Comprehensive network of miRNA-induced intergenic interactions and a biological role of its core in cancer

Vladimir V. Galatenko, Alexey V. Galatenko, Timur R. Samatov, Andrey A. Turchinovich, Maxim Yu. Shkurnikov, Julia A. Makarova, Alexander G. Tonevitsky

Supplementary Information

Network core: a simple example

In order to illustrate the definition of the network core, let us consider the following simple network.



Supplementary Figure 1 | A simple example of a network. Nodes comprising the network core are colored in green. All these nodes have both in-edges and out-edges. The remaining nodes are colored in gray if they also have both in-edges and out-edges, in orange if they have only out-edges (and no in-edges), and in blue if they have only in-edges (and no out-edges). Overall the network contains 9 nodes with both in- and out-edges, 2 nodes with only out-edges and 3 nodes with only in-edges.

This network has two nontrivial (i.e., containing at least two nodes) strongly connected components: $\{A, D\}$ and $\{C, E, F, G, K\}$. In each component every node is reachable from every other node via a directed path. E.g., node C is reachable from node F via a path

 $F \longrightarrow G \longrightarrow K \longrightarrow E \longrightarrow C.$

Nodes B, G and N are reachable from the component {C, E, F, G, K}, but they do not belong to this component as the opposite reachability is violated (i.e., there is no directed path from these nodes to the nodes of the component). Similarly, the component {A, D} is reachable from nodes H, I and L, but these nodes can't be added to the component due to absence of reverse reachability.

The enrichment analysis of lists of nodes with the highest in-degree

Lists of network nodes with in-degrees of at least 10 were formed. For the F-network, this list consisted of 142 genes (these are genes that are targeted by intragenic miRNAs of at least 10 other genes). For the IS-network, this list consisted of 90 genes (these are genes that are targeted by intronic sense miRNAs of at least 10 other genes).

Functional categories overrepresented in these lists were identified using DAVID 6.7 online service. These categories are presented in Supplementary Tables 1-4.

Category Term		Count	%	Fold Enrichment	P-Value	Benjamini
SP PIR KEYWORDS	Phosphoprotein	97	71.3	1.9	3.24×10 ⁻¹⁵	6.63×10 ⁻¹³
SP PIR KEYWORDS	Acetylation	47	34.6	2.5	1.40×10 ⁻⁹	9.61×10 ⁻⁸
SP PIR KEYWORDS	rna-binding	21	15.4	5.5	1.23×10 ⁻⁹	1.27×10 ⁻⁷
KEGG PATHWAY	hsa04110:Cell cycle	11	8.1	9.3	1.35×10 ⁻⁷	1.09×10 ⁻⁵
KEGG PATHWAY	hsa05220:Chronic myeloid leukemia	9	6.6	12.7	3.04×10 ⁻⁷	1.23×10 ⁻⁵
SP PIR KEYWORDS	Cytoplasm	49	36.0	2.1	2.68×10 ⁻⁷	1.38×10 ⁻⁵
KEGG PATHWAY	hsa05200:Pathways in cancer	15	11.0	4.8	7.98×10 ⁻⁷	2.15×10 ⁻⁵
KEGG PATHWAY	hsa05214:Glioma	8	5.9	13.5	1.36×10 ⁻⁶	2.75×10 ⁻⁵
KEGG PATHWAY	hsa05219:Bladder cancer	7	5.1	17.7	1.83×10 ⁻⁶	2.97×10 ⁻⁵
KEGG PATHWAY	hsa04115:p53 signaling pathway	8	5.9	12.5	2.30×10 ⁻⁶	3.11×10 ⁻⁵
SP PIR KEYWORDS	ubl conjugation	18	13.2	4.3	8.04×10 ⁻⁷	3.31×10 ⁻⁵
COTEDM DD EAT	GO:0010608~posttranscriptional regulation of	1.4	10.2	70	2.42×10-8	2 22 10-5
GOTERM_BP_FAT	gene expression	14	10.5	/.8	2.42×10	3.32×10
KEGG PATHWAY	hsa05218:Melanoma	8	5.9	11.9	3.09×10 ⁻⁶	3.58×10 ⁻⁵
SP PIR KEYWORDS	nucleus	56	41.2	1.8	1.06×10 ⁻⁶	3.62×10 ⁻⁵
	and and a sector l	(4.4	2	2 22 10-6	C 92 10-5
SP_PIK_KE1 WORDS	cen cycle control	0	4.4	7.4	2.52×10	0.85×10
_GOTERM_BP_FAT	GO:0010941~regulation of cell death	24	17.6	3.5	2.46×10 ⁻⁷	8.42×10 ⁻⁵
GOTERM CC FAT	GO:0000307~cyclin-dependent protein kinase	5	37	61.8	8 33×10 ⁻⁷	9.83×10 ⁻⁵
dorline_cc_rm	holoenzyme complex	5	5.7	01.0	0.55.10	2.05*10
GOTERM BP FAT	GO:0043067~regulation of programmed cell	24	17.6	3.5	2 31×10 ⁻⁷	1.05×10^{-4}
Sollian_bi_inii	death	21	17.0	5.5	2.51 10	1.05 10
SP_PIR_KEYWORDS	atp-binding	26	19.1	2.8	5.06×10 ⁻⁶	1.30×10 ⁻⁴
GOTERM_BP_FAT	GO:0042981~regulation of apoptosis	24	17.6	3.5	1.93×10 ⁻⁷	1.32×10 ⁻⁴
KEGG_PATHWAY	hsa05215:Prostate cancer	8	5.9	9.5	1.41×10 ⁻⁵	1.43×10 ⁻⁴
GOTERM_CC_FAT	GO:0031981~nuclear lumen	29	21.3	2.7	7.77×10-7	1.83×10 ⁻⁴
GOTERM BP FAT	GO:0010629~negative regulation of gene	18	13.2	4.2	1.03×10 ⁻⁶	2.81×10 ⁻⁴
COTEDM CO EAT	expression	22	22.5	2.2	2.76×10-6	2.05×10-4
GOTERM_CC_FAT	GO:0001974~memoran×10-enclosed lumen	32	23.5	2.3	3.70×10^{-6}	2.95×10
GOTERM_MF_FAT	GO:0003723~KNA binding	22	10.2	3.4	1.13×10^{-6}	5.42×10
GOTERM DD FAT	GO:0043233~organelle lumen	31	22.8	2.3	7.5/×10	$4.4/\times 10$
GUIERM_BP_FAI	GO:0042127~regulation of cell profileration	14	10.2	3.3	2.20×10^{-5}	5.02×10
SP_PIR_KEY WORDS		14	10.5	4.5	2.24×10	5.12×10
SP_PIK_KEY WORDS		0	4.4	17.0	2.00×10 ⁻⁵	5.55×10
CD DID KEVINODDC	hsa04510.Focal adhesion	10	/.4	5.5	7.27×10 ⁻⁵	6.54×10
SP_PIR_KEYWORDS		28	20.6	2.3	3.85×10 ⁻⁵	6.62×10
GUIERM CC_FAI	GO:00/0013~intracellular organelle lumen	30	22.1	2.3	1.43×10^{-5}	$6./3 \times 10^{-4}$
SP_PIR_KEYWORDS	Proto-oncogene	10	/.4	0.1	3.62×10^{-4}	6./8×10 ⁻⁴
KEGG_PATHWAY	hsa05222:Small cell lung cancer	/	5.1	8.8	1.06×10	8.59×10 ⁺
SP_PIR_KEYWORDS	repressor	13	9.6	4.2	5./9×10 ⁻²	9.1/×10
GOTERM BP FAT	GO:000/16/~enzyme linked receptor protein	14	10.3	4.8	5.97×10 ⁻⁶	0.001165
	signaling pathway	10	0.0	15	7.0(~10-5	0.00117
SP_PIR_KEYWORDS	Apoptosis	12	8.8	4.3	/.96×10	0.00117
GOTERM_BP_FAT	proliferation	15	11.0	4.3	9.77×10 ⁻⁶	0.00167
GOTERM BP FAT	GO:0010942~positive regulation of cell death	15	11.0	4.1	1.70×10 ⁻⁵	0.001792
	GO:0009891~positive regulation of	10	14.0	2.2	1.02.10-5	0.001007
GOTERM_BP_FAT	biosynthetic process	19	14.0	3.2	1.93×10	0.001886
INTERDRO	IPR012677:Nucleotid×10-binding, alpha-beta	11	Q 1	6.6	6.63×10 ⁻⁶	0.001014
INTERFRO	plait	11	0.1	0.0	0.03~10	0.001914
GOTERM BP FAT	GO:0048008~platelet-derived growth factor	5	37	31.0	1.68×10 ⁻⁵	0.001915
GOTEKIM_BI_IMI	receptor signaling pathway	5	5.7	51.0	1.00.10	0.001/15
GOTERM BP FAT	GO:0043068~positive regulation of	15	11.0	4.1	1.62×10 ⁻⁵	0.002011
	programmed cell death		11.0		1.02 10	0.002011
GOTERM BP FAT	GO:0031328~positive regulation of cellular	19	14.0	3.3	1.59×10 ⁻⁵	0.002174
	biosynthetic process	10	1 / 0			0.000107
GOTERM_CC_FAT	GO:0005654~nucleoplasm	19	14.0	2.9	5.56×10 ⁻⁵	0.002185
GOTERM_BP_FAT	GO:0043065~positive regulation of apoptosis	15	11.0	4.1	1.50×10-5	0.002274
THP NELL FEATURE	miliagenesis site	4/1	15.0	14		1111/33/

