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Supplementary Information

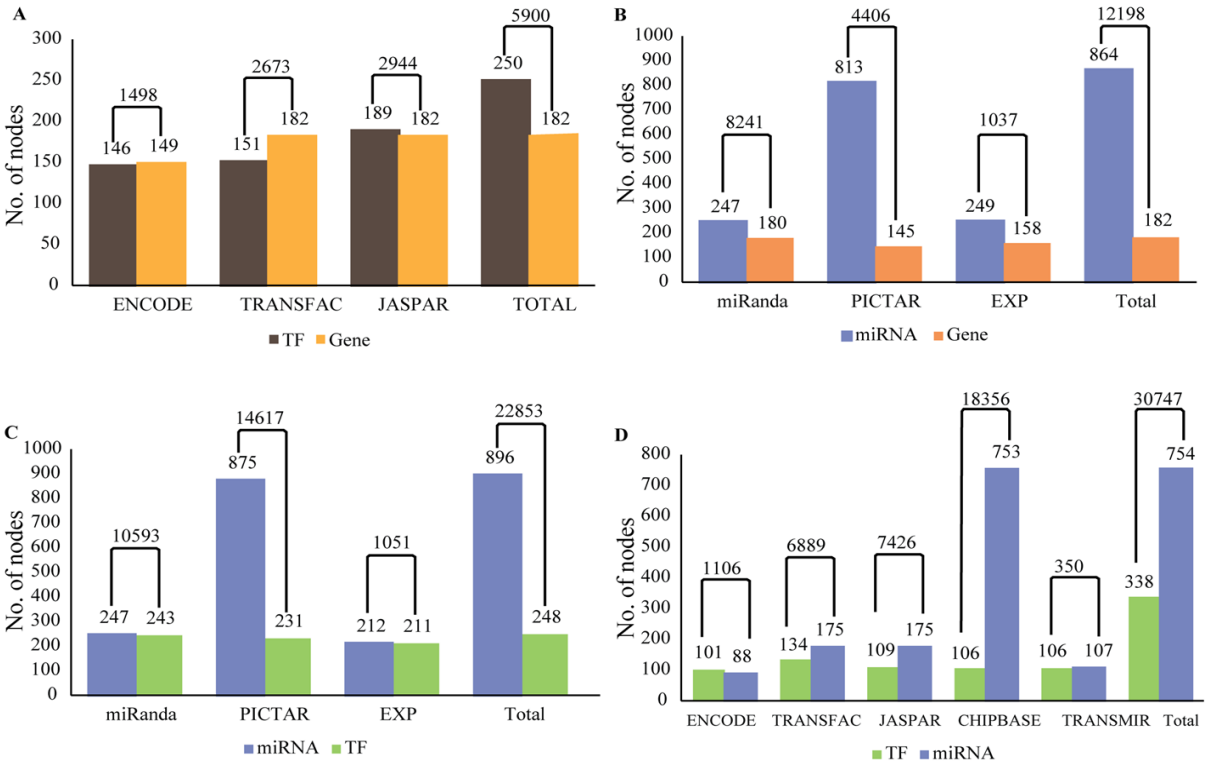

Figure S1. Combinatorial regulatory relationship of apoptosis genes.

A. Association of Transcription factors with ARGs: Identification of different Transcription factor binding to ARGs using various databases. ENCODE database found 149 genes regulated by 146 TFs, binding at 1498 sites; whereas, in case of TRANSFAC and JASPAR, it was found 182 genes were regulated by 151 (TFBS: 2673) and 189 (TFBS: 2944) TFs, respectively. The totals of 182 ARGs were regulated by 250 TFs with 5900 Transcription Factor Binding Sites (TFBS) from this analysis.

B. miRNA target prediction results of ARGs: Out of 182 ARGs, miRanda results identified 180 ARGs targeted by 247 miRNAs with 8241 interactions, whereas PICTAR prediction and experimentally validated data (miRTarBase and miRecords) found 145 and 158 ARGs were targeted by 813 and 249 miRNAs with 4406 and 1037 interactions, respectively. The miRNA target prediction of ARGs showed 864 miRNAs targeting 182 ARGs with 12198 interactions

C. miRNA target prediction results of TFs: miRanda identified 243 TFs targeted by 247 miRNAs with 10593 interactions; whereas PICTAR prediction and experimentally validated data (miRTarBase and miRecords), found 231and 211 TFs targeted by 875 and 212 miRNAs with 14617 and 1051 interactions, respectively. The miRNA regulation of TFs showed 896 miRNAs and 248 TFs with 22853 interactions.

D. TFs binding to microRNA: From ENCODE prediction, 88 microRNAs were regulated by 101 TFs which involved 1106 interactions. In case of TRANSFAC and JASPAR prediction results, 175 microRNAs were regulated by 134 and 109 TFs with 6889 and 7426 interactions, respectively. The result of ChiPBase showed that 106 TFs were binding to 753 microRNAs with 18356 interactions. The experimentally validated TFs binding to microRNA were retrieved from TransmiR database which included 107 microRNAs regulated by 106 TFs with 350 interactions. The TF regulation of miRNA showed 338 TFs regulating 754 miRNAs with 30747 interactions.

