

Supplementary Table 1. Performance of ACNN models on the test subsets of the PDBbind (five random seeds). The averaged Pearson R^2 values and standard errors are reported.

Splitting method	Binding component	Core	Refined	General
Random	Complex	0.04 (± 0.05)	0.80 (± 0.00)	0.70 (± 0.02)
	Ligand alone	0.09 (± 0.08)	0.71 (± 0.06)	0.60 (± 0.08)
	Protein alone	0.08 (± 0.12)	0.84 (± 0.02)	0.73 (± 0.03)
Scaffold	Complex	0.14 (± 0.12)	0.60 (± 0.04)	0.61 (± 0.03)
	Ligand alone	0.16 (± 0.20)	0.48 (± 0.09)	0.42 (± 0.07)
	Protein alone	0.29 (± 0.08)	0.79 (± 0.03)	0.69 (± 0.02)
Sequence	complex	0.08 (± 0.13)	0.54 (± 0.06)	0.47 (± 0.04)
	Ligand alone	0.13 (± 0.15)	0.35 (± 0.07)	0.23 (± 0.04)
	Protein alone	0.16 (± 0.09)	0.63 (± 0.05)	0.54 (± 0.02)

Supplementary Table 2. Performance of ACNN model on PDBbind core set (five random seeds). The averaged Pearson R^2 values and standard errors are reported.

Splitting method	Binding component	Training set (refined)	Training set (general)
Random	Complex	0.70 (± 0.03)	0.73 (± 0.04)
	Ligand alone	0.73 (± 0.03)	0.79 (± 0.02)
	Protein alone	0.70 (± 0.03)	0.76 (± 0.01)
Scaffold	Complex	0.69 (± 0.02)	0.76 (± 0.03)
	Ligand alone	0.77 (± 0.02)	0.76 (± 0.01)
	Protein alone	0.67 (± 0.02)	0.69 (± 0.04)
Sequence	Complex	0.64 (± 0.05)	0.71 (± 0.03)
	Ligand alone	0.75 (± 0.03)	0.73 (± 0.02)
	Protein alone	0.63 (± 0.05)	0.73 (± 0.02)

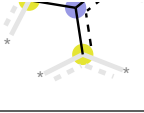
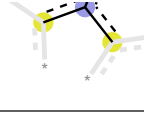
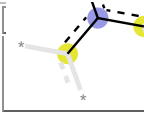
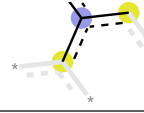
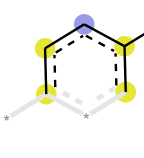

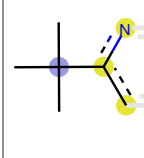
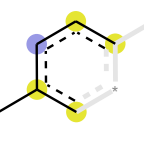
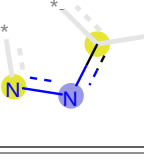
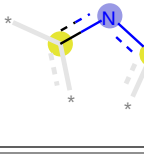
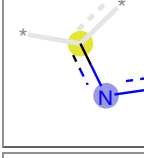
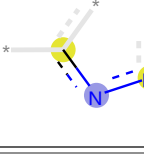
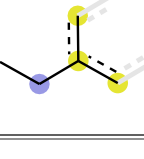
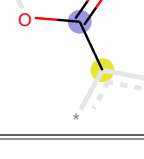
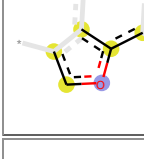
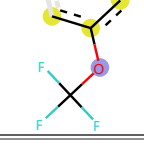
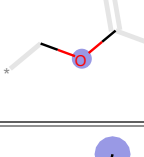
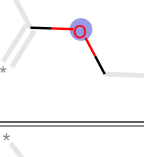
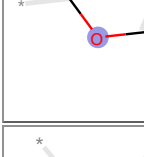