Supplementary Table 1 | **Categories (terms) overrepresented in the list of genes with the highest in-degree in the F-network.** All categories with Benjamini-corrected p-values less than 0.05 are listed.

Category	Term		%	Fold Enrichment	P-Value	Benjamini
GOTERM_BP_FAT	GO:0010605~negative regulation of macromolecule metabolic process	19	14.0	3.0	3.98×10 ⁻⁵	0.003624
SP_PIR_KEYWORDS	ATP	9	6.6	5.4	2.65×10 ⁻⁴	0.003636
GOTERM_BP_FAT	GO:0043066~negative regulation of apoptosis	13	9.6	4.3	4.30×10-5	0.003671
GOTERM_BP_FAT	GO:0060548~negative regulation of cell death	13	9.6	4.2	5.06×10^{-3}	0.003839
SP_PIR_KEYWORDS	serine/threonin×10-protein kinase	11	8.1	4.1	3.62×10^{-4}	0.003923
UP SEO FEATURE	nucleotide phosphat×10-binding region: ATP	21	15.4	3.1	1.38×10^{-5}	0.003924
GOTERM_BP_FAT	GO:0043069~negative regulation of	13	9.6	4.3	4.93×10 ⁻⁵	0.003957
SP_PIR_KEYWORDS	Kinase	15	11.0	3.1	3.46×10 ⁻⁴	0.003958
SP_PIR_KEYWORDS	transcription regulation	29	21.3	2.0	3.40×10 ⁻⁴	0.004116
BIOCARTA	Regulation	6	4.4	11.5	9.39×10 ⁻⁵	0.004356
SP_PIR_KEYWORDS	Transcription GO:0012502~induction of programmed cell	29	21.3	2.0	4.86×10 ⁻⁴	0.004991
GOTERM_BP_FAT	death	12	8.8	4.4	8.27×10 ⁻⁵	0.005129
GOTERM_MF_FAT	GO:0000166~nucleotide binding	38	27.9	1.9	6.97×10 ⁻⁵	0.005266
GOTERM ME FAT	GO:0007049~cell cycle	13	9.6	2.9	3.18×10^{-5}	0.005312
GOTERM BP FAT	GO:00019904~protein domain specific binding GO:0006917~induction of apoptosis	12	8.8	4.4	8.04×10 ⁻⁵	0.005486
GOTERM BP FAT	GO:0010604~positive regulation of	20	14.7	2.7	9.25×10 ⁻⁵	0.005489
GOTERM BR FAT	macromolecule metabolic process	16	11.8	3 3	7 76×10 ⁻⁵	0.005571
GOTERM BP FAT	GO:0022402~cell cycle process	40	29.4	1.8	1.09×10^{-4}	0.005571
GOTERM MF FAT	GO:0019899~enzyme binding	16	11.8	3.4	5.69×10 ⁻⁵	0.005734
GOTERM_BP_FAT	GO:0016265~death	18	13.2	2.9	1.14×10 ⁻⁴	0.005744
GOTERM_BP_FAT	GO:0010033~response to organic substance	18	13.2	2.9	1.08×10^{-4}	0.005899
GOTERM_BP_FAT	GO:0008219~cell death	18	13.2	2.9	1.05×10 ⁻⁴	0.00594
INTERPRO	h_RacCycDPathway:Influence of Ras and Rho	10	7.4	6.0	4.15×10^{-5}	0.005973
DIOCARTA	proteins on G1 to S Transition GO:0051252~regulation of RNA metabolic	0	4.4	12.0	7.02×10	0.007039
GOTERM_BP_FAT	process	31	22.8	2.0	1.68×10 ⁻⁴	0.008167
GOTERM_BP_FAT	GO:0022403~cell cycle phase	13	9.6	3.7	1.90×10^{-4}	0.008617
GOTER_BP_FAT	GO:0012501~programmed cell death	16	5.1	3.1	1.84×10^{-4}	0.008655
GOTERM BP FAT	GO:0051325~interphase	7	5.1	8.0 7.8	2.31×10 2.70×10 ⁻⁴	0.010141
SP PIR KEYWORDS	dna-binding	26	19.1	2.0	0.001186	0.011569
SP_PIR_KEYWORDS	translation regulation	5	3.7	10.6	0.001263	0.011767
GOTERM_BP_FAT	GO:0048534~hemopoietic or lymphoid organ development	10	7.4	4.5	3.49×10 ⁻⁴	0.014346
GOTERM BP FAT	GO:0010557~positive regulation of	16	11.8	2.9	3.82×10 ⁻⁴	0.015256
SP_PIR_KEYWORDS	isopeptide bond	9	6.6	4.0	0.001881	0.016719
GOTERM BP FAT	GO:0006468~protein amino acid	16	11.8	2.8	4 70×10 ⁻⁴	0.018201
	phosphorylation GO:0016481~negative regulation of	10	0.6	2.0	4.05 10-4	0.010240
GOTERM_BP_FAT	transcription	13	9.6	3.3	4.85×10 ⁻⁴	0.018249
GOTERM BP FAT	GO:0002320~initiatie system development	15	11.0	4.5	5.38×10^{-4}	0.019185
GOTERM BP FAT	GO:0007169~transmembrane receptor protein	9	6.6	4.7	6.09×10 ⁻⁴	0.021154
GOTERM BP FAT	GO:0032268~regulation of cellular protein	13	9.6	3.2	6 44×10 ⁻⁴	0.021802
SP PIR KEYWORDS	metabolic process	8	5.0	43	0.002644	0.021802
GOTERM BP FAT	GO:0007423~sensory organ development	9	6.6	4.6	7.04×10 ⁻⁴	0.022400
GOTERM_BP_FAT	GO:0010558~negative regulation of	14	10.3	3.0	6.90×10 ⁻⁴	0.022757
GOTERM BP FAT	GO:0045892~negative regulation of	11	8 1	3.6	8 44×10 ⁻⁴	0.026513
SMADT	transcription, DNA-dependent	10	7.4	4.5	2.21×10-4	0.02(502
SMARI	GO:0031327~negative regulation of cellular	10	/.4	4.5	3.21×10	0.020392
GOTERM_BP_FAT	biosynthetic process	14	10.3	2.9	8.71×10 ⁻⁴	0.026732
GOTERM_BP_FAT	GO:0051253~negative regulation of RNA metabolic process	11	8.1	3.6	9.59×10 ⁻⁴	0.028741
GOTERM_BP_FAT	GO:0009890~negative regulation of biosynthetic process	14	10.3	2.9	0.001057	0.029099
SP_PIR_KEYWORDS	chromosomal rearrangement	8	5.9	4.1	0.003587	0.029173
GOTERM_BP_FAT	GO:0051173~positive regulation of nitrogen compound metabolic process	15	11.0	2.7	0.00102	0.029259
GOTERM_BP_FAT	GO:0000079~regulation of cyclin-dependent	5	3.7	10.9	0.001093	0.029491
GOTERM BP FAT	GO:0006417~regulation of translation	7	51	6.0	0.001054	0.029596
GOTERM_BP_FAT	GO:0001889~liver development	5	3.7	11.1	0.001019	0.029866

