

Network pharmacology and verification experiment-based prediction of active components and potential targets of *Alpiniae Oxyphyllae Fructus-Saposhnikoviae Radix* (Yizhiren-Fangfeng) for treatment of diabetic kidney disease

Supplementary Table S1 (A) *Alpiniae Oxyphyllae Fructus* and *Saposhnikoviae Radix* components in Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform database

Pubchem CID	Name	Oral bioavailability	Drug-likeness	Molecular formula
637517	Oleic acid	33.13	0.14	C ₁₈ H ₃₄ O ₂
5742590	Daucosterol	36.91	0.75	C ₃₅ H ₆₀ O ₆
12303645	Sitosterol	36.91	0.75	C ₂₉ H ₅₀ O
5280794	Stigmasterol	43.83	0.76	C ₂₉ H ₄₈ O
5282457	Linoleic	41.90	0.14	C ₁₈ H ₃₂ O ₂
10082923	(4S,5S,6R)-5,6-dihydroxy-4-isopropyl-6-methyl-2,3,4,5,7,8-hexahydro-1-naphthalen-1-one	38.51	0.11	C ₁₄ H ₂₂ O ₃
10857540	(1S,4R,4aS,6R,8aS)-6-isopropenyl-4,4a-dimethyldecalin-1,8a-diol	44.20	0.12	C ₁₅ H ₂₆ O ₂
5281607	Chrysin	22.61	0.18	C ₁₅ H ₁₀ O ₄
5280934	Linolenic acid	45.01	0.15	C ₁₈ H ₃₀ O ₂
5281607	Chrysin	22.61	0.18	C ₁₅ H ₁₀ O ₄
442510	(2R,3R)-3-(4-hydroxy-3-methoxyphenyl)-5-methoxy-2-methylol-2,3-dihydropyrano[5,6-h][1,4]benzodioxin-9-one	68.83	0.66	C ₂₀ H ₁₈ O ₈
MOL011730*	11-hydroxy-sec-o-beta-d-glucosylhamaudol_qt	50.24	0.24	None
6859585	Anomalin	59.65	0.66	C ₂₄ H ₂₆ O ₇
101866715	Divaricacatol	87.00	0.32	C ₁₆ H ₁₆ O ₇
9974111	Divaricatol	31.62	0.38	C ₁₇ H ₁₈ O ₇
10212	Ammidin	34.55	0.22	C ₁₆ H ₁₄ O ₄
5318962	Ledebourielol	32.05	0.51	C ₂₀ H ₂₂ O ₇
MOL011749*	Phelloptorin	43.39	0.28	None
441970	5-O-Methylvisamminol	37.99	0.25	C ₁₆ H ₁₈ O ₅
98608	Phellopterin	40.19	0.28	C ₁₇ H ₁₆ O ₅
5281703	Wogonin	30.68	0.23	C ₁₆ H ₁₂ O ₅
222284	Beta-sitosterol	36.91	0.75	C ₂₉ H ₅₀ O
5282184	Mandenol	42.00	0.19	C ₂₀ H ₃₆ O ₂
69502	Prangenidin	36.31	0.22	C ₁₆ H ₁₄ O ₄
442126	Decursin	39.27	0.38	C ₁₉ H ₂₀ O ₅

The parts below the dotted line are the components of the *Saposhnikoviae Radix* in the database. *The Pubchem CID and molecular formula of MOL011730 and MOL011749 have not been retrieved. But they were retained in the same study:

1. Yin Y, Liu J, Zhang M, et al. Mechanism of YuPingFeng in the Treatment of COPD Based on Network Pharmacology. *BioMed Res Int* 2020;2020(9):1–13. Available at: <http://doi.org/10.1155/2020/1630102>
2. Xia Q, Liu M, Li H, et al. Network Pharmacology Strategy to Investigate the Pharmacological Mechanism of HuangQiXiXin Decoction on Cough Variant Asthma and Evidence-Based Medicine Approach Validation. *Evid Based Complement Altern Med* 2020;2020(1):1–15. <http://doi.org/10.1155/2020/3829092>

Supplementary Table S1 (B) *Alpiniae Oxyphyllae Fructus* components in Encyclopedia of Traditional Chinese Medicine database

Pubchem CID	Name	Drug-likeness weight	Drug-likeness grading	Molecular formula
1268142	Nootkatone	0.613	Moderate	C ₁₅ H ₂₂ O
5318691	Izalpinin	0.885	Good	C ₁₆ H ₁₂ O ₅
14076604	Isocyperol	0.668	Moderate	C ₁₅ H ₂₄ O
44576208	6-Isopropenyl-4,4A-Dimethyl-1,2,3,4,4A,5,6,7-Octahydro-Naphthalen-1-ol	0.669	Moderate	C ₁₅ H ₂₄ O
182645	Nootkatol	0.669	Moderate	C ₁₅ H ₂₄ O
10082923	Oxyphyllenodiol A	0.732	Good	C ₁₄ H ₂₂ O ₃
5279294	Oxyphyllenodiol B	0.732	Good	C ₁₄ H ₂₂ O ₃
10262534	Oxyphyllenone A	0.624	Moderate	C ₁₂ H ₁₈ O ₃
44310512	Oxyphyllenone B	0.624	Moderate	C ₁₂ H ₁₈ O ₃
637451	Oxyphyllol A	0.669	Moderate	C ₁₅ H ₂₄ O
11128252	Oxyphyllol B	0.708	Good	C ₁₅ H ₂₂ O ₂
10857540	Oxyphyllol C	0.690	Good	C ₁₅ H ₂₆ O ₂
5281954	Tectochrysin	0.909	Good	C ₁₆ H ₁₂ O ₄

Supplementary Table S2 Four topological features shown in Figure 4 (The compounds-diseases-targets network (334 nodes and 3567 edges))

Target	Degree	Closeness centrality	Betweenness centrality	Average shortest path length
TP53	269	0.474170	0.13338428	2.10894705
ESR1	188	0.463339	0.07508256	2.15824711
EP300	141	0.437666	0.02782080	2.28484480
CASP3	130	0.420205	0.04255570	2.37979306
CREBBP	128	0.435347	0.02141013	2.29701765
SRC	128	0.434082	0.02539069	2.30371272
AR	120	0.450631	0.03013742	2.21911138
PRKCA	120	0.430781	0.03381159	2.32136336
MAPK1	118	0.444655	0.02740746	2.24893488
AKT1	117	0.431687	0.03830986	2.31649422
JUN	116	0.418492	0.02773221	2.38953135
CSNK2A1	114	0.434082	0.03156422	2.30371272
RELA	113	0.420958	0.02710828	2.37553256
ACTB	101	0.385500	0.04331679	2.59403530
GRB2	98	0.409624	0.01754404	2.44126598
EGFR	95	0.423345	0.01746643	2.36214242
SMAD3	92	0.436620	0.01858000	2.29032258
RB1	89	0.419454	0.01527414	2.38405356
STAT3	85	0.427197	0.01721246	2.34083993
PRKCD	84	0.417960	0.01971859	2.39257456
MAPK14	84	0.393627	0.01752462	2.54047474
FYN	83	0.408808	0.01085729	2.44613512
MAPK3	82	0.425758	0.01291889	2.34875228
NR3C1	81	0.419561	0.01249155	2.38344492
CTNNB1	80	0.426532	0.01456387	2.34449178
BRCA1	78	0.436736	0.01333554	2.28971394
PIK3R1	78	0.405479	0.01019982	2.46622033
CDK1	78	0.405079	0.01110126	2.46865490
YWHAG	77	0.411367	0.01716657	2.43091905
HDAC1	77	0.403487	0.01076911	2.47839318
SHC1	75	0.406180	0.00705331	2.46195983
PRKACA	74	0.404879	0.01644066	2.46987219
FN1	74	0.350694	0.02829070	2.85149117
SMAD2	73	0.424548	0.01012471	2.35544735
GSK3B	73	0.407086	0.02363542	2.45648205
RXRA	73	0.391750	0.00963672	2.55264760
CASP8	71	0.394857	0.01455308	2.53256239
JAK2	70	0.382627	0.00932462	2.61351187
ABL1	68	0.422256	0.00964733	2.36822885
HSP90AA1	67	0.432027	0.01807676	2.31466829
SP1	66	0.424877	0.00800306	2.35362142
JAK1	66	0.372985	0.00755025	2.68107121
NFKB1	65	0.397821	0.00921110	2.51369446
HDAC2	65	0.386861	0.01254925	2.58490566
PTPN11	65	0.385500	0.00433490	2.59403530
SMAD4	63	0.413646	0.01400411	2.41752891
LCK	63	0.405980	0.00620716	2.46317712
RAF1	61	0.408402	0.00737336	2.44856969
LYN	61	0.395237	0.00752854	2.53012781
STAT1	60	0.409930	0.00946123	2.43944005
UBE2I	59	0.401810	0.00706554	2.48874011
MAPK8	58	0.406180	0.00771675	2.46195983
YWHAZ	58	0.402499	0.00664049	2.48447961
CDKN1A	57	0.391097	0.01757399	2.55690809
PRKCB	57	0.378136	0.00721111	2.64455265
PLCG1	57	0.371972	0.00344572	2.68837492

