

Fifty-nine candidate compounds were acquired from the initial virtually screening which was designed to target the bacterial loop of e β G and its active site. The docking energy scores of 59 candidate compounds measured by the DOCK program are -43 to -55 kcal/mol. (Table S1) The candidate compounds were purchased from SPECS (Zoetermeer, The Netherlands). Each candidate was provided as a solid power and dissolved in 100% DMSO (Sigma-Aldrich, MO, USA) to 10 mM as stock. Candidates were screening for their inhibition specificity of e β G verse h β G, which were conducted at pH 7.3 or pH 5.4 in triplicate, respectively. 40 μ L purified β G was treated with 10 μ L compound solution at 37 °C for 30 min, and sequentially incubated with 50 μ L of pNPG (Sigma-Aldrich) at 37 °C for 30 min. Reactions were quenched with 5 μ L of 2 N sodium hydroxide (Sigma-Aldrich). Each reaction consisted of 3.75 ng purified β G, 50 μ M compound, and 5 mM pNPG in PBS containing 10% DMSO and 0.05% BSA (Sigma-Aldrich). β G-activities were measured by color development of pNP detected on a microplate reader at OD 405 nm. Results are displayed as percent of β G activity compared with the untreated control. The result showed that all the 59 candidate compounds displayed selective inhibition against e β G activity. Especially, the inhibiting ability against e β G activity was >95% in 7 candidates of e β G specific inhibitors (Table S1).

Table S1. The β G activity assay and docking energy score of β G specific inhibitor candidates

	Compound	SPECS ID number	Rank	Docking energy score (kcal/mol)	e β G activity (%) with 50 μ M compound	h β G activity (%) with 50 μ M compound
1	6368	AK-968/13146368	46	-50.74	44.87	116.03
2	9183	AF-399/42309183	48	-50.67	39.67	107.36
3	5259	AK-968/41025259	167	-48.26	34.05	106.20
4	0136	AQ-405/42300136	289	-47.43	19.16	108.76
5	3043	AG-205/10703043	316	-47.30	25.14	103.55
6	1013	AK-918/12271013	343	-47.16	34.76	126.45
7	3959	AK-968/40733959	428	-46.75	42.88	105.45
8	2715	AG-690/13702715	606	-46.11	53.06	114.38
9	9665	AM-807/42859665	1146	-45.02	8.97	100.83
10	1501	AK-968/41171501	1339	-44.70	27.85	105.12
11	0956	AQ-776/42800956	2155	-43.72	29.70	103.31
12	9107	AG-690/11669107	7	-53.90	29.70	105.37
13	1306	AK-918/13161306	15	-52.64	29.20	105.45
14	5003	AK-968/12345003	99	-49.25	17.02	105.54
15	1046	AF-399/12151046	119	-48.84	45.94	106.69
16	8329	AF-399/40918329	482	-46.59	33.19	97.77
17	8889	AN-329/40718889	483	-46.59	11.40	102.15
18	8010	AG-690/36828010	644	-45.99	23.58	98.84
19	0030	AO-365/15160030	649	-45.98	58.19	111.74
20	8074	AG-690/15438074	773	-45.70	22.15	109.09
21	9572	AQ-750/41789572	833	-45.56	42.66	106.78
22	0523	AN-068/42800523	1142	-45.03	31.77	109.26
23	7145	AQ-390/12597145	1283	-44.79	1.00	119.83
24	6843	AK-968/40946843	1369	-44.66	27.49	108.76
25	8572	AG-389/41558572	1648	-44.26	17.66	102.81
26	4465	AQ-390/40194465	1935	-43.95	10.04	99.50

27	9063	AG-690/33359063	2000	-43.88	32.48	105.45
28	3379	AP-124/43383379	2019	-43.87	31.70	102.56
29	4043	AG-205/36564043	2027	-43.86	32.98	81.24
30	1035	AK-968/06451035	2054	-43.82	25.00	102.48
31	3927	AG-690/12883927	2093	-43.78	18.73	106.86
32	9274	AF-399/15599274	2158	-43.72	32.34	106.69
33	1448	AP-853/42931448	2185	-43.70	11.11	109.67
34	7100	AL-398/12677100	2220	-43.66	20.58	112.56
35	6019	AG-690/36516019	2239	-43.64	33.83	104.96
36	5012	AE-641/00585012	127	-48.76	14.96	108.51
37	0015	AI-204/31730015	180	-48.14	17.59	108.51
38	1135	AO-081/15571135	201	-47.95	3.70	118.10
39	1089	AJ-292/14921089	249	-47.58	47.22	119.17
40	0220	AO-476/43380220	518	-46.43	47.15	113.55
41	4011	AE-641/14824011	626	-46.05	37.54	96.28
42	7670	AP-263/40917670	677	-45.91	43.16	93.31
43	2138	AO-476/40672138	947	-45.37	19.23	107.27
44	7007	AN-919/15527007	1032	-45.21	44.30	105.79
45	5244	AJ-292/41945244	1082	-45.12	26.21	44.38
46	4277	AQ-911/42464277	1247	-44.85	44.37	115.21
47	5033	AG-670/36765033	1412	-44.60	9.33	116.12
48	4021	AE-848/30744021	1441	-44.55	28.56	103.06
49	7036	AF-399/37297036	1628	-44.28	6.70	95.45
50	3250	AO-365/42033250	1667	-44.24	33.62	96.94
51	8013a	AF-407/13078013	1718	-44.17	60.40	100.33
52	3181	AR-434/11133181	1741	-44.14	30.27	88.02
53	8013b	AE-848/33858013	1837	-44.04	32.91	93.72
54	2074	AF-407/13462074	1868	-44.01	12.46	101.07
55	5905	AJ-292/41685905	2048	-43.83	24.93	104.96
56	9927	AN-465/43399927	2209	-43.67	25.00	113.80
57	6015	AO-476/14976015	2331	-43.55	10.40	72.07
58	2020	AJ-292/42032020	2355	-43.53	13.68	84.13
59	6003	AG-690/13506003	2365	-43.52	9.76	93.06