Category	Term	Count	%	Fold Enrichment	P-Value	Benjamini
GOTERM_BP_FAT	GO:0000278~mitotic cell cycle	11	8.1	3.5	0.001131	0.029903
KEGG_PATHWAY	hsa05212:Pancreatic cancer	5	3.7	7.4	0.004164	0.030257
GOTERM_BP_FAT	GO:0045934~negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	13	9.6	3.0	0.001257	0.031369
SP PIR KEYWORDS	host-virus interaction	8	59	4.0	0.004028	0.031475
GOTERM BP FAT	GO:0051270~regulation of cell motion	8	5.9	49	0.001228	0.031801
GOTERM BP FAT	GO:0016458~gene silencing	5	37	10.5	0.001254	0.031861
GOTERM_BP_FAT	GO:0000082~G1/S transition of mitotic cell cycle	5	3.7	10.5	0.001254	0.031861
GOTERM_BP_FAT	GO:0006355~regulation of transcription, DNA-dependent	28	20.6	1.9	0.001412	0.033927
GOTERM_BP_FAT	GO:0051172~negative regulation of nitrogen compound metabolic process	13	9.6	2.9	0.001411	0.034516
INTERPRO	IPR017442:Serine/threonine protein kinas×10- related	11	8.1	3.9	5.14×10 ⁻⁴	0.036485
SP_PIR_KEYWORDS	protein kinase inhibitor	3	2.2	26.5	0.005501	0.041215
GOTERM_BP_FAT	GO:0006916~anti-apoptosis	8	5.9	4.6	0.001785	0.041964
INTERPRO	IPR008271:Serine/threonine protein kinase, active site	11	8.1	4.0	4.61×10 ⁻⁴	0.043451
GOTERM_MF_FAT	GO:0004674~protein serine/threonine kinase activity	12	8.8	3.1	0.001493	0.044273
GOTERM_BP_FAT	GO:0043627~response to estrogen stimulus	6	4.4	6.7	0.001924	0.044409
_GOTERM_MF_FAT	GO:0019900~kinase binding	8	5.9	5.0	0.001056	0.044722
GOTERM_MF_FAT	GO:0032559~adenyl ribonucleotide binding	26	19.1	1.9	0.001223	0.045299
GOTERM_BP_FAT	GO:0045768~positive regulation of anti- apoptosis	4	2.9	15.7	0.002005	0.045464
GOTERM_MF_FAT	GO:0030528~transcription regulator activity	26	19.1	1.9	0.001409	0.046366
KEGG_PATHWAY	hsa05210:Colorectal cancer	5	3.7	6.3	0.007204	0.04763
GOTERM_BP_FAT	GO:0060541~respiratory system development	6	4.4	6.5	0.002177	0.048482
INTERPRO	IPR017441:Protein kinase, ATP binding site	12	8.8	3.4	8.79×10 ⁻⁴	0.049551
KEGG_PATHWAY	hsa04012:ErbB signaling pathway	5	3.7	6.1	0.008145	0.04968
GOTERM_MF_FAT	GO:0005524~ATP binding	26	19.1	2.0	0.001009	0.049687

Supplementary Table 2 | **Categories (terms) overrepresented in the list of genes with the highest in-degree in the IS-network.** All categories with Benjamini-corrected p-values less than 0.05 are listed.

Category	Term	Count	%	Fold Enrichment	P-Value	Benjamini
SP PIR KEYWORDS	phosphoprotein	60	69.8	1.8	3.07×10 ⁻⁹	4.79×10 ⁻⁷
KEGG_PATHWAY	hsa04110:Cell cycle	9	10.5	12.6	2.19×10 ⁻⁷	1.16×10 ⁻⁵
KEGG_PATHWAY	hsa04115:p53 signaling pathway	7	8.1	18.1	1.37×10 ⁻⁶	3.62×10 ⁻⁵
SP_PIR_KEYWORDS	Cytoplasm	34	39.5	2.3	2.09×10 ⁻⁶	1.09×10 ⁻⁴
SP_PIR_KEYWORDS	ubl conjugation	14	16.3	5.3	1.75×10 ⁻⁶	1.37×10 ⁻⁴
KEGG_PATHWAY	hsa05214:Glioma	6	7.0	16.7	1.96×10 ⁻⁵	3.46×10 ⁻⁴
KEGG_PATHWAY	hsa05220:Chronic myeloid leukemia	6	7.0	14.0	4.60×10 ⁻⁵	4.06×10 ⁻⁴
KEGG_PATHWAY	hsa05200:Pathways in cancer	10	11.6	5.3	4.00×10 ⁻⁵	4.24×10 ⁻⁴
KEGG PATHWAY	hsa05218:Melanoma	6	7.0	14.8	3.52×10 ⁻⁵	4.67×10 ⁻⁴
KEGG_PATHWAY	hsa05222:Small cell lung cancer	6	7.0	12.5	7.95×10 ⁻⁵	4.68×10 ⁻⁴
KEGG PATHWAY	hsa04510:Focal adhesion	8	9.3	7.0	7.92×10 ⁻⁵	5.25×10 ⁻⁴
KEGG PATHWAY	hsa05219:Bladder cancer	5	5.8	20.9	7.13×10 ⁻⁵	5.40×10 ⁻⁴
KEGG PATHWAY	hsa05215:Prostate cancer	6	7.0	11.8	1.05×10 ⁻⁴	5.56×10 ⁻⁴
UP SEQ FEATURE	mutagenesis site	26	30.2	2.8	1.71×10 ⁻⁶	7.02×10 ⁻⁴
SP PIR KEYWORDS	nucleus	37	43.0	1.9	2.70×10 ⁻⁵	8.44×10 ⁻⁴
SP PIR KEYWORDS	rna-binding	12	14.0	5.0	2.52×10 ⁻⁵	9.81×10 ⁻⁴
GOTERM BP FAT	GO:0010941~regulation of cell death	17	19.8	3.9	4.43×10 ⁻⁶	0.001078
SP PIR KEYWORDS	Apoptosis	10	11.6	5.9	4.67×10 ⁻⁵	0.001212
GOTERM_BP_FAT	GO:0043067~regulation of programmed cell death	17	19.8	3.9	4.23×10 ⁻⁶	0.001371
SP PIR KEYWORDS	cyclin	5	5.8	22.4	7.00×10 ⁻⁵	0.00156
GOTERM_BP_FAT	GO:0010608~posttranscriptional regulation of gene expression	10	11.6	8.8	1.67×10 ⁻⁶	0.00163
GOTERM BP FAT	GO:0042981~regulation of apoptosis	17	19.8	3.9	3.72×10 ⁻⁶	0.00181
GOTERM_CC_FAT	GO:0000307~cyclin-dependent protein kinase holoenzyme complex	4	4.7	80.1	1.35×10 ⁻⁵	0.002054
GOTERM BP FAT	GO:0042127~regulation of cell proliferation	16	18.6	3.8	1.33×10 ⁻⁵	0.002585
SP PIR KEYWORDS	atp-binding	17	19.8	2.9	2.01×10 ⁻⁴	0.003483
GOTERM BP FAT	GO:0010033~response to organic substance	15	17.4	3.9	2.20×10 ⁻⁵	0.003569
SP PIR KEYWORDS	cell cycle	10	11.6	4.9	1.98×10^{-4}	0.003857
SP PIR KEYWORDS	cell cycle control	4	4.7	28.9	3.42×10 ⁻⁴	0.005327
GOTERM_BP_FAT	GO:0060548~negative regulation of cell death	10	11.6	5.1	1.17×10 ⁻⁴	0.007128
GOTERM_BP_FAT	GO:0010942~positive regulation of cell death	11	12.8	4.7	9.60×10 ⁻⁵	0.007165