Supplementary Table S2 Four topological features shown in Figure 4 (The compounds-diseases-targets network (334 nodes and 3567 edges)) (continued)

Target	Degree	Closeness centrality	Betweenness centrality	Average shortest path length
PTK2	56	0.400536	0.00753854	2.49665247
MYC	54	0.394667	0.00640527	2.53377967
PTPN6	53	0.389152	0.00479341	2.56968959
YWHAB	53	0.386952	0.00392704	2.58429702
NCOA1	53	0.382004	0.00290452	2.61777237
CBL	53	0.377788	0.00206476	2.64698722
PRKCZ	52	0.400732	0.00645410	2.49543518
CDK2	50	0.381030	0.00643465	2.62446744
NCOR2	50	0.379533	0.00331889	2.63481436
PTK2B	50	0.377875	0.00362789	2.64637858
BCL2	49	0.398303	0.00964303	2.51065125
IRS1	49	0.391563	0.00293994	2.55386488
TBP	49	0.386952	0.00326863	2.58429702
CSNK2A2	49	0.385681	0.00484965	2.59281802
INSR	49	0.380236	0.00225349	2.62994522
PML	48	0.401123	0.00466664	2.49300061
CAV1	47	0.399562	0.00546996	2.50273889
ESR2	47	0.381207	0.00306659	2.62325015
SYK	47	0.376662	0.00230472	2.65489957
RARA	47	0.370128	0.00277465	2.70176506
TGFBR1	46	0.376576	0.00637589	2.65550822
CEBPB	45	0.394478	0.00412477	2.53499696
HDAC3	45	0.392593	0.00500372	2.54716981
APP	44	0.378571	0.01443973	2.64150943
MDM2	43	0.409114	0.00469820	2.44430919
FOS	43	0.385138	0.00294326	2.59646987
SUMO1	43	0.383520	0.00229198	2.60742544
VIM	43	0.382627	0.00503623	2.61351187
KDR	43	0.365761	0.00685951	2.73402313
HCK	43	0.363415	0.00575800	2.75167377
CRK	43	0.363174	0.00125277	2.75349970
CALM1	42	0.387409	0.00593141	2.58125380
YWHAE	42	0.385409	0.00372647	2.59464394
VAV1	42	0.377008	0.00223038	2.65246500
PAK1	41	0.405879	0.00470036	2.46378576
PXN	41	0.387866	0.00324629	2.57821059
NCOA3	41	0.380412	0.00202607	2.62872794
CASP7	41	0.368551	0.00316314	2.71332928
UNC119	41	0.355705	0.00332496	2.81132075
STAT5A	40	0.388324	0.00212082	2.57516738
EEF1A1	40	0.373834	0.00547609	2.67498478
CHUK	39	0.407490	0.00293467	2.45404747
NFKBIA	38	0.395142	0.00370841	2.53073646
IGF1R	38	0.385953	0.00329741	2.59099209
RAC1	38	0.385771	0.00413787	2.59220937
RASA1	38	0.369131	0.00157452	2.70906878
YWHAQ	38	0.368882	0.00254743	2.71089470
SIN3A	38	0.362613	0.00261374	2.75776019
TRAF2	38	0.354630	0.00224984	2.81984175
XRCC6	37	0.391470	0.00362163	2.55447352
GNB2L1	37	0.387866	0.00357856	2.57821059
CASP9	37	0.373070	0.00551422	2.68046257
NRIP1	37	0.368882	0.00264741	2.71089470
PDGFRB	37	0.366496	0.00107182	2.72854534
PCNA	37	0.356476	0.00294748	2.80523433
PIAS1	36	0.398303	0.00280195	2.51065125

Supplementary Table S2 Four topological features shown in Figure 4 (The compounds-diseases-targets network (334 nodes and 3567 edges)) (continued)

Target	Degree	Closeness centrality	Betweenness centrality	Average shortest path length
DAXX	36	0.389613	0.00518037	2.56664638
MAPT	36	0.385771	0.00429904	2.59220937
ACTA1	36	0.381561	0.00574650	2.62081558
IKBKB	36	0.379358	0.00185537	2.63603165
PRKCG	36	0.351820	0.00167012	2.84236153
KAT5	35	0.397628	0.00385563	2.51491175
BTB	35	0.386588	0.00295027	2.58673159
CCND1	35	0.384958	0.00518738	2.59768716
HNF4A	35	0.382894	0.00300394	2.61168594
ZBTB16	35	0.378049	0.00339587	2.64516129
CDKN1B	35	0.375801	0.00436004	2.66098600
SMAD1	35	0.370964	0.00435395	2.69567864
THRB	35	0.365273	0.00366410	2.73767498
PRKCE	35	0.364949	0.00242169	2.74010956
COPS6	35	0.363737	0.00266595	2.74923920
GRIN1	35	0.357563	0.00347439	2.79671333
UBB	34	0.391563	0.00290298	2.55386488
HSPA1A	34	0.383431	0.00349740	2.60803408
KAT2B	34	0.379008	0.00171042	2.63846622
PPARG	34	0.351143	0.00147337	2.84783932
CSNK2B	33	0.395332	0.00369694	2.52951917
YWHAH	33	0.377268	0.00160648	2.65063907
STAT5B	33	0.374174	0.00111559	2.67255021
NCOA2	33	0.372056	0.00134940	2.68776628
VDR	33	0.367233	0.00452615	2.72306756
ITGB1	33	0.363737	0.00605124	2.74923920
KIT	33	0.363415	0.00089133	2.75167377
NCOR1	33	0.363254	0.00137157	2.75289105
NCK1	33	0.352273	0.00076150	2.83870968
E2F1	32	0.372647	0.00157043	2.68350578
BCL2L1	32	0.366905	0.00311074	2.72550213
PIN1	31	0.397628	0.00261251	2.51491175
PPP2CA	31	0.389891	0.00364574	2.56482045
TP73	31	0.385681	0.00126944	2.59281802
SRF	31	0.382182	0.00292215	2.61655508
FLNA	31	0.381207	0.00446816	2.62325015
PPP1CA	31	0.379271	0.00345462	2.63664029
SNCA	31	0.372731	0.00260176	2.68289714
HTT	30	0.401025	0.00369016	2.49360925
MYOD1	30	0.384958	0.00188663	2.59768716
NCOA6	30	0.369131	0.00099334	2.70906878
IKBKG	30	0.365030	0.00166698	2.73950091
TRAF6	30	0.363656	0.00158391	2.74984784
CDC42	29	0.384148	0.00229189	2.60316494
BCR	29	0.380765	0.00155832	2.62629337
PPARA	29	0.372225	0.00351514	2.68654900
ATXN1	29	0.371048	0.00355706	2.69506999
CHD3	29	0.367479	0.00175199	2.72124163
CASP1	29	0.357796	0.00243299	2.79488740
SKIL	29	0.355166	0.00492467	2.81558125
HIF1A	28	0.393627	0.00205479	2.54047474
PTPN1	28	0.391563	0.00143710	2.55386488
CDK5	28	0.380765	0.00278584	2.62629337
BCAR1	28	0.377614	0.00131461	2.64820450
ERBB2	28	0.376145	0.00123472	2.65855143
PIAS4	28	0.373749	0.00145079	2.67559343