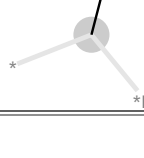
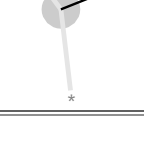
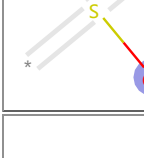
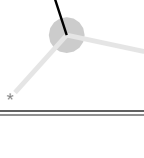
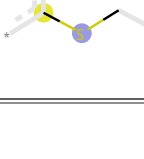

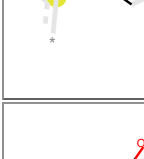
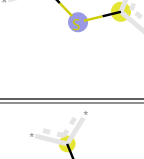


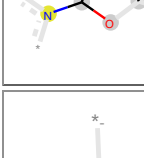
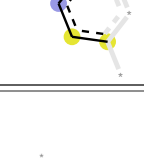


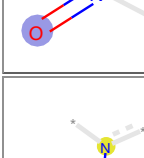


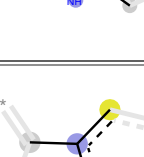
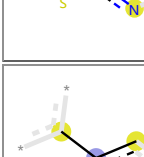

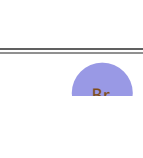
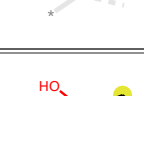

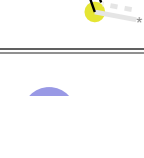




Supplementary Table 3. Performance of ACNN model on a kinase inhibitor dataset. The averaged EF₂₀, PI values and standard errors are reported.

Inhibitor (HET ID)	Physics-based approach ^a		ACNN ^b	
	EF ₂₀ ^c	PI ^d	EF ₂₀	PI
VX-745 (52P)	5.00	0.60	0.00 (±0.00)	-0.10 (±0.18)
Gefitinib (IRE)	5.00	0.57	0.51 (±1.13)	-0.07 (±0.11)
BI-2536 (R78)	5.00	0.38	2.03 (±1.13)	0.13 (±0.14)
LY-333531 (LY4)	5.00	0.35	2.01 (±2.76)	0.08 (±0.13)
CP-690550 (MI1)	3.80	0.59	1.28 (±0.90)	0.19 (±0.19)
Erlotinib (AQ4)	3.04	0.44	1.42 (±0.91)	-0.08 (±0.08)
Dasatinib (1N1)	2.75	0.64	0.97 (±0.44)	0.10 (±0.09)
Vandetanib (ZD6)	2.32	0.25	0.84 (±0.39)	0.03 (±0.07)
A-674563 (SS3)	2.27	0.45	2.61 (±0.51)	0.37 (±0.04)
Flavopiridol (CPB)	1.70	0.07	1.70 (±1.20)	0.15 (±0.11)
VX-680 (VX6)	1.69	0.29	1.01 (±0.47)	-0.01 (±0.07)
Sunitinib (B49)	1.68	0.04	1.31 (±0.37)	0.07 (±0.09)
TAE-684 (GUI)	1.61	0.13	0.84 (±0.06)	-0.08 (±0.09)
Staurosporine (STU)	1.32	0.29	1.22 (±0.14)	0.03 (±0.10)
Crizotinib (VGH)	1.28	0.31	0.00 (±0.00)	-0.19 (±0.09)
SB-203580 (SB2)	1.25	0.15	0.75 (±1.12)	-0.21 (±0.18)
R406 (585)	1.21	0.30	0.61 (±0.15)	-0.22 (±0.06)
Mean	2.70	0.34	1.12 (±1.09)	0.01 (±0.18)

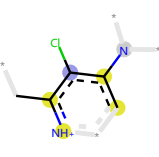
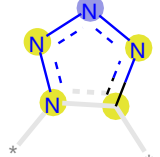
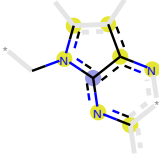
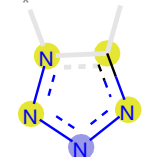
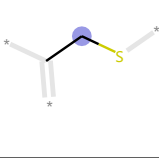
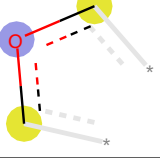
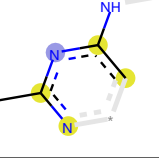
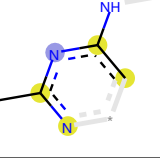