GOTERM_BP_FAT GO 003566-negative regulation of programmed cell death 10 11 6 5.2 1.03×10 ⁺¹ 0.00717 GOTERM_BP_FAT GO 0003609-negative regulation of programmed cell death 10 11.6 5.2 1.15×10 ⁺¹ 0.00747 GOTERM_BP_FAT GO 0003009-natest-derived growth factor 1 12.8 4.7 39.0 1.32×10 ⁺¹ 0.00752 GOTERM_BP_FAT GO 000308-postore regulation of appoison 1 12.8 4.7 39.0 1.32×10 ⁺¹ 0.00762 GOTERM_BP_FAT GO 000308-postore regulation of appoison 12 1.0 4.4 6.64×10 ⁺¹ 0.008027 GOTERM_BP_FAT GO 0007167-array to the for factor protein 10 11.6 5.4 7.95×10 ⁺² 0.008053 GOTERM_BP_FAT GO 00007167-array to the for factor protein 10 11.6 5.4 7.95×10 ⁺² 0.008051 GOTERM_BP_FAT GO 0000707-regulation of cellin-dependent 5 8.8 17.2 1.91×10 ⁺¹ 0.010014 GOTERM_BP_FAT GO 0000707-regulation of cellin-dependent 5 8.8 <t< th=""><th>Category</th><th colspan="2">tegory Term</th><th>%</th><th>Fold Enrichment</th><th>P-Value</th><th>Benjamini</th></t<>	Category	tegory Term		%	Fold Enrichment	P-Value	Benjamini
GOTERM_BP_FAT GÖ 0003000-negative regulation of programmed cell death 10 11.6 5.2 1.15×10 ⁴ 0.007443 GOTERM_BP_FAT GÖ 0004086-negative regulation of GO 0004008-placet-derived growth factor 4 4.7 39.0 1.35×10 ⁴ 0.007527 GOTERM_BP_FAT GÖ 0004008-placet-derived growth factor 4 4.7 39.0 1.35×10 ⁴ 0.007527 GOTERM_BP_FAT GÖ 0001002-neggative regulation of groppose 1 12.8 4.7 8.72×10 ⁷ 0.0006077 GOTERM_BP_FAT GÖ 0001062-neggative regulation of gene 12 1.4.0 4.4 6.64×10 ¹⁰ 0.0008077 GOTERM_BP_FAT GÖ 0000167-fenzyme linked receptor procin 10 1.1 5.4 7.95×10 ⁴ 0.000855 GOTERM_BP_FAT GÖ 0000167-senzyme linked receptor procin 10 1.1.6 5.4 8.94×10 ⁴ 0.000811 SP JPR KEYWORDS kinase 11 12.8 3.6 8.94×10 ⁴ 0.000811 GOTERM_BP_FAT GÖ 0000179-regutation of cyclin dependent 5 5.8 17.2 1.91×10 ⁴ 0.01024	GOTERM_BP_FAT	GO:0043066~negative regulation of apoptosis	10	11.6	5.2	1.03×10 ⁻⁴	0.00717
GOTERM, BP_FAT GO000300S-pinition ergulation of programmed cell death 11 12.8 4.7 924-10 ¹ 0.00747 GOTERM, BP_FAT GO1004300S-pinite-d-drived growth factor receptor signaling pathway 4 7 30 1.32×10 ⁴ 0.007704 GOTERM, BP_FAT GO00405S-positive regulation of gene cytosian 7 8.1 6.8 5.45×10 ¹ 0.007804 GOTERM, BP_FAT GO00012S-positive regulation of gene cytosian 7 8.1 6.6 6.24×10 ⁻¹ 0.008032 GOTERM, BP_FAT GO00002S-positive regulation of cell signaling pathway 7 8.1 6.6 6.24×10 ⁻¹ 0.008032 GOTERM, BP_FAT GO00002S-positive regulation of cell signaling pathway 7 8.1 6.8 6.36×10 ⁻¹ 0.008033 GOTERM, BP_FAT GO000007S-argulation of cell signaling pathway 7 8.1 6.3 6.36×10 ⁻¹ 0.008033 GOTERM, BP_TAT GO000007S-argulation of cell signaling pathway 7 9.1 2.3 2.13×10 ⁻¹ 0.001631 GOTERM, BP_TAT GO00007S-argulation of cyclin-dependert 5 5.8 17.2	GOTERM_BP_FAT	GO:0043069~negative regulation of	10	11.6	5.2	1.15×10 ⁻⁴	0.007443
GOTERM_BP_FAT GOO048008-patientereduction factor 4 4 7 39.0 1.32-10 ⁻⁴ 0.007522 GOTERM_BP_FAT GOO043065-positive regulation of approxis 11 12.8 4.7 87.21 10 ⁻⁰ 0.007704 GOTERM_BP_FAT GOO002305-positive regulation of gent 12 14.0 4.4 6.64-10 ⁻⁶ 0.008522 SP_PIR_KEYWORDS GOTOMOS-regulative regulation of gent 12 14.0 4.4 6.64-10 ⁻⁶ 0.008525 GOTERM_BP_FAT GOO002324-positive regulation of cell 11 12.8 4.9 6.36-10 ⁻⁴ 0.008811 GOTERM_BP_FAT GOO002324-positive regulation of cell 5 5.8 17.2 1.91-10 ⁻⁴ 0.01081 GOTERM_BP_FAT GOO00029-regulation of cell-depended 5 5.8 1.72 1.91-10 ⁻⁴ 0.01081 GOTERM_BP_FAT GOO0009-regulation of cell-depended 5 7.8 1.22 0.001181 0.01081 GOTERM_BP_FAT GOO009-regulation of cell-depended 5 7.8 1.22 0.001081 0.01081 <td< td=""><td>GOTERM_BP_FAT</td><td>GO:0043068~positive regulation of programmed cell death</td><td>11</td><td>12.8</td><td>4.7</td><td>9.24×10⁻⁵</td><td>0.00747</td></td<>	GOTERM_BP_FAT	GO:0043068~positive regulation of programmed cell death	11	12.8	4.7	9.24×10 ⁻⁵	0.00747
COTERM IP FAT CO/0043065-positive regulation of apopuosis 11 12.8 4.7 8.72-10 ² 0.007704 GOTERM, BP_FAT GO/0105290-programmed cell death 13 15.1 3.9 8.75-10 ⁴ 0.008052 GOTERM, BP_FAT GO/0010529-organity regulation of gene expression 12 14.0 4.4 6.64-10 ⁻³ 0.008052 GOTERM, BP_FAT GO/0007167-m27me linked receptor protein signaling pathway 7 8.1 6.6 6.24+10 ⁴ 0.008052 GOTERM, BP_FAT GO/0007167-m27me linked receptor protein signaling pathway 7 8.1 6.8 8.95+10 ⁴ 0.008814 SP PIR KEYWORDS Katese 11 12.8 3.6 8.95+10 ⁴ 0.010014 GOTERM, BP_TAT GO/000739-engulation of cell-ne-pendent 5.5 1.7 1.91+10 ⁴ 0.01014 SP PIR KEYWORDS transcription 20 2.3 2.2 0.001145 0.01145 SP PIR KEYWORDS transcription 2.0 2.3 2.2 0.001145 0.01145 SP PIR KEYWORDS transcription 2.0<	GOTERM_BP_FAT	GO:0048008~platelet-derived growth factor receptor signaling pathway	4	4.7	39.0	1.32×10 ⁻⁴	0.007522
