C(C=C3)CC4C(=O)NC(=O)S4)C)O
71	Cayman CAY15243	IWP-L6	O=C1C2=C(CCS2)N=C(SCC(NC3=NC=C(C4=CC=CC=C4)C=C3)=O)N1C5=CC=CC=C5
72	Aldrich 712264	Cytisine	C1C2CNCC1C3=CC=CC(=O)N3C2
73	Cayman CAY13118	Metformin	CN(C)C(=N)N=C(N)N
74	Cayman CAY16930	Allopregnanolone	CC(=O)C1CCC2C1(CCC3C2CCC4C3(CCC(C4)O)C)C
75	Cayman CAY10004386	Sulindac	CC1=C(C2=C(C1=CC3=CC=C(C=C3)S(=O)C)C=CC(=C2)F)CC(=O)O
76	Cayman CAY90250	Elaidic Acid	CCCCCCCC=CCCCCCCCC(=O)O
77	Sigma ADV509448406	EVP-6124	C1CN2CCC1C(C2)NC(=O)C3=CC4=C(S3)C(=CC=C4)Cl
78	Cayman CAY14184	Memantine	CC12CC3CC(C1)(CC(C3)(C2)N)C
79	Sigma C4024	Carbamazepine	C1=CC=C2C(=C1)C=CC3=CC=CC=C3N2C(=O)N
80	Sigma A3145	Apigenin	C1=CC(=CC=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O
81	Cayman CAY16987	Cryptotanshinone	CC1COC2=C1C(=O)C(=O)C3=C2C=CC4=C3CCCC4(C)C
82	Sigma G6649	Genistein	C1=CC(=CC=C1C2=COC3=CC(=CC(=C3C2=O)O)O)O
83	Cayman CAY10004161	Luteolin	C1=CC(=C(C=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O)O
84	Cayman CAY12059	Clozapine	CN1CCN(CC1)C2=C3C=CC=CC3=NC4=C(N2)C=C(C=C4)Cl
85	Sigma SML1271	TWS 119	C1=CC(=CC(=C1)N)C2=CC3=C(N2)N=CN=C3OC4=CC=CC(=C4)O
86	Sigma M107	MK801 (Dizocilpine)	C[C@]1(C2=C(C[C@H]3N1)C=CC=C2)C4=C3C=CC=C4
87	Cayman CAY14015	Kahweol	OC[C@@]5(O)C[C@@]43[C@H]([C@@]2/C=C\C1occc1[C@H]2CC3)C)CC[C@@H]5C4
88	Cayman CAY13999	Cafestol	CC12CCC3=C(C1CCC45C2CCC(C4)C(C5)(CO)O)C=CO3
89	Cayman CAY70930	Chlorogenic acid	C1C(C(C(C1(C=O)O)O)OC(=O)C=CC2=CC(=C(C=C2)O)O)O
90	Sigma 03960590	(-)-epigallocatechin	O=C(O[C@@H]2Cc3c(O[C@@H]2c1cc(O)c(O)c1)cc(O)cc3O)c4cc(O)c(O)c(O)c4
91	Cayman CAY10011132	Rolipram	COC1=C(C=C(C=C1)C2CC(=O)NC2)OC3CCCC3

92	Sigma S5696	SKI II	<chem>C1=CC(=CC=C1C2=CSC(=N2)NC3=CC=C(C=C3)O)Cl</chem>
93	Sigma X2754	Xanomeline	<chem>CCCCCOC1=NSN=C1C2=CCN(C2)C</chem>
94	Sigma CDS021620	fasudil	<chem>C1CNCCN(C1)S(=O)(=O)C2=CC=CC3=C2C=CN=C3</chem>
95	Sigma 128125	Aloisine	<chem>CCCCC1=C(NC2=NC=CN=C12)C3=CC=C(C=C3)OC</chem>
96	Sigma D6821	Donepezil	<chem>COC1=C(C=C2C(=C1)CC(C2=O)CC3CCN(CC3)CC4=CC=CC=C4)OC</chem>
97	Sigma BP773	Mercaptopurine (6MP)	<chem>S=C2/N=C\Nc1ncnc12</chem>
98	Sigma A3656	Decitabine	<chem>C1C(C(OC1N2C=NC(=NC2=O)N)CO)O</chem>
99	Sigma Q3251	Quinacrine	<chem>CCN(CC)CCCC(C)Nc1c2ccc(cc2nc3c1cc(cc3)OC)Cl</chem>
10 0	Sigma A4638	Azathioprine	<chem>[O-][N+](=O)c3ncn(c3Sc1ncnc2ncnc12)C</chem>
10 1	Sigma K0133	Kaempferol	<chem>C1=CC(=CC=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O</chem>
10 2	Sigma B5016	Bepiridil	<chem>CC(C)COCC(CN(CC1=CC=CC=C1)C2=CC=CC=C2)N3CCCC3</chem>



**Supplementary Figure S1** Size-exclusion chromatography of FZD\_CRD profiles using a Superdex 200 16/60 column (self-repacked). (A) FZD8\_CRD. (B) FZD5\_CRD. (C) FZD7\_CRD.