Supplementary Table S2 Four topological features shown in Figure 4 (The compounds-diseases-targets network (334 nodes and 3567 edges)) (continued)

Target	Degree	Closeness centrality	Betweenness centrality	Average shortest path length
CREB1	28	0.370546	0.00229927	2.69872185
HSPA8	28	0.369712	0.00354830	2.70480828
MAP3K7	28	0.364706	0.00170437	2.74193548
THRA	28	0.363737	0.00092956	2.74923920
HRAS	28	0.362213	0.00167140	2.76080341
SUMO4	28	0.360623	0.00205035	2.77297626
UBQLN4	28	0.358734	0.00382152	2.78758369
CASP6	28	0.357563	0.00119032	2.79671333
GRIN2B	28	0.355936	0.00317308	2.80949483
PRKDC	27	0.399174	0.00202954	2.50517346
KHDRBS1	27	0.375629	0.00083615	2.66220329
PDPK1	27	0.369380	0.00151972	2.70724285
IRS2	27	0.352273	0.00070582	2.83870968
HMGB1	26	0.390725	0.00345068	2.55934267
KRT18	26	0.381383	0.00219336	2.62203287
COPS5	26	0.373239	0.00163587	2.67924528
PSEN1	26	0.372225	0.00164582	2.68654900
TNFRSF1A	26	0.371972	0.00185469	2.68837492
ATF2	26	0.369629	0.00112709	2.70541692
CSK	26	0.369131	0.00069548	2.70906878
PARP1	26	0.365680	0.00218233	2.73463177
GAPDH	26	0.364544	0.00272542	2.74315277
DYNLL1	26	0.355397	0.00272740	2.81375533
DLG4	26	0.354936	0.00380915	2.81740718
PRMT1	25	0.381207	0.00326843	2.62325015
EIF2AK2	25	0.380853	0.00146332	2.62568472
EZR	25	0.369380	0.00275395	2.70724285
HSF1	25	0.369048	0.00075571	2.70967742
MAP2K1	25	0.366332	0.00160706	2.72976263
PGR	25	0.364059	0.00117009	2.74680463
ITGB3	25	0.363656	0.00356611	2.74984784
CEBPA	25	0.362293	0.00096753	2.76019477
ATN1	25	0.353561	0.00377307	2.82836275
CCNE1	25	0.353485	0.00170698	2.82897139
SMARCA4	24	0.382360	0.00273447	2.61533780
MED1	24	0.366823	0.00107010	2.72611077
EWSR1	24	0.366332	0.00214748	2.72976263
MBP	24	0.365599	0.00241086	2.73524041
TGFBR2	24	0.364221	0.00267876	2.74558734
GTF2B	24	0.362453	0.00060940	2.75897748
BAD	24	0.362134	0.00086950	2.76141205
MAP3K5	24	0.355859	0.00106693	2.81010347
CDK4	24	0.355474	0.00118308	2.81314668
SOCS1	24	0.355474	0.00062296	2.81314668
HDAC4	24	0.352122	0.00092274	2.83992696
CXCR4	24	0.351820	0.00247471	2.84236153
TSC2	23	0.378223	0.00094128	2.64394400
ETS1	23	0.376059	0.00087710	2.65916007
CSNK1A1	23	0.374943	0.00285376	2.66707243
MAPK9	23	0.370964	0.00100107	2.69567864
ING1	23	0.368716	0.00158328	2.71211199
ADRBK1	23	0.366577	0.00197416	2.72793670
PTMA	23	0.365924	0.00108017	2.73280584
AHR	23	0.364868	0.00072003	2.74071820
POU2F1	23	0.364221	0.00055137	2.74558734
CCNA2	23	0.355166	0.00115785	2.81558125

Supplementary Table S2 Four topological features shown in Figure 4 (The compounds-diseases-targets network (334 nodes and 3567 edges)) (continued)

Target	Degree	Closeness centrality	Betweenness centrality	Average shortest path length
MDM4	22	0.385048	0.00065557	2.59707851
CHEK1	22	0.375200	0.00139471	2.66524650
CDH1	22	0.374174	0.00178217	2.67255021
FAS	22	0.367808	0.00123824	2.71880706
NOTCH1	22	0.367315	0.00196187	2.72245892
PAK2	22	0.364706	0.00111243	2.74193548
TUBB	22	0.364382	0.00231964	2.74437005
RPS6KB1	22	0.358421	0.00083376	2.79001826
CSF2RB	22	0.357718	0.00075909	2.79549604
TUBA4A	22	0.357485	0.00157336	2.79732197
MAP3K3	22	0.357485	0.00078942	2.79732197
PPARGC1A	22	0.352122	0.00106967	2.83992696
FHL2	21	0.374430	0.00265951	2.67072428
BCL3	21	0.373155	0.00079899	2.67985393
RUNX2	21	0.369546	0.00073845	2.70602556
RPS6KA1	21	0.367973	0.00075762	2.71758977
ELK1	21	0.365111	0.00079503	2.73889227
JUND	21	0.362773	0.00084507	2.75654291
HIPK2	21	0.360703	0.00060273	2.77236762
WAS	21	0.358186	0.00076898	2.79184419
NEDD9	21	0.355474	0.00053250	2.81314668
PTPRC	21	0.355397	0.00224984	2.81375533
PPARD	21	0.355090	0.00081305	2.81618990
SMAD9	21	0.353714	0.00309948	2.82714547
FOXO1	20	0.385229	0.00085190	2.59586123
NCF1	20	0.379096	0.00257378	2.63785758
NR4A1	20	0.377614	0.00075176	2.64820450
PIAS3	20	0.374686	0.00060472	2.66889836
CDC25A	20	0.363335	0.00051472	2.75228241
KPNB1	20	0.361020	0.00140144	2.76993305
ZHX1	20	0.360623	0.00075469	2.77297626
RHOA	20	0.355166	0.00074674	2.81558125
GIT1	20	0.353181	0.00137964	2.83140596
RPS6KA5	20	0.353030	0.00082748	2.83262325
POLR2A	20	0.352954	0.00174400	2.83323189
CDC25C	19	0.368468	0.00077571	2.71393792
MET	19	0.363979	0.00133804	2.74741327
RPS6KA3	19	0.363656	0.00176727	2.74984784
SVIL	19	0.361337	0.00239622	2.76749848
GADD45G	19	0.358890	0.00091694	2.78636640
PRKD1	19	0.358030	0.00071738	2.79306147
SFN	19	0.358030	0.00070475	2.79306147
IL6ST	19	0.356245	0.00133936	2.80706026
PECAM1	19	0.355551	0.00050689	2.81253804
SNW1	19	0.353638	0.00060302	2.82775411
VTN	19	0.351895	0.00428644	2.84175289
AXIN1	19	0.350021	0.00064799	2.85696896
TOP2A	18	0.382805	0.00084739	2.61229458
PTEN	18	0.376576	0.00232654	2.65550822
TGM2	18	0.376489	0.00533015	2.65611686
HABP4	18	0.370629	0.00065539	2.69811321
KPNA2	18	0.367397	0.00086305	2.72185027
HNRNPU	18	0.366905	0.00190151	2.72550213
CAPN1	18	0.366414	0.00229034	2.72915399
TEC	18	0.361258	0.00079693	2.76810712
HNFI1A	18	0.361099	0.00252863	2.76932441