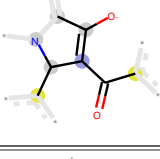
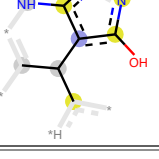
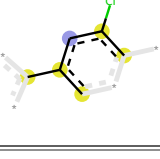
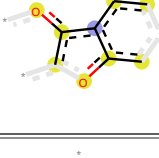
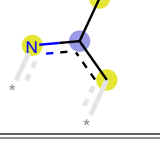
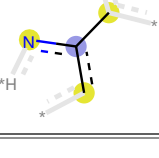
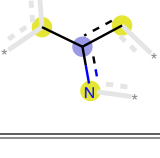
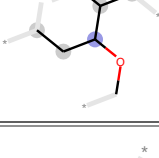
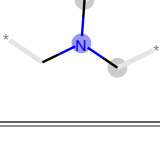
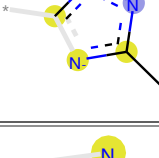
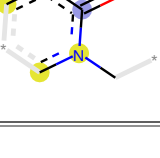
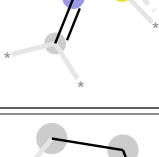
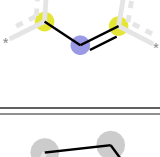
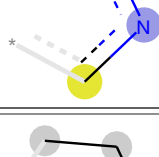
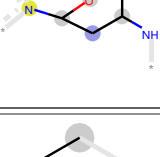
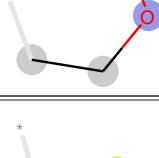
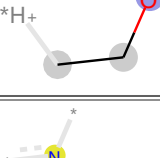
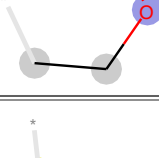
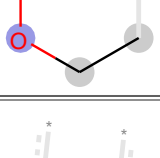
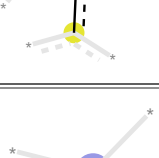


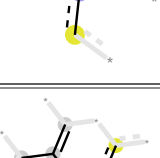
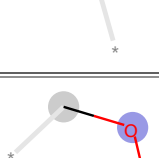
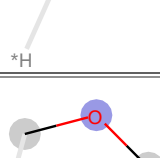
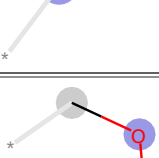
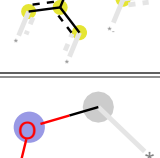
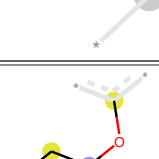
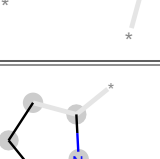
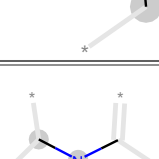





^a Results from (Wan et al., 2013). ^b ACNN models (binding complex) trained on PDBbind refined set (with removal of structures overlapping with core set). ^c Number of predicted targets in top 20% denotes the number of true positives in top 20% of ranked kinase targets, which corresponds to the enrichment factors (EF₂₀) compared to random selection. ^d PI is semi-quantitative measurement of the correlation of predicted binding affinity with experimental values.

Supplementary Table 4. Visualization of fingerprint bits.