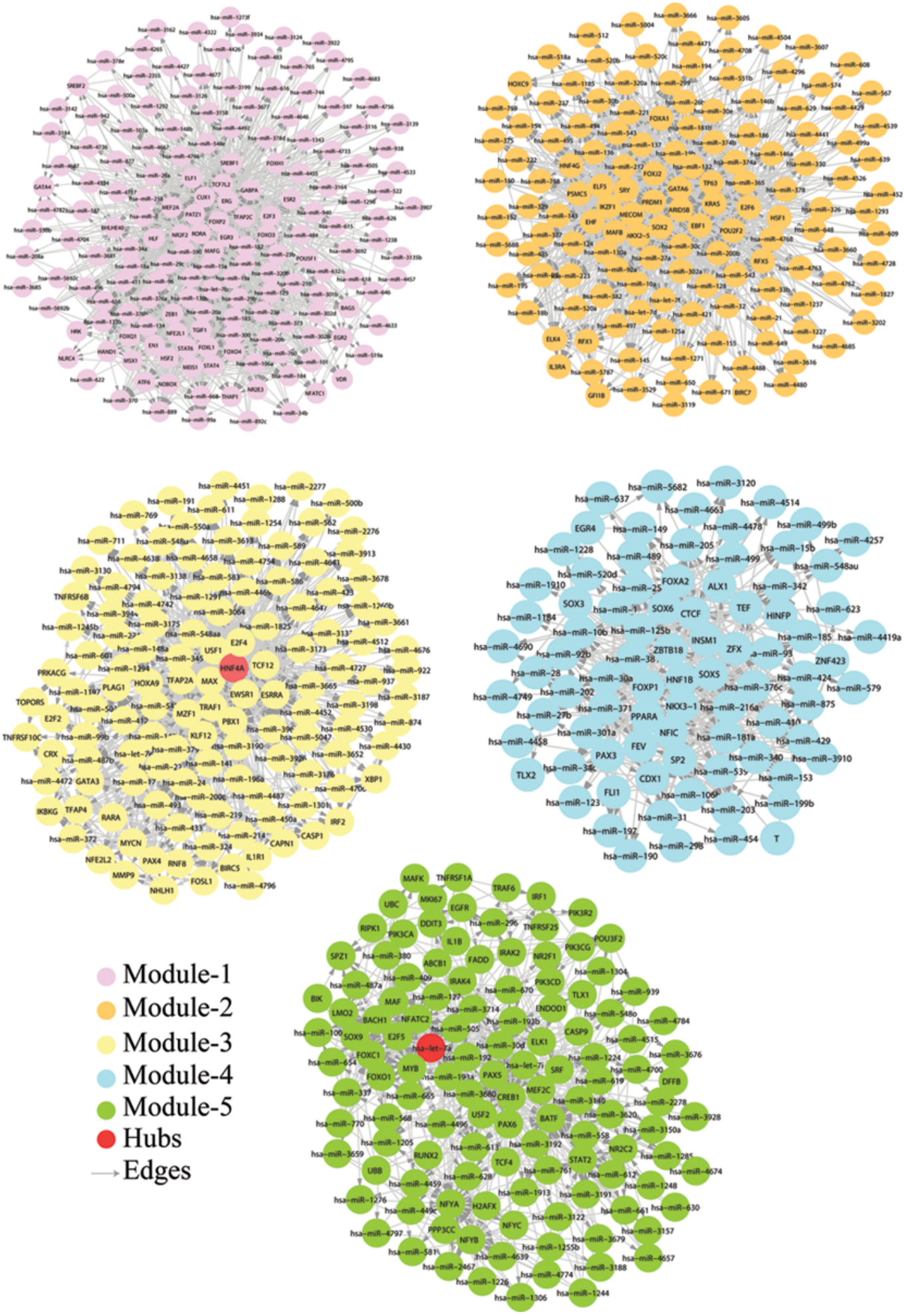
Module-1
Module-2
Module-3
Module-4
Module-5
Hubs
Edges

Figure S2. Skeletal structures of the Modules in the combinatorial network.

All the five modules were constructed and analyzed using MCODE. Modules 1-5 show all the nodes in filled circles with pink, orange, yellow, blue and green color, respectively and the corresponding edges in gray lines. Two of the significant hubs, *HNF4A* and *hsa-let-7a* (red) are present in modules 3 and 5.

Table S1. Significant global apoptotic regulatory genes and their related information

S.No	Gene Name	Gene-ID	Uniprot-ID	Description
1	ABCB1	5243	P08183	ATP-binding cassette, sub-family B (MDR/TAP), member 1
2	AIFM1	9131	O95831	Apoptosis-inducing factor, mitochondrion-associated, 1
3	AKT1	207	P31749	V-akt murine thymoma viral oncogene homolog 1
4	AKT2	208	P31751	V-akt murine thymoma viral oncogene homolog 2
5	AKT3	10000	Q9Y243	V-akt murine thymoma viral oncogene homolog 3
6	APAF1	317	O14727	Apoptotic peptidase activating factor 1
7	APC	324	P25054	Adenomatous polyposis coli
8	APP	351	P05067	Amyloid beta (A4) precursor protein
9	ATM	472	Q13315	ATM serine/threonine kinase
10	BAD	572	Q92934	BCL2-associated agonist of cell death
11	BAG1	573	Q99933	BCL2-associated athanogene
12	BAG3	9531	O95817	BCL2-associated athanogene 3
13	BAG4	9530	O95429	BCL2-associated athanogene 4
14	BAG5	9529	Q9UL15	BCL2-associated athanogene 5
15	BAK1	578	Q16611	BCL2-antagonist/killer 1
16	BAX	581	Q07812	BCL2-associated X protein
17	BBC3	27113	Q96PG8	BCL2 binding component 3
18	BCL2	596	P10415	B-cell CLL/lymphoma 2
19	BCL2L1	598	Q07817	BCL2-like 1
20	BCL2L13	23786	Q9BXK5	BCL2-like 13 (apoptosis facilitator)