Supplementary Table S2 Four topological features shown in Figure 4 (The compounds-diseases-targets network (334 nodes and 3567 edges)) (continued)

Target	Degree	Closeness centrality	Betweenness centrality	Average shortest path length
PSEN2	18	0.360940	0.00073266	2.77054169
GSK3A	18	0.359519	0.00091134	2.78149726
EPHB2	18	0.352802	0.00148123	2.83444918
PRPF40A	18	0.352273	0.00212531	2.83870968
FLT1	18	0.352122	0.00055815	2.83992696
DAB2	17	0.368056	0.00097902	2.71698113
NCL	17	0.363818	0.00111744	2.74863055
NPM1	17	0.363496	0.00061723	2.75106512
IRAK1	17	0.362134	0.00073506	2.76141205
PRKCQ	17	0.358655	0.00075890	2.78819233
SAT1	17	0.357407	0.00096694	2.79793061
HNRNPK	17	0.355782	0.00070818	2.81071211
SMAD7	17	0.354936	0.00058537	2.81740718
AKT2	17	0.352575	0.00090125	2.83627511
CAMK2G	17	0.352348	0.00052727	2.83810103
BID	17	0.351369	0.00053471	2.84601339
IGFBP3	17	0.350395	0.00379264	2.85392575
LMNA	16	0.368138	0.00114025	2.71637249
TERT	16	0.365599	0.00071024	2.73524041
DVL2	16	0.365273	0.00176876	2.73767498
RAD51	16	0.364544	0.00058368	2.74315277
FASLG	16	0.362293	0.00170083	2.76019477
ARRB2	16	0.354936	0.00101102	2.81740718
PLK1	16	0.352878	0.00061958	2.83384054
GSN	15	0.369546	0.00279631	2.70602556
BRCA2	15	0.361815	0.00082071	2.76384662
CREM	15	0.361815	0.00052437	2.76384662
PLD2	15	0.355551	0.00074794	2.81253804
UBTF	15	0.355551	0.00062309	2.81253804
SPTAN1	15	0.353030	0.00115051	2.83262325
NUMB	15	0.351294	0.00065381	2.84662203
YBX1	14	0.371132	0.00088642	2.69446135
TP53BP2	14	0.370295	0.00099720	2.70054778
TSG101	14	0.369380	0.00100449	2.70724285
CDK9	14	0.365517	0.00053006	2.73584906
TGFB1I1	14	0.358969	0.00065579	2.78575776
MAPKAPK5	14	0.358577	0.00057323	2.78880097
PKD1	14	0.358108	0.00142227	2.79245283
C1QBP	14	0.357329	0.00158797	2.79853926
TIAM1	14	0.357019	0.00059259	2.80097383
HSPD1	14	0.351971	0.00093462	2.84114425
IQGAP1	14	0.351444	0.00067045	2.84540475
TFAP2A	13	0.367808	0.00062218	2.71880706
WEE1	13	0.362054	0.00057104	2.76202069
JUNB	13	0.353714	0.00056537	2.82714547
PRKAR1A	13	0.352802	0.00080039	2.83444918
ANXA2	13	0.351143	0.00153386	2.84783932
DNM2	13	0.351068	0.00069832	2.84844796
PEA15	12	0.354171	0.00050859	2.82349361
EIF2S2	11	0.353638	0.00051497	2.82775411
RAB4A	10	0.361496	0.00138363	2.76628119
NFE2L2	10	0.351895	0.00059252	2.84175289
NMT1	8	0.354706	0.00058117	2.81923311
PBK	8	0.352726	0.00055589	2.83505782

Supplementary Table S3 (A) Gene Ontology (GO) map of target genes (biological process)

Term		Count	Pop hits	P value
GO: 0045944	Positive regulation of transcription from RNA polymerase II promoter	33	981	2.78472E – 19
GO: 0006351	Transcription, DNA-templated	25	1955	8.06402E – 06
GO: 0045893	Positive regulation of transcription, DNA-templated	20	515	2.60345E – 12
GO: 0007165	Signal transduction	19	1161	6.67532E – 06
GO: 0006367	Transcription initiation from RNA polymerase II promoter	18	152	4.46266E – 19
GO: 0043066	Negative regulation of apoptotic process	18	455	3.59241E – 11
GO: 0000122	Negative regulation of transcription from RNA polymerase II promoter	17	720	2.29156E – 07
GO: 0006355	Regulation of transcription, DNA-templated	17	1504	0.001725879
GO: 0043401	Steroid hormone mediated signaling pathway	14	57	4.79484E – 19
GO: 0042493	Response to drug	14	304	1.84777E – 09
GO: 0006915	Apoptotic process	14	567	2.55976E – 06
GO: 0006468	Protein phosphorylation	13	456	1.57377E – 06
GO: 0032355	Response to estradiol	11	91	1.58744E – 11
GO: 0008284	Positive regulation of cell proliferation	11	466	7.12243E – 05
GO: 0006366	Transcription from RNA polymerase II promoter	11	513	0.000156911
GO: 0006954	Inflammatory response	10	379	7.80155E – 05
GO: 0008285	Negative regulation of cell proliferation	10	396	0.000108947
GO: 0045892	Negative regulation of transcription, DNA-templated	10	499	0.000599576
GO: 0030522	Intracellular receptor signaling pathway	9	38	8.07597E – 12
GO: 0006974	Cellular response to DNA damage stimulus	9	208	6.53884E – 06
GO: 1901796	Regulation of signal transduction by p53 class mediator	8	124	2.0524E – 06
GO: 0001525	Angiogenesis	8	223	9.25592E – 05
GO: 0010628	Positive regulation of gene expression	8	262	0.000250168
GO: 0008283	Cell proliferation	8	366	0.001791387
GO: 0071456	Cellular response to hypoxia	7	96	6.37192E – 06
GO: 0018105	Peptidyl-serine phosphorylation	7	125	2.88982E – 05
GO: 0010629	Negative regulation of gene expression	7	137	4.83927E – 05
GO: 0032496	Response to lipopolysaccharide	7	164	0.000131027
GO: 0043065	Positive regulation of apoptotic process	7	300	0.00307297
GO: 0035556	Intracellular signal transduction	7	403	0.012454197
GO: 0046677	Response to antibiotic	6	32	3.93699E – 07
GO: 0097192	Extrinsic apoptotic signaling pathway in absence of ligand	6	34	5.39965E – 07
GO: 0034644	Cellular response to UV	6	44	2.03042E – 06
GO: 0048146	Positive regulation of fibroblast proliferation	6	54	5.69674E – 06
GO: 0007265	Ras protein signal transduction	6	70	2.05426E – 05
GO: 0045471	Response to ethanol	6	105	0.000143927
GO: 0030308	Negative regulation of cell growth	6	121	0.000279252
GO: 0043524	Negative regulation of neuron apoptotic process	6	132	0.000417174
GO: 0007568	Aging	6	165	0.001144493
GO: 0046777	Protein autophosphorylation	6	172	0.001376277
GO: 0042127	Regulation of cell proliferation	6	185	0.001896293
GO: 0042981	Regulation of apoptotic process	6	213	0.0034858
GO: 0000165	MAPK cascade	6	262	0.008272961
GO: 0015721	Bile acid and bile salt transport	5	27	7.71125E – 06
GO: 0018107	Peptidyl-threonine phosphorylation	5	38	3.11681E – 05
GO: 0044255	Cellular lipid metabolic process	5	41	4.22996E – 05
GO: 0045429	Positive regulation of nitric oxide biosynthetic process	5	43	5.11761E – 05
GO: 0043525	Positive regulation of neuron apoptotic process	5	43	5.11761E – 05

Supplementary Table S3 (A) Gene Ontology (GO) map of target genes (biological process) (continued)