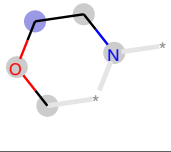
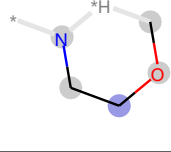
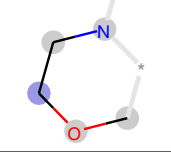
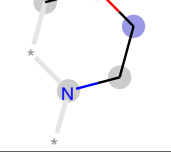
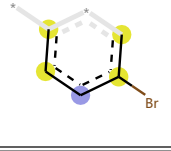
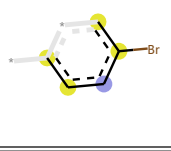
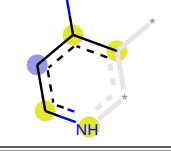
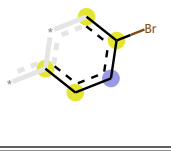
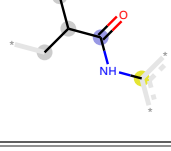
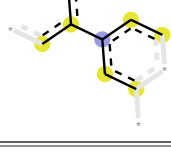
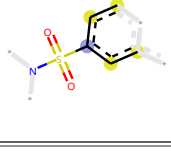
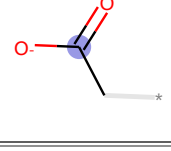
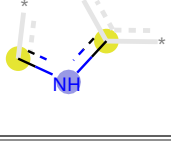
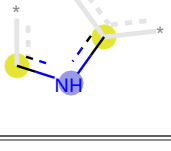
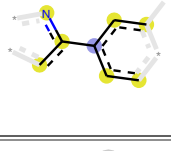
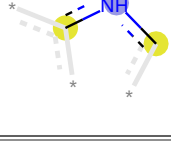
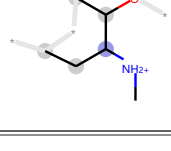
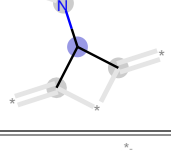
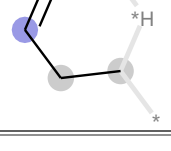
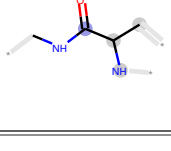
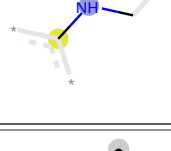
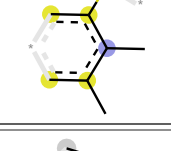
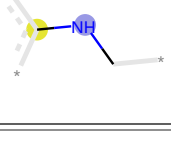
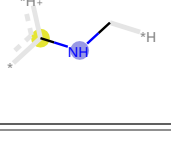
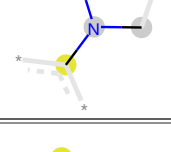
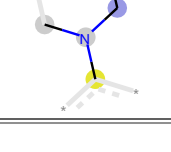
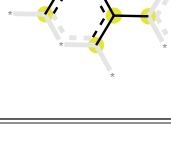
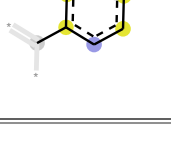
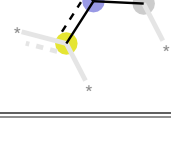
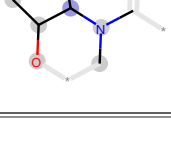
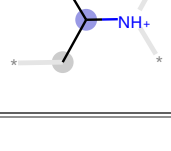
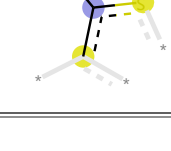
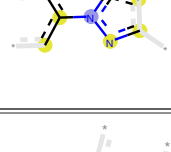
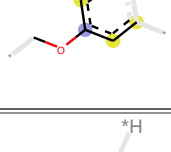
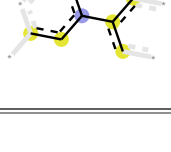
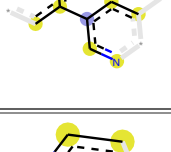
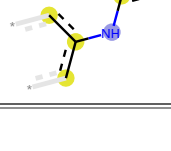
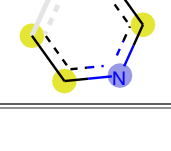
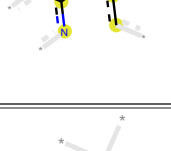
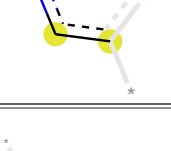
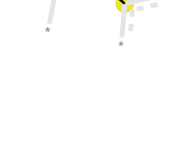
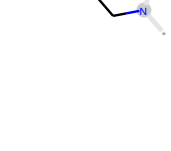
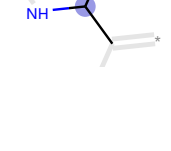
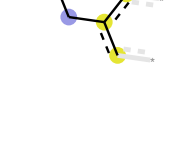
	bit	zinc_freq	log2_FC	mean_freq	active_freq	decoy_freq	example_1	example_2	example_3	example_4
1	bit: 1452	zinc_freq: 22.7%	log2(FC): 1.14	mean_freq: 27.5%	active_freq: 37.9%	decoy_freq: 17.2%				
2	bit: 283	zinc_freq: 19.2%	log2(FC): -1.03	mean_freq: 15.3%	active_freq: 10.0%	decoy_freq: 20.6%				
3	bit: 41	zinc_freq: 16.7%	log2(FC): -1.20	mean_freq: 10.6%	active_freq: 6.4%	decoy_freq: 14.8%				
4	bit: 1866	zinc_freq: 10.8%	log2(FC): 1.67	mean_freq: 11.9%	active_freq: 18.1%	decoy_freq: 5.7%				
5	bit: 1160	zinc_freq: 10.4%	log2(FC): 1.45	mean_freq: 16.7%	active_freq: 24.5%	decoy_freq: 8.9%				
6	bit: 116	zinc_freq: 10.2%	log2(FC): -1.36	mean_freq: 9.8%	active_freq: 5.5%	decoy_freq: 14.2%				
7	bit: 1823	zinc_freq: 10.1%	log2(FC): -2.12	mean_freq: 7.1%	active_freq: 2.6%	decoy_freq: 11.5%				
8	bit: 1535	zinc_freq: 9.9%	log2(FC): 1.51	mean_freq: 12.0%	active_freq: 17.8%	decoy_freq: 6.3%				
9	bit: 1066	zinc_freq: 9.9%	log2(FC): 1.20	mean_freq: 10.6%	active_freq: 14.8%	decoy_freq: 6.4%				
10	bit: 1238	zinc_freq: 9.4%	log2(FC): -1.38	mean_freq: 6.3%	active_freq: 3.5%	decoy_freq: 9.2%				
11	bit: 1357	zinc_freq: 8.7%	log2(FC): 1.13	mean_freq: 15.2%	active_freq: 20.9%	decoy_freq: 9.6%				