21	BCL6	604	P41182	B-cell CLL/lymphoma 6
22	BFAR	51283	Q9NZS9	Bifunctional apoptosis regulator
23	BID	637	P55957	BH3 interacting domain death agonist
24	BIK	638	Q13323	BCL2-interacting killer (apoptosis-inducing)
25	BIRC2	329	Q13490	Baculoviral IAP repeat containing 2
26	BIRC3	330	Q13489	Baculoviral IAP repeat containing 3
27	BIRC5	332	O15392	Baculoviral IAP repeat containing 5
28	BIRC7	79444	Q96CA5	Baculoviral IAP repeat containing 7
29	BNIP3L	665	O60238	BCL2/adenovirus E1B 19kDa interacting protein 3-like
30	BRCA1	672	P38398	Breast cancer 1, early onset
31	BRCA2	675	P51587	Breast cancer 2, early onset
32	CAPN1	823	P07384	Calpain 1, (mu/I) large subunit
33	CAPN2	824	P17655	Calpain 2, (m/II) large subunit
34	CARD8	22900	Q9Y2G2	Caspase recruitment domain family, member 8
35	CASP1	834	P29466	Caspase 1, apoptosis-related cysteine peptidase
36	CASP10	843	Q92851	Caspase 10, apoptosis-related cysteine peptidase
37	CASP2	835	P42575	Caspase 2, apoptosis-related cysteine peptidase
38	CASP3	836	P42574	Caspase 3, apoptosis-related cysteine peptidase
39	CASP4	837	P49662	Caspase 4, apoptosis-related cysteine peptidase
40	CASP6	839	P55212	Caspase 6, apoptosis-related cysteine peptidase
41	CASP7	840	P55210	Caspase 7, apoptosis-related cysteine peptidase
42	CASP8	841	Q14790	Caspase 8, apoptosis-related cysteine peptidase

43	CASP8AP2	9994	Q9UKL3	Caspase 8 associated protein 2
44	CASP9	842	P55211	Caspase 9, apoptosis-related cysteine peptidase
45	CCND1	595	P24385	Cyclin D1
46	CDC6	990	Q99741	Cell division cycle 6
47	CDKN1A	1026	P38936	Cyclin-dependent kinase inhibitor 1A (p21, Cip1)
48	CDKN1B	1027	P46527	Cyclin-dependent kinase inhibitor 1B (p27, Kip1)
49	CDKN2A	1029	P42771	Cyclin-dependent kinase inhibitor 2A
50	CFLAR	8837	O15519	CASP8 and FADD-like apoptosis regulator
51	CHEK2	11200	O96017	Checkpoint kinase 2
52	CHP1	11261	Q99653	Calcineurin-like EF-hand protein 1
53	CHP2	63928	O43745	Calcineurin-like EF-hand protein 2
54	CHUK	1147	O15111	Conserved helix-loop-helix ubiquitous kinase
55	CRADD	8738	P78560	CASP2 and RIPK1 domain containing adaptor with death domain
56	CSF2RB	1439	P32927	Colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)
57	CYCS	54205	P99999	Cytochrome c, somatic
58	DAPK1	1612	P53355	Death-associated protein kinase 1
59	DAXX	1616	Q9UER7	Death-domain associated protein
60	DCC	1630	P43146	DCC netrin 1 receptor
61	DEDD	9191	O75618	Death effector domain containing
62	DEDD2	162989	Q8WXF8	Death effector domain containing 2
63	DFFA	1676	O00273	DNA fragmentation factor, 45kDa, alpha polypeptide
64	DFFB	1677	O76075	DNA fragmentation factor, 40kDa, beta polypeptide (caspase-activated DNase)

65	DIABLO	56616	Q9NR28	Diablo, IAP-binding mitochondrial protein
66	E2F1	1869	Q01094	E2F transcription factor 1
67	EGFR	1956	P00533	Epidermal growth factor receptor
68	ENDOD1	23052	O94919	Endonuclease domain containing 1
69	ENDOG	2021	Q14249	Endonuclease G
70	EXOG	9941	Q9Y2C4	Endo/exonuclease (5'-3'), endonuclease G-like
71	FADD	8772	Q13158	Fas (TNFRSF6)-associated via death domain
72	FAS	355	P25445	Fas cell surface death receptor
73	FASLG	356	P48023	Fas ligand (TNF superfamily, member 6)
74	FGFR1	2260	P11362	Fibroblast growth factor receptor 1
75	H2AFX	3014	P16104	H2A histone family, member X
76	HRAS	3265	P01112	Harvey rat sarcoma viral oncogene homolog
77	HRK	8739	O00198	Harakiri, BCL2 interacting protein
78	HSPB1	3315	P04792	Heat shock 27kDa protein 1
79	HTRA2	27429	O43464	HtrA serine peptidase 2
80	IFNG	3458	P01579	Interferon, gamma
81	IGFBP3	3486	P17936	Insulin-like growth factor binding protein 3
82	IKBKB	3551	O14920	Inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta
83	IKBKG	8517	Q9Y6K9	Inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma
84	IL10	3586	P22301	Interleukin 10
85	IL1A	3552	P01583	Interleukin 1, alpha
86	IL1B	3553	P01584	Interleukin 1, beta