Term	Count	Pop hits	P value
GO: 0031100 Organ regeneration	5	47	7.29038E – 05
GO: 0032922 Circadian regulation of gene expression	5	57	0.000155729
GO: 0006977 DNA damage response, signal transduction by p53 class mediator resulting in cell cycle arrest	5	62	0.000215995
GO: 0043627 Response to estrogen	5	65	0.000259326
GO: 0071347 Cellular response to interleukin-1	5	71	0.000364205
GO: 0071260 Cellular response to mechanical stimulus	5	71	0.000364205
GO: 0048010 Vascular endothelial growth factor receptor signaling pathway	5	72	0.000384242
GO: 0009636 Response to toxic substance	5	85	0.000721665
GO: 0042593 Glucose homeostasis	5	101	0.001373915
GO: 0000082 G1/S transition of mitotic cell cycle	5	102	0.001424869
GO: 0071222 Cellular response to lipopolysaccharide	5	113	0.002075362
GO: 0051092 Positive regulation of NF-kappaB transcription factor activity	5	133	0.003737861
GO: 0018108 Peptidyl-tyrosine phosphorylation	5	153	0.006131468
GO: 0001666 Response to hypoxia	5	172	0.0091923
GO: 0070374 Positive regulation of ERK1 and ERK2 cascade	5	175	0.009751936
GO: 0030335 Positive regulation of cell migration	5	184	0.011562557
GO: 0007049 Cell cycle	5	217	0.019998645
GO: 0007268 Chemical synaptic transmission	5	240	0.027663126
GO: 0007267 Cell-cell signaling	5	254	0.033081484
GO: 0035994 Response to muscle stretch	4	16	5.57619E – 05
GO: 0010165 Response to X-ray	4	22	0.000150216
GO: 0035235 Ionotropic glutamate receptor signaling pathway	4	24	0.000196076
GO: 0097421 Liver regeneration	4	29	0.000347963
GO: 0010332 Response to gamma radiation	4	31	0.000425124
GO: 0045907 Positive regulation of vasoconstriction	4	32	0.000467497
GO: 0070059 Intrinsic apoptotic signaling pathway in response to endoplasmic reticulum stress	4	33	0.000512488
GO: 0009409 Response to cold	4	36	0.00066381
GO: 0038083 Peptidyl-tyrosine autophosphorylation	4	40	0.000906057
GO: 0030521 Androgen receptor signaling pathway	4	41	0.000974248
GO: 0007595 Lactation	4	42	0.001045607
GO: 0001541 Ovarian follicle development	4	42	0.001045607
GO: 0008630 Intrinsic apoptotic signaling pathway in response to DNA damage	4	47	0.00145184
GO: 0045600 Positive regulation of fat cell differentiation	4	47	0.00145184
GO: 0042542 Response to hydrogen peroxide	4	51	0.001839299
GO: 0034097 Response to cytokine	4	52	0.001945256
GO: 0048511 Rhythmic process	4	54	0.002168409
GO: 0070301 Cellular response to hydrogen peroxide	4	57	0.002531911
GO: 0032091 Negative regulation of protein binding	4	57	0.002531911
GO: 0071407 Cellular response to organic cyclic compound	4	59	0.002793931
GO: 0048661 Positive regulation of smooth muscle cell proliferation	4	60	0.002930971
GO: 0007613 Memory	4	62	0.003217309
GO: 0050727 Regulation of inflammatory response	4	63	0.003366684
GO: 0007200 Phospholipase C-activating G-protein coupled receptor signaling pathway	4	66	0.003840079
GO: 0050796 Regulation of insulin secretion	4	67	0.004006419
GO: 0009749 Response to glucose	4	68	0.004177089
GO: 0001938 Positive regulation of endothelial cell proliferation	4	69	0.004352121
GO: 0033138 Positive regulation of peptidyl-serine phosphorylation	4	70	0.004531547

Supplementary Table S3 (A) Gene Ontology (GO) map of target genes (biological process) (continued)

Term	Count	Pop hits	P value
GO: 0071300 Cellular response to retinoic acid	4	70	0.004531547
GO: 0097190 Apoptotic signaling pathway	4	71	0.004715401
GO: 0001889 Liver development	4	74	0.005293829
GO: 0007623 Circadian rhythm	4	75	0.005495694
GO: 0006805 Xenobiotic metabolic process	4	78	0.006128848
GO: 0050728 Negative regulation of inflammatory response	4	79	0.006349177
GO: 0043410 Positive regulation of MAPK cascade	4	81	0.006803902
GO: 0006919 Activation of cysteine-type endopeptidase activity involved in apoptotic process	4	83	0.007277548
GO: 0030307 Positive regulation of cell growth	4	84	0.007521524
GO: 0006338 Chromatin remodeling	4	86	0.008023895
GO: 0010468 Regulation of gene expression	4	100	0.012090981
GO: 0051091 Positive regulation of sequence-specific DNA binding transcription factor activity	4	105	0.013782299
GO: 0030168 Platelet activation	4	115	0.017550489
GO: 0016925 Protein sumoylation	4	117	0.018366346
GO: 0038096 Fc-gamma receptor signaling pathway involved in phagocytosis	4	127	0.022758786
GO: 0000086 G2/M transition of mitotic cell cycle	4	137	0.027674094
GO: 0007050 Cell cycle arrest	4	141	0.029786343
GO: 0060745 Mammary gland branching involved in pregnancy	3	3	6.70366E-05
GO: 0000320 Re-entry into mitotic cell cycle	3	4	0.000133658
GO: 0060850 Regulation of transcription involved in cell fate commitment	3	5	0.000222074
GO: 0032025 Response to cobalt ion	3	6	0.000332081
GO: 0035357 Peroxisome proliferator activated receptor signaling pathway	3	7	0.000463475
GO: 0008635 Activation of cysteine-type endopeptidase activity involved in apoptotic process by cytochrome c	3	9	0.000789624
GO: 0031571 Mitotic G1 DNA damage checkpoint	3	11	0.001198929
GO: 0090399 Replicative senescence	3	12	0.001434272
GO: 0006809 Nitric oxide biosynthetic process	3	13	0.001689818
GO: 0035729 Cellular response to hepatocyte growth factor stimulus	3	14	0.001965371
GO: 0021854 Hypothalamus development	3	15	0.002260742
GO: 0097194 Execution phase of apoptosis	3	16	0.002575739
GO: 0060749 Mammary gland alveolus development	3	17	0.002910174
GO: 0030224 Monocyte differentiation	3	17	0.002910174
GO: 0048384 Retinoic acid receptor signaling pathway	3	18	0.003263858
GO: 0051968 Positive regulation of synaptic transmission, glutamatergic	3	19	0.003636607
GO: 0008637 Apoptotic mitochondrial changes	3	19	0.003636607
GO: 0043536 Positive regulation of blood vessel endothelial cell migration	3	19	0.003636607
GO: 0006921 Cellular component disassembly involved in execution Phase of apoptosis	3	21	0.004438555
GO: 0051000 Positive regulation of nitric-oxide synthase activity	3	22	0.004867389
GO: 0001954 Positive regulation of cell-matrix adhesion	3	22	0.004867389
GO: 0045453 Bone resorption	3	22	0.004867389
GO: 0035924 Cellular response to vascular endothelial growth factor stimulus	3	23	0.005314554
GO: 0001836 Release of cytochrome c from mitochondria	3	23	0.005314554
GO: 0034612 Response to tumor necrosis factor	3	25	0.006263158
GO: 0051090 Regulation of sequence-specific DNA binding transcription factor activity	3	25	0.006263158
GO: 0051881 Regulation of mitochondrial membrane potential	3	28	0.007819091
GO: 0097193 Intrinsic apoptotic signaling pathway	3	30	0.008943023
GO: 2000379 Positive regulation of reactive oxygen species metabolic process	3	30	0.008943023
GO: 1900740 Positive regulation of protein insertion into mitochondrial membrane	3	30	0.008943023