SP PR, KEYWORDS Proto-encogene 7 8.1 6.8 5.45-117 0.00704 GOTERM, BP FAT GO:0010523-negrammed cell dath 13 15 3.9 8.27-107 0.008027 GOTERM, BP, FAT GO:0010523-negrammed cell dath 13 15 3.9 8.27-107 0.008027 GOTERM, BP, FAT GO:0007167-enzyme linked receptor protein 10 11.6 5.4 6.24-10 ⁻⁴ 0.008855 GOTERM, BP, FAT GO:0000234-epsilve regulation of cell 11 12.8 3.6 8.85-10 ⁴ 0.008851 SP PR, KEYWORDS kexplation 24 2.79 2.0 8.38-10 ⁴ 0.01014 GOTERM, BP, FAT GO:000079-regulation of cyclin-dependent 5 5.8 17.2 1.91-10 ⁴ 0.01014 GOTERM, BP, FAT GO:000132-metrphase 6 7.3 1.6 2.4 0.001165 0.01138 SP PR, KEYWORDS keynamic and invince cell cycle 6 7.0 0.03 2.1 1.91-10 ⁴ 0.01021 GOTERM, BP, FAT GO:000132-metrphase <td< td=""><td>GOTERM_BP_FAT</td><td>GO:0043065~positive regulation of apoptosis</td><td>11</td><td>12.8</td><td>4.7</td><td>8.72×10⁻⁵</td><td>0.007693</td></td<>	GOTERM_BP_FAT	GO:0043065~positive regulation of apoptosis	11	12.8	4.7	8.72×10 ⁻⁵	0.007693
GOTERM_BP_FAT CO-0010629-regulation of gene signaling pathway 14.0 4.4 6.6 6.24+10 ⁴ 0.088052 SP_PIR_KEFWORDS ATP 7 8.1 6.6 6.24+10 ⁴ 0.088053 GOTERM_BP_FAT GO.0007167-enzyme linked receptor protein ignaling pathway 10 11.6 5.4 7.95+10 ⁴ 0.008811 SP_PIR_KEFWORDS scase 11 12.8 4.9 6.36+10 ⁴ 0.008811 SP_PIR_KEFWORDS scase 11 12.8 5.8 17.2 1.91+10 ⁴¹ 0.010071 GOTERM_BP_FAT GO.000073-regulation of cyclin-dependent SP_PIR_KEFWORDS 5.8 17.2 1.91+10 ⁴¹ 0.011048 SP_PIR_KEFWORDS dau-binding 19 2.21 2.3 0.001165 0.011345 SP_PIR_KEFWORDS dau-binding 19 2.21 2.3 2.0001164 0.011345 GOTERM_BP_FAT GO.0005125-micplation of RNA metabolic 22 25.6 2.2 3.46+10 ⁴ 0.011435 GOTERM_BP_FAT GO.000219-cell death 13 15.1 3.4	SP_PIR_KEYWORDS GOTERM BP_FAT	Proto-oncogene GO:0012501~programmed cell death	7	8.1	6.8 3.9	5.45×10 ⁻⁴ 8.27×10 ⁻⁵	0.007704
SP PIR KEYWORDS ATT 6.6 6.24-10 ⁴ 0.098083 GOTERM, BP_FAT GO.0007167-enzyme linked receptor protein signaling pathway 10 11.6 5.4 7.95-10 ³ 0.0980854 GOTERM, BP_FAT GO.000728-Expositive regulation of cell 11 12.8 4.9 6.36-10 ⁴⁵ 0.098931 SP_PIR_KEYWORDS GO-000709-regulation of cyclin-dependent 5 5.8 17.2 1.91+10 ⁴⁵ 0.009014 GOTERM, BP_FAT GO-000709-regulation of cyclin-dependent 5 5.8 17.2 1.91+10 ⁴⁵ 0.010014 GOTERM, BP_FAT GO-0001329-interphase of minoric cell cycle 6 7 10.5 2.17s+10 ⁴⁵ 0.011035 SP_PIR_KEYWORDS srine-threconin-10-protein kinase 8 9.3 4.7 0.001485 0.011435 GOTERM_BP_FAT GO-000615-s-opeoinsis 12 14.0 3.7 3.16+10 ⁴⁶ 0.015325 GOTERM_BP_FAT GO-0006215-s-cell death 13 15.1 3.3 4.01×10 ⁴⁶ 0.01525 GOTERM_BP_FAT GO-000525-cegulation of RNA metabolic<	GOTERM_BP_FAT	GO:0010629~negative regulation of gene	12	14.0	4.4	6.64×10 ⁻⁵	0.008052
GOTERM_BP_FAT GO.0007167-enzyme linkel receptor protein ing pathway 10 11.6 5.4 7.95×10° 0.008565 GOTERM_BP_FAT GO.0008284-positive regulation of cell protein tamas activity 11 12.8 4.9 6.36×10° 0.009834 SP_PIR_EEYWORDS scriptation 24 27.9 2.0 8.38×10° 0.001001 GOTERM_BP_FAT GO.000079-regulation of cyclin-dependent protein tamas activity 5 5.8 1.72 1.91×10° 0.011048 SP_PIR_EEYWORDS transcription regulation 20 2.3 2.2 0.001148 0.011807 GOTERM_BP_FAT GO.0051329-interphase 6 7.0 10.5 2.48×10° 0.011807 GOTERM_BP_FAT GO.0051329-interphase 6 7.0 10.5 2.48×10° 0.011807 GOTERM_BP_FAT GO.0013252-regulation of RNA metabolic 22 2.2 3.46×10° 0.015325 GOTERM_BP_FAT GO.0006913-sepotos 12 14.0 3.7 3.16×10° 0.016317 GOTERM_BP_FAT GO.0000270×cegulation of RNA metabolic 2	SP PIR KEYWORDS	ATP	7	8.1	6.6	6.24×10 ⁻⁴	0.008083
GOTERM_BP_FAT PIR_KEYWORDS GO-000823-energiation of cell in this as a circle regulation of cell power of the second	GOTERM_BP_FAT	GO:0007167~enzyme linked receptor protein signaling nathway	10	11.6	5.4	7.95×10 ⁻⁵	0.008565
SP PR KryvORDS kinase 11 12.8 3.6 8.9×10 ⁻¹ 0.009933 SP PR KFYWORDS 60.000079-regulation of cyclin-dependent from kinase activity 5 17.2 1.91×10 ⁴ 0.010014 GOTERM_BP_FAT GO.0001329-interphase of mitotic cell cycle 6 7.0 10.8 2.17×10 ⁴ 0.011045 SP PR KFYWORDS achinizing 19 22.1 2.3 0.001146 0.01185 SP PR KFYWORDS achinizing 20 23.3 2.2 0.001485 0.013547 GOTERM_BP_FAT GO.000051325-interphase 6 7.0 10.5 2.48×10 ⁴ 0.011857 GOTERM_BP_FAT GO.000021525-regulation of RNA metabolic 22 25.6 2.2 3.46×10 ⁴ 0.01637 GOTERM_BP_FAT GO.0001232-interphase 5 8 13.7 2.87×10 ⁴ 0.016317 GOTERM_BP_FAT GO.0001232-interphase 5 5.8 13.7 2.87×10 ⁴ 0.016317 GOTERM_BP_FAT GO.0000123-cs	GOTERM_BP_FAT	GO:0008284~positive regulation of cell proliferation	11	12.8	4.9	6.36×10 ⁻⁵	0.008811
SP_PIR_KFYWORDS acetylation 24 279 2.0 8.38-10 ⁴ 0.010014 GOTERM_BP_FAT GO:000079-regulation of cyclin-dependent protein kinase activity 5 5.8 17.2 1.91×10 ⁴ 0.010271 GOTERM_BP_FAT GO:0051329-interphase of nitotic cell cycle 6 7.0 10.8 2.17×10 ⁴ 0.011867 GOTERM_BP_FAT GO:0051329-interphase 6 7.0 10.5 2.48×10 ⁴ 0.011867 GOTERM_BP_FAT GO:00051329-interphase 6 7.0 10.5 2.48×10 ⁴ 0.011867 GOTERM_BP_FAT GO:0005123-cell death 13 15.1 3.4 15.10 ⁴ 0.014535 GOTERM_BP_FAT GO:000620-seqptopoisi 12 14.0 3.7 16.16 ¹⁰⁴ 0.015817 GOTERM_BP_FAT GO:000120-seql death 13 15.1 3.4 3.4 10.11637 BIOCARTA Regluoin 3 5.8 13.7 2.87×10 ⁴ 0.016217 SP_PIR_KEYWORDS activator 9 10.5 3.9 0.002225 <	SP_PIR_KEYWORDS	kinase	11	12.8	3.6	8.95×10 ⁻⁴	0.009933