87	IL1R1	3554	P14778	Interleukin 1 receptor, type I
88	IL1RAP	3556	Q9NPH3	Interleukin 1 receptor accessory protein
89	IL3	3562	P08700	Interleukin 3
90	IL3RA	3563	P26951	Interleukin 3 receptor, alpha (low affinity)
91	IL4	3565	P05112	Interleukin 4
92	IL6	3569	P05231	Interleukin 6
93	IRAK1	3654	P51617	Interleukin-1 receptor-associated kinase 1
94	IRAK2	3656	O43187	Interleukin-1 receptor-associated kinase 2
95	IRAK3	11213	Q9Y616	Interleukin-1 receptor-associated kinase 3
96	IRAK4	51135	Q9NWZ3	Interleukin-1 receptor-associated kinase 4
97	KAT5	10524	Q92993	K(lysine) acetyltransferase 5
98	KRAS	3845	P01116	Kirsten rat sarcoma viral oncogene homolog
99	MALT1	10892	Q9UDY8	Mucosa associated lymphoid tissue lymphoma translocation gene 1
100	MAP3K14	9020	Q99558	Mitogen-activated protein kinase kinase kinase 14
101	MAP3K7	6885	O43318	Mitogen-activated protein kinase kinase kinase 7
102	MAPK1	5594	P28482	Mitogen-activated protein kinase 1
103	MAPK3	5595	P27361	Mitogen-activated protein kinase 3
104	MCL1	4170	Q07820	Myeloid cell leukemia 1
105	MDM2	4193	Q00987	MDM2 proto-oncogene, E3 ubiquitin protein ligase
106	MFN2	9927	O95140	Mitofusin 2
107	MITF	4286	O75030	Microphthalmia-associated transcription factor
108	MKI67	4288	P46013	Marker of proliferation Ki-67

109	MMP9	4318	P14780	Matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)
110	MSH2	4436	P43246	MutS homolog 2
111	MYC	4609	P01106	V-myc avian myelocytomatosis viral oncogene homolog
112	MYD88	4615	Q99836	Myeloid differentiation primary response 88
113	NAIP	4671	Q13075	NLR family, apoptosis inhibitory protein
114	NFKB1	4790	P19838	Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1
115	NFKBIA	4792	P25963	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha
116	NGF	4803	P01138	nerve growth factor (beta polypeptide)
117	NLRC4	58484	Q9NPP4	NLR family, CARD domain containing 4
118	NLRP1	22861	Q9C000	NLR family, pyrin domain containing 1
119	NOD1	10392	Q9Y239	Nucleotide-binding oligomerization domain containing 1
120	NRAS	4893	P01111	Neuroblastoma RAS viral (v-ras) oncogene homolog
121	NTRK1	4914	P04629	Neurotrophic tyrosine kinase, receptor, type 1
122	PARP1	142	P09874	Poly (ADP-ribose) polymerase 1
123	PCNA	5111	P12004	Proliferating cell nuclear antigen
124	PEA15	8682	Q15121	Phosphoprotein enriched in astrocytes 15
125	PECAM1	5175	P16284	Platelet/endothelial cell adhesion molecule 1
126	PIK3CA	5290	P42336	Phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha
127	PIK3CB	5291	P42338	Phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit beta
129	PIK3CG	5294	P48736	Phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit gamma
130	PIK3R1	5295	P27986	Phosphoinositide-3-kinase, regulatory subunit 1 (alpha)

131	PIK3R2	5296	O00459	Phosphoinositide-3-kinase, regulatory subunit 2 (beta)
132	PIK3R3	8503	Q92569	Phosphoinositide-3-kinase, regulatory subunit 3 (gamma)
133	PIK3R5	23533	Q8WYR1	Phosphoinositide-3-kinase, regulatory subunit 5
134	PKMYT1	9088	Q99640	Protein kinase, membrane associated tyrosine/threonine 1
135	PML	5371	P29590	Promyelocytic leukemia
136	PPP3CA	5530	Q08209	Protein phosphatase 3, catalytic subunit, alpha isozyme
137	PPP3CB	5532	P16298	Protein phosphatase 3, catalytic subunit, beta isozyme
138	PPP3CC	5533	P48454	Protein phosphatase 3, catalytic subunit, gamma isozyme
139	PPP3R1	5534	P63098	Protein phosphatase 3, regulatory subunit B, alpha
140	PPP3R2	5535	Q96LZ3	Protein phosphatase 3, regulatory subunit B, beta
141	PRKACA	5566	P17612	Protein kinase, cAMP-dependent, catalytic, alpha
142	PRKACB	5567	P22694	Protein kinase, cAMP-dependent, catalytic, beta
143	PRKACG	5568	P22612	Protein kinase, cAMP-dependent, catalytic, gamma
144	PRKAR1A	5573	P10644	Protein kinase, cAMP-dependent, regulatory, type I, alpha
145	PRKAR1B	5575	P31321	Protein kinase, cAMP-dependent, regulatory, type I, beta
146	PRKAR2A	5576	P13861	Protein kinase, cAMP-dependent, regulatory, type II, alpha
147	PRKAR2B	5577	P31323	Protein kinase, cAMP-dependent, regulatory, type II, beta
148	PRKX	5613	P51817	Protein kinase, X-linked
149	PSEN1	5663	P49768	Presenilin 1
150	PTEN	5728	P60484	Phosphatase and tensin homolog
151	RARG	5916	P13631	Retinoic acid receptor, gamma
152	RELA	5970	Q04206	V-rel avian reticuloendotheliosis viral oncogene homolog A