Supplementary Table S3 (A) Gene Ontology (GO) map of target genes (biological process) (continued)

Term	Count	Pop hits	P value
involved in apoptotic signaling pathway			
GO: 0001975 Response to amphetamine	3	31	0.009530464
GO: 0048147 Negative regulation of fibroblast proliferation	3	31	0.009530464
GO: 0071479 Cellular response to ionizing radiation	3	31	0.009530464
GO: 0042100 B cell proliferation	3	32	0.010134662
GO: 0042220 Response to cocaine	3	32	0.010134662
GO: 0031663 Lipopolysaccharide-mediated signaling pathway	3	32	0.010134662
GO: 0050873 Brown fat cell differentiation	3	32	0.010134662
GO: 0071364 Cellular response to epidermal growth factor stimulus	3	33	0.010755447
GO: 2001244 Positive regulation of intrinsic apoptotic signaling pathway	3	33	0.010755447
GO: 0001890 Placenta development	3	35	0.012046112
GO: 0010507 Negative regulation of autophagy	3	36	0.012715659
GO: 0035094 Response to nicotine	3	37	0.01340113
GO: 2001240 Negative regulation of extrinsic apoptotic signaling pathway in absence of ligand	3	37	0.01340113
GO: 0043124 Negative regulation of I-kappaB kinase/NF-kappaB signaling	3	40	0.015551465
GO: 0007190 Activation of adenylate cyclase activity	3	40	0.015551465
GO: 0032526 Response to retinoic acid	3	41	0.016299014
GO: 0032870 Cellular response to hormone stimulus	3	45	0.019438854
GO: 0051591 Response to cAMP	3	46	0.020260446
GO: 0010595 Positive regulation of endothelial cell migration	3	46	0.020260446
GO: 0042752 Regulation of circadian rhythm	3	49	0.022810691
GO: 0032481 Positive regulation of type I interferon production	3	51	0.024580576
GO: 0019233 Sensory perception of pain	3	52	0.025485988
GO: 0008344 Adult locomotory behavior	3	52	0.025485988
GO: 0021987 Cerebral cortex development	3	56	0.029240709
GO: 0021766 Hippocampus development	3	56	0.029240709
GO: 0007612 Learning	3	57	0.030211938
GO: 0009612 Response to mechanical stimulus	3	59	0.032192463
GO: 0043433 Negative regulation of sequence-specific DNA binding transcription factor activity	3	60	0.03320148
GO: 0006950 Response to stress	3	61	0.034222816
GO: 0060395 SMAD protein signal transduction	3	62	0.035256333
GO: 0000902 Cell morphogenesis	3	62	0.035256333
GO: 0051384 Response to glucocorticoid	3	65	0.038428616
GO: 0006006 Glucose metabolic process	3	67	0.040601911
GO: 0008203 Cholesterol metabolic process	3	68	0.041705693
GO: 0035690 Cellular response to drug	3	69	0.042820725
GO: 0060333 Interferon-gamma-mediated signaling pathway	3	71	0.045084022
GO: 0045444 Fat cell differentiation	3	73	0.047390778
GO: 1904017 Cellular response to Thyroglobulin triiodothyronine	2	2	0.009505932
GO: 0006808 Regulation of nitrogen utilization	2	2	0.009505932
GO: 0070561 Vitamin D receptor signaling pathway	2	3	0.014225379
GO: 0044774 Mitotic DNA integrity checkpoint	2	3	0.014225379
GO: 2000630 Positive regulation of miRNA metabolic process	2	3	0.014225379
GO: 0070141 Response to UV-A	2	3	0.014225379
GO: 0010871 Negative regulation of receptor biosynthetic process	2	3	0.014225379
GO: 0000819 Sister chromatid segregation	2	3	0.014225379
GO: 0060058 Positive regulation of apoptotic process involved in mammary gland involution	2	4	0.01892262

Supplementary Table S3 (A) Gene Ontology (GO) map of target genes (biological process) (continued)

Term		Count	Pop hits	P value
GO: 0045986	Negative regulation of smooth muscle contraction	2	4	0.01892262
GO: 0032079	Positive regulation of endodeoxyribonuclease activity	2	4	0.01892262
GO: 0060750	Epithelial cell proliferation involved in mammary gland duct elongation	2	4	0.01892262
GO: 0090400	Stress-induced premature senescence	2	4	0.01892262
GO: 1900015	Regulation of cytokine production involved in inflammatory response	2	4	0.01892262
GO: 0099565	Chemical synaptic transmission, postsynaptic	2	5	0.023597756
GO: 0010891	Negative regulation of sequestering of triglyceride	2	5	0.023597756
GO: 0034349	Glial cell apoptotic process	2	5	0.023597756
GO: 1904385	Cellular response to angiotensin	2	5	0.023597756
GO: 0046321	Positive regulation of fatty acid oxidation	2	6	0.028250891
GO: 0001661	Conditioned taste aversion	2	6	0.028250891
GO: 0090336	Positive regulation of brown fat cell differentiation	2	6	0.028250891
GO: 0010887	Negative regulation of cholesterol storage	2	6	0.028250891
GO: 0060179	Male mating behavior	2	6	0.028250891
GO: 0034351	Negative regulation of glial cell apoptotic process	2	7	0.032882128
GO: 0045656	Negative regulation of monocyte differentiation	2	7	0.032882128
GO: 0060687	Regulation of branching involved in prostate gland morphogenesis	2	7	0.032882128
GO: 1904628	Cellular response to phorbol 13-acetate 12-myristate	2	7	0.032882128
GO: 0043496	Regulation of protein homodimerization activity	2	7	0.032882128
GO: 0031659	Positive regulation of cyclin-dependent protein serine/threonine kinase activity involved in G1/S transition of mitotic cell cycle	2	8	0.037491566
GO: 0033598	Mammary gland epithelial cell proliferation	2	8	0.037491566
GO: 0071316	Cellular response to nicotine	2	8	0.037491566
GO: 0033601	Positive regulation of mammary gland epithelial cell proliferation	2	8	0.037491566
GO: 2001020	Regulation of response to DNA damage stimulus	2	8	0.037491566
GO: 0043497	Regulation of protein heterodimerization activity	2	8	0.037491566
GO: 0010224	Response to UV-B	2	9	0.042079309
GO: 0006265	DNA topological change	2	9	0.042079309
GO: 0010226	Response to lithium ion	2	9	0.042079309
GO: 0060068	Vagina development	2	9	0.042079309
GO: 0009651	Response to salt stress	2	9	0.042079309
GO: 1901522	Positive regulation of transcription from RNA polymerase II promoter involved in cellular response to chemical stimulus	2	9	0.042079309
GO: 0033148	Positive regulation of intracellular estrogen receptor signaling pathway	2	10	0.046645457
GO: 0001893	Maternal placenta development	2	10	0.046645457
GO: 0043267	Negative regulation of potassium ion transport	2	10	0.046645457
GO: 0033327	Leydig cell differentiation	2	10	0.046645457
GO: 1901030	Positive regulation of mitochondrial outer membrane permeabilization involved in apoptotic signaling pathway	2	10	0.046645457
GO: 0016572	Histone phosphorylation	2	10	0.046645457
GO: 2001022	Positive regulation of response to DNA damage stimulus	2	10	0.046645457
GO: 0051146	Striated muscle cell differentiation	2	10	0.046645457
GO: 0006268	DNA unwinding involved in DNA replication	2	10	0.046645457
GO: 0006983	ER overload response	2	10	0.046645457
GO: 0071383	Cellular response to steroid hormone stimulus	2	10	0.046645457
GO: 0046902	Regulation of mitochondrial membrane permeability	2	10	0.046645457
GO: 0033160	Positive regulation of protein import into nucleus, translocation	2	10	0.046645457