GOTERM_BP_FAT GO:00001/9-regulation of cyclin-dependent 5 5.8 17.2 191:10 ⁴ 0.010271 GOTERM_BP_FAT GO:005132>-interphase of mitotic cell cycle 6 7.0 10.8 2.17:10 ⁴ 0.01135 SP PIR KEYWORDS transcription regulation 20 23.3 2.2 0.001145 0.01135 SP PIR KEYWORDS transcription 20 23.3 2.2 0.001485 0.01282 GOTERM_BP_FAT GO:0005132-supeption 20 23.3 2.2 0.001485 0.01347 GOTERM_BP_FAT GO:000512-supeption fRA metabolic 20 25.6 2.2 3.46×10 ⁴ 0.01547 GOTERM_BP_FAT GO:000512-supeption of RNA metabolic 22 25.6 2.2 3.46×10 ⁴ 0.015187 GOTERM_BP_FAT GO:000620-cell death 13 15.1 3.3 401*10 ⁴ 0.016137 BIOCARTA Kepulation of mithan action bitor 3 3.5 4.19 0.00225 0.01721 SP PIR KEYWORDS protein kinase inbibitor 3 3.5 4	SP_PIR_KEYWORDS	acetylation	24	27.9	2.0	8.38×10 ⁻⁴	0.010014
	GOTERM_BP_FAT	GO:0000079~regulation of cyclin-dependent protein kinase activity	5	5.8	17.2	1.91×10 ⁻⁴	0.010271
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	GOTERM_BP_FAT	GO:0051329~interphase of mitotic cell cycle	6	7.0	10.8	2.17×10 ⁻⁴	0.011048
$ \begin{array}{c} \text{COTTERM BP FAT} & \text{CO-0051325-interphase} & \text{fo} & \text{10.5} & \text{2.6} & \text{2.6} & \text{2.48+10^{+}} & \text{0.011995} \\ \text{SP PIR KEYWORDS} & \text{Transcription} & \text{20} & \text{23.3} & \text{2.2} & \text{0.001485} & \text{0.012827} \\ \text{GOTERM BP FAT} & \text{GO-0051325-interphase} & \text{8} & \text{9.3} & \text{4.7} & \text{0.001485} & \text{0.013827} \\ \text{GOTERM BP FAT} & \text{GO-0051525-regulation of RNA metabolic} \\ \text{process} & \text{22} & \text{25.6} & \text{2.2} & \text{3.46\times10^{+}} & \text{0.01525} \\ \text{GOTERM BP FAT} & \text{GO-0008215-call dism of RNA metabolic} \\ \text{process} & \text{22} & \text{25.6} & \text{13.3} & \text{4.01\times10^{-4}} & \text{0.015817} \\ \text{GOTERM BP FAT} & \text{GO-0006215-call dism of CPU cell dealh} & \text{13} & \text{15.1} & \text{3.4} & \text{3.76\times10^{-4}} & \text{0.016137} \\ \text{BIOCARTA} & \text{Regulation} & \text{gender of CPU cell second cell Cycle} \\ \text{SP PIR KEYWORDS} & \text{activator} & \text{9} & \text{10.5} & \text{3.9} & \text{0.00122} & \text{0.01721} \\ \text{GOTERM BP FAT} & \text{GO-001605-negative regulation of} & \text{3} & \text{3.5} & \text{41.9} & \text{0.002227} & \text{0.01721} \\ \text{GOTERM BP FAT} & \text{GO-001605-negative regulation of} & \text{3} & \text{3.5} & \text{41.9} & \text{0.002228} & \text{0.017221} \\ \text{GOTERM BP FAT} & \text{GO-0010605-negative regulation of} & \text{3} & \text{3.5} & \text{4.19} & \text{0.002228} & \text{0.017221} \\ \text{GOTERM BP FAT} & \text{GO-000505-negative regulation of} & \text{13} & \text{1.5.1} & \text{3.3} & \text{4.54\times10^{-4}} & \text{0.017519} \\ \text{nucleotid-10-binding} & \text{17} & \text{19.8} & \text{2.3} & \text{0.0022665} & \text{0.019626} \\ \text{GOTERM BP FAT} & \text{GO-00022402-cell cycle process} & \text{11} & \text{12.8} & \text{3.6} & \text{7.75\times10^{-4}} & \text{0.023031} \\ \text{SP PIR KEYWORDS} & \text{transfation regulation of} & \text{7} & \text{8.1} & \text{4.9} & \text{0.002324} & \text{0.021864} \\ \text{GOTERM BP FAT} & \text{GO-00022402-cell cycle process} & \text{11} & \text{12.8} & \text{3.6} & \text{7.75\times10^{-4}} & \text{0.023489} \\ \text{GOTERM BP FAT} & \text{GO-00022402-cell cycle process} & \text{11} & \text{12.8} & \text{3.6} & \text{7.75\times10^{-4}} & \text{0.023497} \\ \text{GOTERM BP FAT} & \text{GO-00022402-cell cycle process} & \text{11} & \text{12.8} & \text{4.0} & \text{3.06117^{-4}} & \text{0.023497} \\ \text{GOTERM BP FAT} & \text{GO-0000732-response to normone stimulus} & \text{9} & \text{10.5} & \text{4.5}$	SP_PIR_KEYWORDS	dna-binding transcription regulation	20	22.1	2.3	0.001165	0.011305
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	GOTERM BP FAT	GO:0051325~interphase	6	7.0	10.5	2.48×10^{-4}	0.011995
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	SP_PIR_KEYWORDS	Transcription	20	23.3	2.2	0.001489	0.012827
	SP_PIR_KEYWORDS	serine/threonin×10-protein kinase	8	9.3	4.7	0.001485	0.013547
	GOTERM_BP_FAT	GO:0006915~apoptosis GO:0051252- regulation of RNA metabolic	12	14.0	3.7	3.16×10 ⁻⁴	0.014535
	GOTERM_BP_FAT	process	22	23.0	2.2	3.46×10 ⁻⁴	0.015225
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	GOTERM_BP_FAT	GO:0008219~cell death	13	15.1	3.4	3.76×10 ⁻⁴	0.015817
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	GOTERM_BP_FAT	GO:0016265~death	13	15.1	3.3	4.01×10 ⁻⁴	0.016137