153	RIPK1	8737	Q13546	Receptor (TNFRSF)-interacting serine-threonine kinase 1
154	RNF8	9025	O76064	Ring finger protein 8, E3 ubiquitin protein ligase
155	RPS27A	6233	P62979	Ribosomal protein S27a
156	RTN4	57142	Q9NQC3	Reticulon 4
157	SP1	6667	P08047	Sp1 transcription factor
158	TANK	10010	Q92844	TRAF family member-associated NFKB activator
159	TGFB1	7040	P01137	Transforming growth factor, beta 1
160	TNF	7124	P01375	Tumor necrosis factor
161	TNFRSF10A	8797	O00220	Tumor necrosis factor receptor superfamily, member 10a
162	TNFRSF10B	8795	O14763	Tumor necrosis factor receptor superfamily, member 10b
163	TNFRSF10C	8794	O14798	Tumor necrosis factor receptor superfamily, member 10c, decoy without an intracellular domain
164	TNFRSF10D	8793	Q9UBN6	Tumor necrosis factor receptor superfamily, member 10d, decoy with truncated death domain
165	TNFRSF12A	51330	Q9NP84	Tumor necrosis factor receptor superfamily, member 12A
166	TNFRSF1A	7132	P19438	Tumor necrosis factor receptor superfamily, member 1A
167	TNFRSF1B	7133	P20333	Tumor necrosis factor receptor superfamily, member 1B
168	TNFRSF25	8718	Q93038	Tumor necrosis factor receptor superfamily, member 25
169	TNFRSF6B	8771	O95407	Tumor necrosis factor receptor superfamily, member 6b, decoy
170	TNFSF10	8743	P50591	Tumor necrosis factor (ligand) superfamily, member 10
171	TP53	7157	P04637	Tumor protein p53
172	TRADD	8717	Q15628	TNFRSF1A-associated via death domain

173	TRAF1	7185	Q13077	TNF receptor-associated factor 1
174	TRAF2	7186	Q12933	TNF receptor-associated factor 2
175	TRAF3	7187	Q13114	TNF receptor-associated factor 3
176	TRAF4	9618	Q9BUZ4	TNF receptor-associated factor 4
177	TRAF6	7189	Q9Y4K3	TNF receptor-associated factor 6, E3 ubiquitin protein ligase
178	UBA52	7311	P62987	Ubiquitin A-52 residue ribosomal protein fusion product 1
179	UBB	7314	P0CG47	Ubiquitin B
180	UBC	7316	P0CG48	Ubiquitin C
181	VEGFA	7422	P15692	Vascular endothelial growth factor A
182	XIAP	331	P98170	X-linked inhibitor of apoptosis

Table S2. List of mutations in cancer of hub proteins

Gene	Position	Mutation (CDS)	Mutation (Amino Acid)	Mutation-ID (COSM)
SP1	387	c.1159G>C	p.E387Q	COSM51318
HNF4A	9	c.25G>A	p.D9N	COSM1027061
HNF4A	35	c.104C>A	p.T35K	COSM724511
HNF4A	50	c.148G>A	p.A50T	COSM172628
HNF4A	51	c.152C>G	p.P51R	COSM1326728
HNF4A	54	c.160C>A	p.L54M	COSM1209837
HNF4A	58	c.173C>T	p.A58V	COSM1533746
HNF4A	79	c.236G>C	p.G79A	COSM399420
HNF4A	85	c.253C>T	p.R85W	COSM1731194
HNF4A	94	c.281A>G	p.Y94C	COSM1027064
HNF4A	113	c.337C>G	p.R113G	COSM443867
HNF4A	115	c.345C>G	p.C115W	COSM1027066
HNF4A	123	c.368C>T	p.A123V	COSM1027068
HNF4A	130	c.388G>C	p.V130L	COSM356496
HNF4A	152	c.454A>T	p.I152F	COSM443869
HNF4A	154	c.461C>T	p.A154V	COSM1027072
HNF4A	158	c.473C>T	p.A158V	COSM1027074
HNF4A	163	c.487C>G	p.R163G	COSM1743504
HNF4A	164	c.492G>T	p.Q164H	COSM395878
HNF4A	174	c.520G>A	p.G174S	COSM1533737
HNF4A	175	c.523G>A	p.D175N	COSM1027076
HNF4A	178	c.533C>T	p.A178V	COSM1027078
HNF4A	191	c.573G>A	p.M191I	COSM577678
HNF4A	199	c.595G>A	p.V199I	COSM290659
HNF4A	200	c.598G>A	p.E200K	COSM419385
HNF4A	211	c.632T>C	p.L211P	COSM1713517
HNF4A	226	c.677A>T	p.E226V	COSM1533731
HNF4A	263	c.788G>A	p.R263Q	COSM3405114
HNF4A	294	c.882C>A	p.F294L	COSM1027080
HNF4A	330	c.989C>T	p.S330L	COSM1027084
HNF4A	331	c.991C>G	p.R331G	COSM1027086
HNF4A	387	c.1159C>T	p.H387Y	COSM3405120
HNF4A	408	c.1223T>C	p.M408T	COSM1717357
HNF4A	409	c.1225C>T	p.P409S	COSM1027090
HNF4A	415	c.1243G>A	p.G415R	COSM3423668
HNF4A	415	c.1244G>A	p.G415E	COSM3546876
HNF4A	417	c.1251G>A	p.M417I	COSM724503
HNF4A	418	c.1252T>A	p.C418S	COSM1533729
HNF4A	425	c.1274G>A	p.G425E	COSM228736
HNF4A	439	c.1315G>T	p.G439C	COSM172485
HNF4A	459	c.1375C>A	p.P459T	COSM331215
HNF4A	472	c.1414G>A	p.E472K	COSM1713523
NFKB1	45	c.134T>C	p.L45P	COSM732095
NFKB1	74	c.221C>G	p.S74C	COSM1485562
NFKB1	111	c.332C>T	p.A111V	COSM1328007
NFKB1	136	c.407G>A	p.G136D	COSM222928