	bit	zinc_freq	log2_FC	mean_freq	active_freq	decoy_freq				
12	bit: 235	zinc_freq: 7.8%	log2(FC): -2.13	mean_freq: 5.9%	active_freq: 2.2%	decoy_freq: 9.6%				
13	bit: 1164	zinc_freq: 7.7%	log2(FC): -1.52	mean_freq: 5.8%	active_freq: 3.0%	decoy_freq: 8.6%				
14	bit: 145	zinc_freq: 6.9%	log2(FC): -1.67	mean_freq: 5.0%	active_freq: 2.4%	decoy_freq: 7.6%				
15	bit: 147	zinc_freq: 6.5%	log2(FC): -1.13	mean_freq: 4.7%	active_freq: 3.0%	decoy_freq: 6.5%				
16	bit: 1309	zinc_freq: 6.4%	log2(FC): -1.59	mean_freq: 6.7%	active_freq: 3.4%	decoy_freq: 10.1%				
17	bit: 341	zinc_freq: 6.2%	log2(FC): -2.43	mean_freq: 5.1%	active_freq: 1.6%	decoy_freq: 8.7%				
18	bit: 896	zinc_freq: 6.1%	log2(FC): 1.47	mean_freq: 10.7%	active_freq: 15.8%	decoy_freq: 5.7%				
19	bit: 753	zinc_freq: 5.7%	log2(FC): -1.34	mean_freq: 4.5%	active_freq: 2.6%	decoy_freq: 6.5%				
20	bit: 747	zinc_freq: 5.7%	log2(FC): -1.53	mean_freq: 4.6%	active_freq: 2.4%	decoy_freq: 6.9%				
21	bit: 352	zinc_freq: 5.7%	log2(FC): 1.57	mean_freq: 12.0%	active_freq: 17.9%	decoy_freq: 6.0%				
22	bit: 728	zinc_freq: 5.6%	log2(FC): -1.77	mean_freq: 7.1%	active_freq: 3.2%	decoy_freq: 11.0%				