Supplementary Table S3 (B) Gene Ontology (GO) map of target genes (cellular component)

Term		Count	Pop hits	P value
GO: 0005634	Nucleus	62	5415	2.41E-17
GO: 0005654	Nucleoplasm	51	2784	1.61E-21
GO: 0005737	Cytoplasm	44	5222	3.22E-06
GO: 0005829	Cytosol	37	3315	4.41E-08
GO: 0043234	Protein complex	13	412	2.63E-07
GO: 0005739	Mitochondrion	13	1331	0.01423789
GO: 0005887	Integral component of plasma membrane	12	1415	0.048049018
GO: 0005783	Endoplasmic reticulum	10	828	0.011071624
GO: 0000790	Nuclear chromatin	9	193	2.27E-06
GO: 0043005	Neuron projection	8	237	8.84E-05
GO: 0048471	Perinuclear region of cytoplasm	8	621	0.0204178
GO: 0005856	Cytoskeleton	6	371	0.024759465
GO: 0005741	Mitochondrial outer membrane	5	149	0.004386082
GO: 0005667	Transcription factor complex	5	193	0.010765749
GO: 0045121	Membrane raft	5	206	0.013410123
GO: 0045211	Postsynaptic membrane	5	211	0.01452806
GO: 0017146	NMDA selective glutamate receptor complex	4	11	1.36E-05
GO: 0000307	Cyclin-dependent protein kinase holoenzyme complex	4	15	3.70E-05
GO: 0016363	Nuclear matrix	4	97	0.009241896
GO: 0043235	Receptor complex	4	127	0.019011147
GO: 0072562	Blood microparticle	4	152	0.03025507
GO: 0043209	Myelin sheath	4	152	0.03025507
GO: 0005657	Replication fork	3	17	0.00254119
GO: 0090575	RNA polymerase II transcription factor complex	3	33	0.009422506
GO: 0000781	Chromosome, telomeric region	3	46	0.017796259
GO: 0005901	Caveola	3	65	0.033883176
GO: 0031234	Extrinsic component of cytoplasmic side of plasma membrane	3	68	0.036794514
GO: 0070557	PCNA-p21 complex	2	2	0.008869864
GO: 0009295	Nucleoid	2	2	0.008869864
GO: 0009330	DNA topoisomerase complex (ATP-hydrolyzing)	2	2	0.008869864
GO: 0097124	Cyclin A2-CDK2 complex	2	2	0.008869864
GO: 0097136	Bcl-2 family protein complex	2	3	0.013275612
GO: 0033256	I-kappaB/NF-kappaB complex	2	5	0.022029161
GO: 0031264	Death-inducing signaling complex	2	7	0.030706005
GO: 0046930	Pore complex	2	9	0.039306808
GO: 0032590	Dendrite membrane	2	10	0.043578899

Supplementary Table S3 (C) Gene Ontology (GO) map of target genes (molecular function)

Term		Count	Pop hits	P value
GO: 0003707	Steroid hormone receptor activity	17	56	5.81E – 25
GO: 0004879	RNA polymerase II transcription factor activity, ligand-activated sequence-specific DNA binding	13	36	7.20E – 20
GO: 0008134	Transcription factor binding	19	284	1.25E – 15
GO: 0019899	Enzyme binding	20	333	1.25E – 15
GO: 0043565	Sequence-specific DNA binding	23	518	2.34E – 15
GO: 0005515	Protein binding	74	8785	1.79E – 13
GO: 0003700	Transcription factor activity, sequence-specific DNA binding	26	961	1.39E – 12
GO: 0005496	Steroid binding	8	27	3.69E – 11
GO: 0003682	Chromatin binding	17	391	4.31E – 11
GO: 0001077	Transcriptional activator activity, RNA polymerase II core promoter proximal region sequence-specific binding	13	236	1.27E – 09
GO: 0000978	RNA polymerase II core promoter proximal region sequence-specific DNA binding	15	355	1.31E – 09
GO: 0003677	DNA binding	27	1674	3.37E – 08
GO: 0032403	Protein complex binding	11	206	5.20E – 08
GO: 0000977	RNA polymerase II regulatory region sequence-specific DNA binding	11	208	5.70E – 08
GO: 0046982	Protein heterodimerization activity	14	465	3.03E – 07
GO: 0044212	Transcription regulatory region DNA binding	10	213	8.14E – 07
GO: 0008270	Zinc ion binding	20	1169	1.96E – 06
GO: 0003713	Transcription coactivator activity	10	248	2.86E – 06
GO: 0004972	NMDA glutamate receptor activity	4	8	5.86E – 06
GO: 0042803	Protein homodimerization activity	15	730	8.74E – 06
GO: 0042802	Identical protein binding	15	749	1.17E – 05
GO: 0008144	Drug binding	6	76	3.18E – 05
GO: 0005102	Receptor binding	10	353	4.79E – 05
GO: 0001046	Core promoter sequence-specific DNA binding	5	43	5.27E – 05
GO: 0005524	ATP binding	20	1495	6.47E – 05
GO: 0004886	9-Cis retinoic acid receptor activity	3	3	6.80E – 05
GO: 0004674	Protein serine/threonine kinase activity	10	376	7.78E – 05
GO: 0042826	Histone deacetylase binding	6	102	1.30E – 04
GO: 0051434	BH3 domain binding	3	4	1.36E – 04
GO: 0016301	Kinase activity	8	241	1.57E – 04
GO: 0019903	Protein phosphatase binding	5	63	2.36E – 04
GO: 0000980	RNA polymerase II distal enhancer sequence-specific DNA binding	5	65	2.67E – 04
GO: 0004672	Protein kinase activity	9	359	3.22E – 04
GO: 0030235	Nitric-oxide synthase regulator activity	3	8	6.25E – 04
GO: 0030331	Estrogen receptor binding	4	37	7.35E – 04
GO: 0046983	Protein dimerization activity	6	150	7.72E – 04
GO: 0001228	Transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific binding	5	95	0.001124502
GO: 0004715	Non-membrane spanning protein tyrosine kinase activity	4	46	0.001392428

Supplementary Table S3 (C) Gene Ontology (GO) map of target genes (molecular function) (continued)

Term		Count	Pop hits	P value
GO: 0097153	Cysteine-type endopeptidase activity involved in apoptotic process	3	13	0.00171394
GO: 0030374	Ligand-dependent nuclear receptor transcription coactivator activity	4	51	0.001877634
GO: 0046965	Retinoid X receptor binding	3	15	0.002292908
GO: 0031625	Ubiquitin protein ligase binding	7	287	0.002559863
GO: 0005234	Extracellular-glutamate-gated ion channel activity	3	18	0.003310069
GO: 0004713	Protein tyrosine kinase activity	5	133	0.003835955
GO: 0003705	Transcription factor activity, RNA polymerase II distal enhancer sequence-specific binding	4	66	0.003918602
GO: 0030332	Cyclin binding	3	20	0.004085079
GO: 0016922	Ligand-dependent nuclear receptor binding	3	21	0.004501088
GO: 0035257	Nuclear hormone receptor binding	3	22	0.00493585
GO: 0051087	Chaperone binding	4	81	0.006940374
GO: 0008013	Beta-catenin binding	4	82	0.00717934
GO: 0051879	Hsp90 protein binding	3	27	0.007384538
GO: 0051721	Protein phosphatase 2A binding	3	27	0.007384538
GO: 0035035	Histone acetyltransferase binding	3	28	0.007927983
GO: 0051059	NF-kappaB binding	3	30	0.009067155
GO: 0019901	Protein kinase binding	7	376	0.009374162
GO: 0038052	RNA polymerase II transcription factor activity, estrogen-activated sequence-specific DNA binding	2	2	0.009573847
GO: 0047485	Protein N-terminus binding	4	97	0.011355924
GO: 0070644	Vitamin D response element binding	2	3	0.014326766
GO: 0003918	DNA topoisomerase type II (ATP-hydrolyzing) activity	2	3	0.014326766
GO: 0004882	Androgen receptor activity	2	3	0.014326766
GO: 0005088	Ras guanyl-nucleotide exchange factor activity	4	115	0.017887184
GO: 0005497	Androgen binding	2	4	0.019057157
GO: 0030375	Thyroid hormone receptor coactivator activity	2	4	0.019057157
GO: 0034056	Estrogen response element binding	2	4	0.019057157
GO: 0005080	Protein kinase C binding	3	46	0.020534243
GO: 0001085	RNA polymerase II transcription factor binding	3	47	0.021380998
GO: 0030284	Estrogen receptor activity	2	5	0.023765124
GO: 0051525	NFAT protein binding	2	5	0.023765124
GO: 0000979	RNA polymerase II core promoter sequence-specific DNA binding	3	57	0.030612694
GO: 0031490	Chromatin DNA binding	3	58	0.031609008
GO: 0004197	Cysteine-type endopeptidase activity	3	61	0.034673696
GO: 0004887	Thyroid hormone receptor activity	2	8	0.037755537
GO: 0002039	P53 binding	3	67	0.041131379
GO: 0001223	Transcription coactivator binding	2	10	0.046972276
GO: 0042805	Actinin binding	2	10	0.046972276
GO: 0051117	ATPase binding	3	74	0.049185816