NFKB1	158	c.474G>A	p.M158I	COSM1618203
NFKB1	175	c.524A>T	p.D175V	COSM325945
NFKB1	181	c.541G>C	p.A181P	COSM585322
NFKB1	219	c.655G>A	p.A219T	COSM1217222
NFKB1	270	c.809A>G	p.Y270C	COSM124738
NFKB1	280	c.838G>T	p.D280Y	COSM1049557
NFKB1	284	c.851G>T	p.R284L	COSM1642372
NFKB1	308	c.923G>T	p.R308I	COSM1049559
NFKB1	310	c.930T>G	p.F310L	COSM1049561
NFKB1	321	c.961G>T	p.D321Y	COSM1049563
NFKB1	335	c.1004G>A	p.R335Q	COSM78167
NFKB1	369	c.1105C>T	p.P369S	COSM136425
NFKB1	395	c.1184G>T	p.G395V	COSM380592
NFKB1	399	c.1196G>A	p.G399E	COSM368177
NFKB1	532	c.1594G>A	p.V532I	COSM144954
NFKB1	572	c.1715C>T	p.S572F	COSM447176
NFKB1	585	c.1754C>T	p.T585M	COSM219325
NFKB1	605	c.1813G>A	p.A605T	COSM1618205
NFKB1	611	c.1831C>T	p.L611F	COSM107259
NFKB1	614	c.1840C>T	p.R614C	COSM1049569
NFKB1	678	c.2032G>A	p.V678I	COSM2951881
NFKB1	685	c.2054C>T	p.S685F	COSM1049573
NFKB1	927	c.2779G>A	p.D927N	COSM1049581
NFKB1	931	c.2791G>A	p.E931K	COSM1217221
CDX2	83	c.248G>T	p.G83V	COSM398922
CDX2	104	c.311C>T	p.A104V	COSM3417501
CDX2	185	c.554C>T	p.T185M	COSM946462
CDX2	209	c.626G>A	p.R209H	COSM946461
CDX2	214	c.641G>A	p.R214Q	COSM946460
CDX2	237	c.709C>T	p.R237C	COSM184391