	bit	zinc_freq	log2(FC)	mean_freq	active_freq	decoy_freq				
23	bit: 102	zinc_freq: 5.6%	log2(FC): 1.37	mean_freq: 7.0%	active_freq: 10.1%	decoy_freq: 3.9%				
24	bit: 725	zinc_freq: 5.6%	log2(FC): -1.29	mean_freq: 5.8%	active_freq: 3.4%	decoy_freq: 8.2%				
25	bit: 1279	zinc_freq: 5.5%	log2(FC): -1.04	mean_freq: 7.4%	active_freq: 4.9%	decoy_freq: 10.0%				
26	bit: 1195	zinc_freq: 5.4%	log2(FC): -1.55	mean_freq: 4.1%	active_freq: 2.1%	decoy_freq: 6.2%				
27	bit: 736	zinc_freq: 5.3%	log2(FC): 1.39	mean_freq: 8.2%	active_freq: 11.9%	decoy_freq: 4.5%				
28	bit: 237	zinc_freq: 5.3%	log2(FC): -1.62	mean_freq: 4.7%	active_freq: 2.3%	decoy_freq: 7.1%				
29	bit: 1963	zinc_freq: 5.2%	log2(FC): -1.50	mean_freq: 4.1%	active_freq: 2.1%	decoy_freq: 6.1%				
30	bit: 1013	zinc_freq: 5.2%	log2(FC): -1.95	mean_freq: 3.6%	active_freq: 1.5%	decoy_freq: 5.7%				
31	bit: 1920	zinc_freq: 5.0%	log2(FC): -1.15	mean_freq: 3.7%	active_freq: 2.3%	decoy_freq: 5.2%				
32	bit: 1603	zinc_freq: 4.6%	log2(FC): 1.94	mean_freq: 5.9%	active_freq: 9.4%	decoy_freq: 2.4%				

	bit	zinc_freq	log2_FC	mean_freq	active_freq	decoy_freq				
33	bit: 257	zinc_freq: 4.6%	log2(FC): -1.09	mean_freq: 4.9%	active_freq: 3.1%	decoy_freq: 6.7%				
34	bit: 1959	zinc_freq: 4.5%	log2(FC): -1.85	mean_freq: 3.8%	active_freq: 1.7%	decoy_freq: 6.0%				
35	bit: 1853	zinc_freq: 4.4%	log2(FC): -1.47	mean_freq: 5.2%	active_freq: 2.8%	decoy_freq: 7.6%				
36	bit: 980	zinc_freq: 4.4%	log2(FC): 1.20	mean_freq: 5.0%	active_freq: 7.0%	decoy_freq: 3.0%				
37	bit: 1791	zinc_freq: 4.4%	log2(FC): 1.05	mean_freq: 3.8%	active_freq: 5.1%	decoy_freq: 2.5%				
38	bit: 281	zinc_freq: 4.3%	log2(FC): -1.18	mean_freq: 3.9%	active_freq: 2.4%	decoy_freq: 5.5%				
39	bit: 1405	zinc_freq: 4.1%	log2(FC): 1.02	mean_freq: 4.0%	active_freq: 5.4%	decoy_freq: 2.7%				
40	bit: 45	zinc_freq: 4.1%	log2(FC): 1.35	mean_freq: 4.9%	active_freq: 7.1%	decoy_freq: 2.8%				
41	bit: 2031	zinc_freq: 4.1%	log2(FC): -1.35	mean_freq: 4.9%	active_freq: 2.7%	decoy_freq: 7.0%				
42	bit: 523	zinc_freq: 4.0%	log2(FC): 1.02	mean_freq: 3.9%	active_freq: 5.2%	decoy_freq: 2.6%				
43	bit: 193	zinc_freq: 3.9%	log2(FC): 1.35	mean_freq: 4.3%	active_freq: 6.2%	decoy_freq: 2.4%				