$\begin{array}{llllllllllllllllllllllllllllllllllll$	BIOCARTA	h_cellcyclePathway:Cyclins and Cell Cycle Regulation	5	5.8	13.7	2.87×10 ⁻⁴	0.016217
SP PIR KEY WORDS protein kinase minitor 3 3.5 41.9 0.002225 0.017221 GOTERM_BP_FAT GC:0010605-negative regulation of macromolecule metabolic process 13 15.1 3.3 4.54×10 ⁴ 0.017519 SP PIR KEYWORDS mucleotid×10-binding 17 19.8 2.3 0.002665 0.019626 GOTERM_BP_FAT GC:0050678-regulation of epithelial cell 5 5.8 13.1 5.48×10 ⁴ 0.02036 SP PIR KEYWORDS translation regulation 4 4.7 13.4 0.003254 0.021864 GOTERM BP_FAT GO:0002740-cell cycle process 11 12.8 3.6 7.75×10 ⁴ 0.022497 GOTERM BP_FAT GO:000728-response to hormone stimulus 9 10.5 4.5 7.16×10 ⁴ 0.022497 GOTERM BP_FAT GO:000719-cell cycle 13 15.1 3.1 7.44×10 ⁴ 0.02249 GOTERM_BP_FAT GO:000719-response to hormone stimulus 9 10.5 4.5 7.16×10 ⁴ 0.02249 GOTERM_BP_FAT GO:000719-response to normone stimulus 9 10.5 4.1 0.001380 0.040185	SP_PIR_KEYWORDS	activator	9	10.5	3.9	0.002102	0.017129
GOTERM_BP_FAT GO:0007000-regainer teguation of a macromolecule metabolic process 13 13.1 <th13.1< th=""> 13.1 <th13.1< th=""> <t< td=""><td>SP_PIR_KEY WORDS</td><td>GO:0010605- negative regulation of</td><td>3</td><td>3.5 15.1</td><td>41.9</td><td>0.002225</td><td>0.01/221</td></t<></th13.1<></th13.1<>	SP_PIR_KEY WORDS	GO:0010605- negative regulation of	3	3.5 15.1	41.9	0.002225	0.01/221
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	GOTERM_BP_FAT	macromolecule metabolic process	13	13.1	5.5	4.54×10 ⁻⁴	0.017519
GOTERM_BP_FAT CO.000078*regulation of epinenation 5 3.8 13.1 5.48×10 ⁴ 0.02031 SP_PIR_KEYWORDS isopeptide bond 7 8.1 4.9 0.002897 0.02036 SP_PIR_KEYWORDS translation regulation 4 4.7 13.4 0.003254 0.021864 GOTERM BP_FAT GO:00022402-cell cycle process 11 12.8 3.6 7.75×10 ⁴ 0.022497 GOTERM BP_FAT GO:0000725-response to hormone stimulus 9 10.5 4.5 7.16×10 ⁴ 0.025497 GOTERM_BP_FAT GO:0007049-cell cycle 13 15.1 3.1 7.44×10 ⁴ 0.025497 GOTERM_BP_FAT GO:0007169-transmembrane receptor protein trose in transe signaling pathway 7 8.1 5.8 0.001212 0.037377 SP_PIR_KEYWORDS ma-mediated gene silencing 3 3.5 24.9 0.006305 0.048699 GOTERM_BP_FAT GO:000719-response to endogenous stimulus 9 10.5 4.1 0.001389 0.040185 SP_PIR_KEYWORDS cell division <	SP_PIR_KEYWORDS	nucleotid×10-binding	17	19.8	2.3	0.002665	0.019626
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	GOTERM_BP_FAT	proliferation	5	5.8	15.1	5.48×10 ⁻⁴	0.02031
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	SP_PIR_KEYWORDS	isopeptide bond	7	8.1	4.9	0.002897	0.02036
GOTERM_BP_FATGO:0022402-cell cycle process1112.83.6 7.75×10^{-4} 0.02486GOTERM_BP_FATGO:0000278-mitotic cell cycle910.54.5 7.55×10^{-4} 0.025039GOTERM_BP_FATGO:0007049-cell cycle1315.13.1 7.44×10^{-4} 0.025497GOTERM_BP_FATGO:0007169-cell cycle1315.13.1 7.44×10^{-4} 0.025269GOTERM_BP_FATGO:0007169-crass esignaling pathway78.15.80.0012120.037377SP_PIR_KEYWORDSma-mediated gene silencing33.524.90.0063050.038699GOTERM_BP_FATGO:0045449-regulation of transcription2630.21.90.0013890.040185SP_PIR_KEYWORDScell division67.05.10.0063050.040278GOTERM_BP_FATGO:009719-response to endogenous stimulus910.54.10.0013510.0403GOTERM_BP_FATGO:0015202-induction of programmed cell death89.34.60.001560.041362GOTERM_BP_FATGO:0010604-rositive regulation of macromolecule metabolic process1112.84.03.66 \times 10^40.042384GOTERM_BP_FATGO:00060575-regulation of transcription death155.89.40.0015520.042316GOTERM_BP_FATGO:0010604-rositive regulation of macromolecule metabolic process1315.12.80.0017540.045383GOTERM_BP_FATGO:0010604-rositive regulation of macromolecule metabol	SP_PIR_KEYWORDS	translation regulation	4	4.7	13.4	0.003254	0.021864
GOTERM_BP_FATGO:0002725-response to hormone stimulus910.54.37.33×100.0023039GOTERM_BP_FATGO:000725-response to hormone stimulus910.54.57.16×10 ⁴ 0.025569GOTERM_CC_FATGO:0007169transmembrane receptor protein tyrosine kinase signaling pathway78.15.80.0012120.037377SP_PIR_KEYWORDSma-mediated gene silencing33.524.90.0063050.038699GOTERM_BP_FATGO:0007169transmembrane receptor protein tyrosine kinase signaling pathway78.15.80.0012120.037377SP_PIR_KEYWORDSma-mediated gene silencing33.524.90.0063050.038699GOTERM_BP_FATGO:0009719-response to endogenous stimulus910.54.10.0013510.0403GOTERM_BP_FATGO:0009719-response to endogenous stimulus910.54.10.0013510.0403GOTERM_BP_FATGO:0012502-induction of programmed cell death89.34.60.001560.041362GOTERM_MF_FATGO:0019899-enzyme binding1112.84.03.66×10 ⁻⁴ 0.041436GOTERM_BP_FATGO:0010604-positive regulation of macromolecule metabolic process1315.12.80.0015520.042316GOTERM_BP_FATGO:0006017-induction of apoptosis89.34.60.0015520.042316GOTERM_BP_FATGO:0010604-positive regulation of macromolecule metabolic process1315.12.80.0018760.045184<	GOTERM_BP_FAT	GO:0022402~cell cycle process	11	12.8	3.6	7.75×10^{-4}	0.02486