Table S3. List of genes in each module of combinatorial apoptosis network

Modules	Gene List
Module1	ATF6, BAG5, BHLHE40, CUX1, E2F3, EGR2, EGR3, ELF1, EN1, ERG, ESR2, FOXH1, FOXL1, FOXO3, FOXO4, FOXP2, FOXQ1, GABPA, GATA4, HAND1, HLF, HRK, hsa-let-7b, hsa-miR-101, hsa-miR-103a, hsa-miR-106a, hsa-miR-1238, hsa-miR-1273f, hsa-miR-129, hsa-miR-1292, hsa-miR-1296, hsa-miR-130b, hsa-miR-133b, hsa-miR-134, hsa-miR-1343, hsa-miR-148b, hsa-miR-15a, hsa-miR-16, hsa-miR-182, hsa-miR-183, hsa-miR-184, hsa-miR-187, hsa-miR-18a, hsa-miR-19a, hsa-miR-208a, hsa-miR-20a, hsa-miR-20b, hsa-miR-210, hsa-miR-218, hsa-miR-2355, hsa-miR-23a, hsa-miR-23b, hsa-miR-26a, hsa-miR-29b, hsa-miR-29c, hsa-miR-300, hsa-miR-301b, hsa-miR-302b, hsa-miR-302d, hsa-miR-3116, hsa-miR-3124, hsa-miR-3126, hsa-miR-3135b, hsa-miR-3139, hsa-miR-3142, hsa-miR-3158, hsa-miR-3162, hsa-miR-3164, hsa-miR-3184, hsa-miR-3199, hsa-miR-320b, hsa-miR-34a, hsa-miR-34b, hsa-miR-3677, hsa-miR-3681, hsa-miR-3685, hsa-miR-3692, hsa-miR-370, hsa-miR-373, hsa-miR-376a, hsa-miR-376b, hsa-miR-378d, hsa-miR-378e, hsa-miR-3907, hsa-miR-3922, hsa-miR-3934, hsa-miR-411, hsa-miR-4265, hsa-miR-4322, hsa-miR-4426, hsa-miR-4427, hsa-miR-4455, hsa-miR-4457, hsa-miR-4492, hsa-miR-4505, hsa-miR-4533, hsa-miR-4534, hsa-miR-4633, hsa-miR-4646, hsa-miR-4667, hsa-miR-4677, hsa-miR-4683, hsa-miR-4687, hsa-miR-4704, hsa-miR-4717, hsa-miR-4733, hsa-miR-4736, hsa-miR-4756, hsa-miR-4766, hsa-miR-4782, hsa-miR-4795, hsa-miR-483, hsa-miR-484, hsa-miR-496, hsa-miR-500a, hsa-miR-519a, hsa-miR-522, hsa-miR-548e, hsa-miR-550b, hsa-miR-5692b, hsa-miR-5692c, hsa-miR-590, hsa-miR-597, hsa-miR-615, hsa-miR-616, hsa-miR-618, hsa-miR-622, hsa-miR-626, hsa-miR-632, hsa-miR-646, hsa-miR-656, hsa-miR-668, hsa-miR-7, hsa-miR-744, hsa-miR-760, hsa-miR-765, hsa-miR-877, hsa-miR-889, hsa-miR-892c, hsa-miR-9, hsa-miR-938, hsa-miR-940, hsa-miR-942, hsa-miR-96, hsa-miR-99a, HSF2, MAFG, MEF2A, MEIS1, MSX1, NFATC1, NFE2L1, NLRC4, NOBOX, NR2E3, NR2F2, PATZ1, POU5F1, RORA, SREBF1, SREBF2, STAT4, STAT6, TCF7L2, TFAP2C, TGIF1, THAP1, VDR, ZEB1.
Module2	ARID5B, BIRC7, E2F6, EBF1, EHF, ELF5, ELK4, FOXA1, FOXJ2, GATA6, GFI1B, HNF4G, HOXC9, hsa-let-7d, hsa-let-7f, hsa-miR-10a, hsa-miR-1185, hsa-miR-1227, hsa-miR-1237, hsa-miR-124, hsa-miR-125a, hsa-miR-1271, hsa-miR-128, hsa-miR-1293, hsa-miR-130a, hsa-miR-132, hsa-miR-136, hsa-miR-137, hsa-miR-143, hsa-miR-145, hsa-miR-146a, hsa-miR-146b, hsa-miR-150, hsa-miR-152, hsa-miR-154, hsa-miR-155, hsa-miR-181b, hsa-miR-1827, hsa-miR-186, hsa-miR-18b, hsa-miR-194, hsa-miR-195, hsa-miR-19b, hsa-miR-200b, hsa-miR-21, hsa-miR-212, hsa-miR-217, hsa-miR-221, hsa-miR-222, hsa-miR-223, hsa-miR-26b, hsa-miR-27a, hsa-miR-299, hsa-miR-29a, hsa-miR-302a, hsa-miR-30b, hsa-miR-30c, hsa-miR-30e, hsa-miR-3119, hsa-miR-32, hsa-miR-3202, hsa-miR-320a, hsa-miR-326, hsa-miR-329, hsa-miR-330, hsa-miR-33b, hsa-miR-3529, hsa-miR-3605, hsa-miR-3607, hsa-miR-3616, hsa-miR-365, hsa-miR-3660, hsa-miR-3666, hsa-miR-374a, hsa-miR-374b, hsa-miR-375, hsa-miR-377, hsa-miR-378, hsa-miR-382, hsa-miR-421, hsa-miR-4296, hsa-miR-4429, hsa-miR-4441, hsa-miR-4471, hsa-miR-4480, hsa-miR-4488, hsa-miR-4504, hsa-miR-452, hsa-miR-4526, hsa-miR-4539, hsa-miR-4685, hsa-miR-4708, hsa-miR-4728, hsa-miR-4762, hsa-miR-4763, hsa-miR-4768, hsa-miR-485, hsa-miR-494, hsa-miR-495, hsa-miR-497, hsa-miR-499a, hsa-miR-5004, hsa-miR-512, hsa-miR-518a, hsa-miR-520a, hsa-miR-520b, hsa-miR-520c, hsa-miR-542, hsa-miR-543, hsa-miR-551b, hsa-miR-567, hsa-miR-5688, hsa-miR-574, hsa-miR-5787, hsa-miR-608, hsa-miR-609, hsa-miR-629, hsa-miR-639, hsa-miR-648, hsa-miR-649, hsa-miR-650, hsa-miR-671, hsa-miR-758, hsa-miR-759, hsa-miR-92a, HSF1, IKZF1, IL3RA, KRAS, MAFB, MECOM, NKX2-5, POU2F2, PRDM1, PSMC5, RFX1, RFX5, SOX2, SRY, TP63.
Module3	BIRC5, CAPN1, CASP1, CRX, E2F2, E2F4, ESRRA, EWSR1, FOSL1, GATA3, HNF4A, HOXA9, hsa-let-7e, hsa-miR-1197, hsa-miR-1245b, hsa-miR-1254, hsa-miR-1260b, hsa-miR-1288, hsa-miR-1291, hsa-miR-1294, hsa-miR-1301, hsa-miR-141, hsa-miR-142, hsa-miR-148a, hsa-miR-17, hsa-miR-1825, hsa-miR-191, hsa-miR-196a, hsa-miR-200c, hsa-miR-214, hsa-miR-219, hsa-miR-22, hsa-miR-224, hsa-miR-2276, hsa-miR-2277, hsa-miR-24, hsa-miR-3064, hsa-miR-3130, hsa-miR-3133, hsa-miR-3138, hsa-miR-3173, hsa-miR-3175, hsa-miR-3176, hsa-miR-3187, hsa-miR-3190, hsa-miR-3198, hsa-miR-324, hsa-miR-345, hsa-miR-3613, hsa-miR-3652, hsa-miR-3661, hsa-miR-3665, hsa-miR-3678, hsa-miR-372, hsa-miR-379, hsa-miR-3913, hsa-miR-3926, hsa-miR-3944, hsa-miR-3960, hsa-miR-412, hsa-miR-423, hsa-miR-433, hsa-miR-4430, hsa-miR-4451, hsa-miR-4452, hsa-miR-4469, hsa-miR-4472, hsa-miR-4487, hsa-miR-450a, hsa-miR-4512, hsa-miR-4530, hsa-miR-4638, hsa-miR-4641, hsa-miR-4647, hsa-miR-4658, hsa-miR-4676, hsa-miR-4706, hsa-miR-4727, hsa-miR-4742, hsa-miR-4754, hsa-miR-4794, hsa-miR-4796, hsa-miR-487b, hsa-miR-493, hsa-miR-500b, hsa-miR-503, hsa-miR-5047, hsa-miR-541, hsa-miR-548aa, hsa-miR-548u, hsa-miR-550a, hsa-miR-562, hsa-miR-583, hsa-miR-586, hsa-miR-589, hsa-miR-601, hsa-miR-611, hsa-miR-711, hsa-miR-769, hsa-miR-874, hsa-miR-922, hsa-miR-937, hsa-miR-99b, IKBKG, IL1R1, IRF2, KLF12, MAX, MMP9, MYCN, MZF1, NFE2L2, NHLH1, PAX4, PBX1, PLAG1, PRKACG, RARA, RNF8, TCF12, TFAP2A, TFAP4, TNFRSF10C, TNFRSF6B, TOPORS, TRAF1, USF1, XBP1.