	bit	zinc_freq	log2_FC	mean_freq	active_freq	decoy_freq				
44	bit: 879	zinc_freq: 3.9%	log2(FC): -1.12	mean_freq: 4.6%	active_freq: 2.9%	decoy_freq: 6.2%				
45	bit: 241	zinc_freq: 3.7%	log2(FC): -1.06	mean_freq: 3.3%	active_freq: 2.1%	decoy_freq: 4.5%				
46	bit: 29	zinc_freq: 3.7%	log2(FC): 1.03	mean_freq: 3.9%	active_freq: 5.3%	decoy_freq: 2.6%	H^+ 			
47	bit: 502	zinc_freq: 3.7%	log2(FC): -1.01	mean_freq: 3.6%	active_freq: 2.4%	decoy_freq: 4.8%				
48	bit: 1043	zinc_freq: 3.6%	log2(FC): 1.31	mean_freq: 3.2%	active_freq: 4.6%	decoy_freq: 1.9%			H^+ 	
49	bit: 448	zinc_freq: 3.6%	log2(FC): 1.30	mean_freq: 3.3%	active_freq: 4.7%	decoy_freq: 1.9%				
50	bit: 1034	zinc_freq: 3.3%	log2(FC): 1.37	mean_freq: 5.5%	active_freq: 7.9%	decoy_freq: 3.1%				
51	bit: 909	zinc_freq: 3.3%	log2(FC): -2.05	mean_freq: 4.1%	active_freq: 1.6%	decoy_freq: 6.6%				
52	bit: 97	zinc_freq: 3.2%	log2(FC): -1.58	mean_freq: 3.4%	active_freq: 1.7%	decoy_freq: 5.1%				
53	bit: 984	zinc_freq: 3.2%	log2(FC): 1.05	mean_freq: 4.7%	active_freq: 6.4%	decoy_freq: 3.1%				
54										

	bit	zinc_freq	log2_FC	mean_freq	active_freq	decoy_freq				
	bit: 1441	zinc_freq: 3.1%	log2(FC): 1.03	mean_freq: 3.3%	active_freq: 4.5%	decoy_freq: 2.2%				
55	bit: 1157	zinc_freq: 3.0%	log2(FC): -1.01	mean_freq: 3.8%	active_freq: 2.5%	decoy_freq: 5.0%				
56	bit: 785	zinc_freq: 3.0%	log2(FC): 1.10	mean_freq: 6.0%	active_freq: 8.2%	decoy_freq: 3.8%				
57	bit: 806	zinc_freq: 2.8%	log2(FC): 1.05	mean_freq: 5.0%	active_freq: 6.8%	decoy_freq: 3.3%				
58	bit: 1427	zinc_freq: 2.8%	log2(FC): -1.91	mean_freq: 3.6%	active_freq: 1.5%	decoy_freq: 5.6%				
59	bit: 1416	zinc_freq: 2.8%	log2(FC): 1.05	mean_freq: 4.3%	active_freq: 5.9%	decoy_freq: 2.8%				
60	bit: 680	zinc_freq: 2.8%	log2(FC): 1.45	mean_freq: 4.7%	active_freq: 6.8%	decoy_freq: 2.5%				
61	bit: 42	zinc_freq: 2.8%	log2(FC): -2.37	mean_freq: 3.2%	active_freq: 1.0%	decoy_freq: 5.3%				
62	bit: 1501	zinc_freq: 2.6%	log2(FC): 1.02	mean_freq: 3.3%	active_freq: 4.5%	decoy_freq: 2.2%				
63	bit: 1586	zinc_freq: 2.6%	log2(FC): 2.19	mean_freq: 3.6%	active_freq: 6.0%	decoy_freq: 1.3%				
64	bit: 1507	zinc_freq: 2.4%	log2(FC): -1.58	mean_freq: 3.2%	active_freq: 1.6%	decoy_freq: 4.9%				