Supplementary Table S4 Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis

Term		Count	Pop hits	P value
Hsa05200	Pathways in cancer	28	393	8.19E-17
Hsa04151	PI3K-Akt signaling pathway	18	345	2.34E-08
Hsa04919	Thyroid hormone signaling pathway	16	115	1.86E-13
Hsa05203	Viral carcinogenesis	16	205	8.58E-10
Hsa04657	IL-17 signaling pathway	16	92	1.04E-13
Hsa05222	Small cell lung cancer	15	85	4.61E-14
Hsa05169	Epstein-Barr virus infection	14	122	1.24E-10
Hsa05166	HTLV-I infection	14	254	8.92E-07
Hsa04659	Th17 cell differentiation	14	102	5.03E-11
Hsa05152	Tuberculosis	13	177	1.20E-07
Hsa05215	Prostate cancer	12	88	6.71E-10
Hsa05206	MicroRNAs in cancer	12	286	9.78E-05
Hsa04630	Jak-STAT signaling pathway	12	160	3.72E-07
Hsa05145	Toxoplasmosis	11	110	9.69E-08
Hsa04110	Cell cycle	11	124	3.02E-07
Hsa05162	Measles	11	133	5.83E-07
Hsa05202	Transcriptional misregulation in cancer	11	167	4.69E-06
Hsa05205	Proteoglycans in cancer	11	200	2.30E-05
Hsa05210	Colorectal cancer	10	62	7.00E-09
Hsa04115	p53 signaling pathway	10	67	1.42E-08
Hsa04071	Sphingolipid signaling pathway	10	120	2.30E-06
Hsa04722	Neurotrophin signaling pathway	10	120	2.30E-06
Hsa04932	Non-alcoholic fatty liver disease (NAFLD)	10	151	1.52E-05
Hsa05164	Influenza A	10	174	4.71E-05
Hsa05168	Herpes simplex infection	10	183	6.98E-05
Hsa04024	cAMP signaling pathway	10	198	1.28E-04
Hsa04010	MAPK signaling pathway	10	253	7.88E-04
Hsa04080	Neuroactive ligand-receptor interaction	10	277	1.49E-03
Hsa05014	Amyotrophic lateral sclerosis (ALS)	9	50	2.31E-08
Hsa05223	Non-small cell lung cancer	9	56	5.83E-08
Hsa04210	Apoptosis	9	62	1.32E-07
Hsa05220	Chronic myeloid leukemia	9	72	4.34E-07
Hsa04668	TNF signaling pathway	9	107	8.98E-06
Hsa04020	Calcium signaling pathway	9	179	3.50E-04
Hsa05016	Huntington's disease	9	192	5.61E-04
Hsa05212	Pancreatic cancer	8	65	2.98E-06
Hsa04917	Prolactin signaling pathway	8	71	5.43E-06
Hsa04064	NF-kappa B signaling pathway	8	87	2.11E-05
Hsa04380	Osteoclast differentiation	8	131	2.85E-04
Hsa04310	Wnt signaling pathway	8	138	3.92E-04
Hsa04510	Focal adhesion	8	206	0.00402126
Hsa05216	Thyroid cancer	7	29	2.96E-07
Hsa05030	Cocaine addiction	7	49	7.47E-06
Hsa04920	Adipocytokine signaling pathway	7	70	5.95E-05

Supplementary Table S4 Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis (continued)

Term		Count	Pop hits	P value
Hsa05140	Leishmaniasis	7	71	6.45E-05
Hsa04066	HIF-1 signaling pathway	7	96	3.44E-04
Hsa04660	T cell receptor signaling pathway	7	100	4.29E-04
Hsa05142	Chagas disease (American trypanosomiasis)	7	104	5.29E-04
Hsa05010	Alzheimer's disease	7	168	0.006080133
Hsa04062	Chemokine signaling pathway	7	186	0.009839285
Hsa04015	Rap1 signaling pathway	7	210	0.017117947
Hsa04014	Ras signaling pathway	7	226	0.023654995
Hsa05213	Endometrial cancer	6	52	1.48E-04
Hsa05134	Legionellosis	6	54	1.77E-04
Hsa05221	Acute myeloid leukemia	6	56	2.10E-04
Hsa05416	Viral myocarditis	6	57	2.29E-04
Hsa04370	VEGF signaling pathway	6	61	3.15E-04
Hsa05214	Glioma	6	65	4.25E-04
Hsa05031	Amphetamine addiction	6	66	4.56E-04
Hsa05133	Pertussis	6	75	8.22E-04
Hsa05132	Salmonella infection	6	83	0.001301675
Hsa04914	Progesterone-mediated oocyte maturation	6	87	0.001606961
Hsa04012	ErbB signaling pathway	6	87	0.001606961
Hsa04915	Estrogen signaling pathway	6	99	0.002839818
Hsa04620	Toll-like receptor signaling pathway	6	106	0.003815837
Hsa04931	Insulin resistance	6	108	0.004134108
Hsa04728	Dopaminergic synapse	6	128	0.008435092
Hsa04261	Adrenergic signaling in cardiomyocytes	6	138	0.011460221
Hsa04550	Signaling pathways regulating pluripotency of stem cells	6	140	0.01214373
Hsa04921	Oxytocin signaling pathway	6	150	0.015980399
Hsa04621	NOD-like receptor signaling pathway	5	56	0.002179673
Hsa05120	Epithelial cell signaling in Helicobacter pylori infection	5	67	0.004193758
Hsa03320	PPAR signaling pathway	5	67	0.004193758
Hsa04662	B cell receptor signaling pathway	5	69	0.004660832
Hsa05218	Melanoma	5	71	0.005161781
Hsa04912	GnRH signaling pathway	5	91	0.012257455
Hsa05146	Amoebiasis	5	106	0.020414731
Hsa04152	AMPK signaling pathway	5	123	0.03296272
Hsa04068	FoxO signaling pathway	5	134	0.043045592
Hsa04630	Jak-STAT signaling pathway	5	145	0.04769282
Hsa05033	Nicotine addiction	4	40	0.007029647
Hsa05219	Bladder cancer	4	41	0.007531597
Hsa05321	Inflammatory bowel disease (IBD)	4	64	0.025070566
Hsa05131	Shigellosis	4	64	0.025070566
Hsa04720	Long-term potentiation	4	66	0.027155519
Hsa04664	Fc epsilon RI signaling pathway	4	68	0.029330716
Hsa04622	RIG-I-like receptor signaling pathway	4	70	0.031595883
Hsa04666	Fc gamma R-mediated phagocytosis	4	84	0.049928878