Module4	ALX1, CDX1, CTCF, EGR4, FEV, FLI1, FOXA2, FOXP1, HINFP, HNF1B, hsa-miR-1, hsa-miR-106b, hsa-miR-10b, hsa-miR-1184, hsa-miR-1228, hsa-miR-1231, hsa-miR-125b, hsa-miR-149, hsa-miR-153, hsa-miR-15b, hsa-miR-181a, hsa-miR-185, hsa-miR-190, hsa-miR-1910, hsa-miR-197, hsa-miR-199b, hsa-miR-202, hsa-miR-203, hsa-miR-205, hsa-miR-216a, hsa-miR-25, hsa-miR-27b, hsa-miR-28, hsa-miR-298, hsa-miR-301a, hsa-miR-30a, hsa-miR-31, hsa-miR-3120, hsa-miR-340, hsa-miR-342, hsa-miR-34c, hsa-miR-371, hsa-miR-376c, hsa-miR-381, hsa-miR-3910, hsa-miR-410, hsa-miR-424, hsa-miR-4257, hsa-miR-429, hsa-miR-4419a, hsa-miR-4458, hsa-miR-4478, hsa-miR-4514, hsa-miR-454, hsa-miR-4663, hsa-miR-4690, hsa-miR-4749, hsa-miR-489, hsa-miR-499, hsa-miR-499b, hsa-miR-520d, hsa-miR-539, hsa-miR-548au, hsa-miR-5682, hsa-miR-579, hsa-miR-623, hsa-miR-637, hsa-miR-875, hsa-miR-92b, hsa-miR-93, INSM1, NFIC, NKX3-1, PAX3, PPARA, SOX3, SOX5, SOX6, SP2, T, TEF, TLX2, ZBTB18, ZFX, ZNF423.
Module5	ABCB1, BACH1, BATF, BIK, CASP9, CREB1, DDIT3, DFFB, E2F5, EGFR, ELK1, ENDOD1, FADD, FOXC1, FOXO1, H2AFX, hsa-let-7a, hsa-let-7i, hsa-miR-100, hsa-miR-1205, hsa-miR-1224, hsa-miR-1226, hsa-miR-1244, hsa-miR-1248, hsa-miR-1255b, hsa-miR-127, hsa-miR-1276, hsa-miR-1285, hsa-miR-1304, hsa-miR-1306, hsa-miR-1913, hsa-miR-192, hsa-miR-193a, hsa-miR-193b, hsa-miR-2278, hsa-miR-2467, hsa-miR-296, hsa-miR-30d, hsa-miR-3122, hsa-miR-3140, hsa-miR-3150a, hsa-miR-3157, hsa-miR-3188, hsa-miR-3191, hsa-miR-3192, hsa-miR-337, hsa-miR-3620, hsa-miR-3659, hsa-miR-3676, hsa-miR-3679, hsa-miR-3680, hsa-miR-3714, hsa-miR-380, hsa-miR-3928, hsa-miR-409, hsa-miR-4459, hsa-miR-4496, hsa-miR-449c, hsa-miR-4515, hsa-miR-4639, hsa-miR-4657, hsa-miR-4674, hsa-miR-4700, hsa-miR-4774, hsa-miR-4784, hsa-miR-4797, hsa-miR-487a, hsa-miR-505, hsa-miR-548o, hsa-miR-558, hsa-miR-568, hsa-miR-581, hsa-miR-612, hsa-miR-613, hsa-miR-619, hsa-miR-628, hsa-miR-630, hsa-miR-654, hsa-miR-661, hsa-miR-665, hsa-miR-670, hsa-miR-761, hsa-miR-770, hsa-miR-939, IL1B, IRAK2, IRAK4, IRF1, LMO2, MAF, MAFK, MEF2C, MKI67, MYB, NFATC2, NFYA, NFYB, NFYC, NR2C2, NR2F1, PAX5, PAX6, PIK3CA, PIK3CD, PIK3CG, PIK3R2, POU3F2, PPP3CC, RIPK1, RUNX2, SOX9, SPZ1, SRF, STAT2, TCF4, TLX1, TNFRSF1A, TNFRSF25, TRAF6, UBB, UBC, USF2.