	bit	zinc_freq	log2_FC	mean_freq	active_freq	decoy_freq				
65	1045	zinc_freq: 2.4%	log2(FC): 1.52	mean_freq: 3.4%	active_freq: 5.1%	decoy_freq: 1.8%				
66	927	zinc_freq: 2.3%	log2(FC): -1.18	mean_freq: 3.0%	active_freq: 1.9%	decoy_freq: 4.2%				
67	489	zinc_freq: 2.3%	log2(FC): 1.41	mean_freq: 4.3%	active_freq: 6.3%	decoy_freq: 2.4%				
68	79	zinc_freq: 2.2%	log2(FC): 1.15	mean_freq: 3.9%	active_freq: 5.4%	decoy_freq: 2.4%				
69	323	zinc_freq: 2.1%	log2(FC): 1.44	mean_freq: 4.6%	active_freq: 6.7%	decoy_freq: 2.5%				
70	878	zinc_freq: 1.9%	log2(FC): 1.46	mean_freq: 4.3%	active_freq: 6.4%	decoy_freq: 2.3%				
71	708	zinc_freq: 1.9%	log2(FC): 1.59	mean_freq: 4.2%	active_freq: 6.3%	decoy_freq: 2.1%				
72	271	zinc_freq: 1.9%	log2(FC): -1.28	mean_freq: 3.7%	active_freq: 2.2%	decoy_freq: 5.3%				
73	491	zinc_freq: 1.8%	log2(FC): 2.27	mean_freq: 5.7%	active_freq: 9.4%	decoy_freq: 1.9%				
74	381	zinc_freq: 1.7%	log2(FC): 1.47	mean_freq: 4.6%	active_freq: 6.7%	decoy_freq: 2.4%				
75	203	zinc_freq: 1.7%	log2(FC): 1.08	mean_freq: 3.0%	active_freq: 4.1%	decoy_freq: 2.0%				

	bit	zinc_freq	log2_FC	mean_freq	active_freq	decoy_freq				
76	bit: 2010	zinc_freq: 1.7%	log2(FC): 1.57	mean_freq: 3.4%	active_freq: 5.1%	decoy_freq: 1.7%				
77	bit: 832	zinc_freq: 1.6%	log2(FC): 1.43	mean_freq: 3.1%	active_freq: 4.5%	decoy_freq: 1.7%				
78	bit: 1747	zinc_freq: 1.5%	log2(FC): 1.30	mean_freq: 4.5%	active_freq: 6.5%	decoy_freq: 2.6%				
79	bit: 1733	zinc_freq: 1.5%	log2(FC): 1.12	mean_freq: 3.0%	active_freq: 4.1%	decoy_freq: 1.9%				
80	bit: 1313	zinc_freq: 1.4%	log2(FC): 1.51	mean_freq: 4.0%	active_freq: 5.9%	decoy_freq: 2.1%				
81	bit: 1617	zinc_freq: 1.4%	log2(FC): 1.84	mean_freq: 3.5%	active_freq: 5.5%	decoy_freq: 1.5%				
82	bit: 457	zinc_freq: 1.0%	log2(FC): 1.74	mean_freq: 6.2%	active_freq: 9.5%	decoy_freq: 2.9%				
83	bit: 1459	zinc_freq: 0.9%	log2(FC): 1.32	mean_freq: 3.4%	active_freq: 4.8%	decoy_freq: 1.9%				
84	bit: 1868	zinc_freq: 0.8%	log2(FC): 1.94	mean_freq: 3.5%	active_freq: 5.6%	decoy_freq: 1.5%				