GOTERM_BP_FAT GO:0007049-cell cycle 13 10.5 1.5 1.13 7.44×10 ⁴ 0.022556 GOTERM_BP_FAT GO:0007049-cell cycle 13 15.1 3.1 7.44×10 ⁴ 0.032249 GOTERM_BP_FAT GO:0007169-cransmembrane receptor protein tyrosine kinase signaling pathway 7 8.1 5.8 0.001212 0.037377 SP_PIR_KEYWORDS ma-mediated gene silencing 3 3.5 24.9 0.006305 0.038699 GOTERM_BP_FAT GO:0003194/-regulation of transcription 26 30.2 1.9 0.001389 0.040185 SP_PIR_KEYWORDS cell division 6 7.0 5.1 0.006305 0.038699 GOTERM_BP_FAT GO:00031974regulation of transcription 26 30.2 1.9 0.001351 0.403 GOTERM_BP_FAT GO:0012502-induction of programmed cell death 9 10.5 4.1 0.001351 0.403 GOTERM_BP_FAT GO:0022403-cell cycle phase 9 10.5 4.0 0.366×10 ⁴ 0.41436 GOTERM_BP_FAT GO:00060917induct	GOTERM BP FAT	GO:0000278~Initotic cell cycle	9	10.5	4.5	7.55×10	0.025039
GOTERM_CC_FAT GO:0031981-nuclear lunen 17 19.8 2.6 4.31×10 ⁴ 0.032249 GOTERM_BP_FAT GO:0007169-transmembrane receptor protein tyrosine kinase signaling pathway 7 8.1 5.8 0.001212 0.037377 SP_PIR_KEYWORDS ma-mediated gene silencing 3 3.5 24.9 0.006305 0.038699 GOTERM_BP_FAT GO:0045449-regulation of transcription 26 30.2 1.9 0.001389 0.040185 SP_PIR_KEYWORDS cell division 6 7.0 5.1 0.006305 0.040278 GOTERM_BP_FAT GO:0009719-response to endogenous stimulus 9 10.5 4.1 0.001351 0.0403 GOTERM_BP_FAT GO:0012502induction of programmed cell death 8 9.3 4.6 0.00156 0.041362 GOTERM_MF_FAT GO:0022403-cell cycle phase 9 10.5 4.0 3.66×10 ⁴ 0.041436 GOTERM_BP_FAT GO:0022403-cell cycle phase 9 10.5 4.0 0.001552 0.042316 GOTERM_BP_FAT GO:0019899-enzyme binding 11 12.8 4.6 0.001552 0.042316 <t< td=""><td>GOTERM BP FAT</td><td>GO:0007749~cell cvcle</td><td>13</td><td>15.1</td><td>3.1</td><td>7.44×10^{-4}</td><td>0.025569</td></t<>	GOTERM BP FAT	GO:0007749~cell cvcle	13	15.1	3.1	7.44×10^{-4}	0.025569
GOTERM_BP_FAT GO:0007169transmembrane receptor protein tyrosine kinase signaling pathway 7 8.1 5.8 0.001212 0.037377 SP_PIR_KEYWORDS ma-mediated gene silencing 3 3.5 24.9 0.006305 0.038699 GOTERM_BP_FAT GO:0045449-regulation of transcription 26 30.2 1.9 0.001389 0.040185 SP_PIR_KEYWORDS cell division 6 7.0 5.1 0.006305 0.040278 GOTERM_BP_FAT GO:0009719~response to endogenous stimulus 9 10.5 4.1 0.001351 0.0403 GOTERM_BP_FAT GO:0012502~induction of programmed cell death 9 2.1 2.3 8.24×10 ⁴ 0.040899 GOTERM_BP_FAT GO:0012502~induction of programmed cell death 8 9.3 4.6 0.00156 0.041362 GOTERM_BP_FAT GO:0022403~cell cycle phase 9 10.5 4.0 0.66×10 ⁴ 0.042316 GOTERM_BP_FAT GO:0010604~positive regulation of macromolecule metabolic process 13 15.1 2.8 0.001754 0.042384 GOTER	GOTERM_CC_FAT	GO:0031981~nuclear lumen	17	19.8	2.6	4.31×10 ⁻⁴	0.032249
SP_PIR_KEYWORDS ma-mediated gene silencing 3 3.5 24.9 0.006305 0.038699 GOTERM_BP_FAT GO:0045449~regulation of transcription 26 30.2 1.9 0.001389 0.040185 SP_PIR_KEYWORDS cell division 6 7.0 5.1 0.006305 0.040278 GOTERM_BP_FAT GO:009719~response to endogenous stimulus 9 10.5 4.1 0.001351 0.0403 GOTERM_CC_FAT GO:001974~membran×10-enclosed lumen 19 22.1 2.3 8.24×10 ⁻⁴ 0.040899 GOTERM_BP_FAT GO:0012502~induction of programmed cell death 8 9.3 4.6 0.00156 0.041362 GOTERM_BP_FAT GO:0022403~cell cycle phase 9 10.5 4.0 0.066810 ⁻⁴ 0.041436 GOTERM_BP_FAT GO:0010604~positive regulation of macromolecule metabolic process 13 15.1 2.8 0.001754 0.042984 GOTERM_BP_FAT GO:00030324~lung development 5 5.8 9.4 0.001858 0.045383 GOTERM_BP_FAT GO:00051726~regulation of tr	GOTERM_BP_FAT	GO:0007169~transmembrane receptor	7	8.1	5.8	0.001212	0.037377
GOTERM_BP_FAT GO:0045449-regulation of transcription 26 30.2 1.9 0.001389 0.040185 SP_PIR_KEYWORDS cell division 6 7.0 5.1 0.006305 0.040278 GOTERM_BP_FAT GO:0009719~response to endogenous stimulus 9 10.5 4.1 0.001351 0.0403 GOTERM_CC_FAT GO:0012502~induction of programmed cell death 9 10.5 4.1 0.00156 0.04185 GOTERM_BP_FAT GO:0012502~induction of programmed cell death 8 9.3 4.6 0.00156 0.041362 GOTERM_BP_FAT GO:0012802~induction of programmed cell death 8 9.3 4.6 0.00156 0.041362 GOTERM_BP_FAT GO:0012802~induction of apoptosis 8 9.3 4.6 0.001552 0.042316 GOTERM_BP_FAT GO:0006917~induction of apoptosis 8 9.3 4.6 0.001552 0.042984 GOTERM_BP_FAT GO:001604~positive regulation of macromolecule metabolic process 13 15.1 2.8 0.001754 0.045158 GOTERM_BP_FAT GO:00030324~lung development 5 5.8 9.4 0.001858	SP PIR KEYWORDS	rna-mediated gene silencing	3	35	24.9	0.006305	0.038699
SP_PIR_KEYWORDS cell division 6 7.0 5.1 0.006305 0.040278 GOTERM_BP_FAT GO:0009719~response to endogenous stimulus 9 10.5 4.1 0.001351 0.0403 GOTERM_CC_FAT GO:0012502~induction of programmed cell death 9 22.1 2.3 8.24×10 ⁻⁴ 0.040899 GOTERM_BP_FAT GO:0012502~induction of programmed cell death 8 9.3 4.6 0.00156 0.041362 GOTERM_BP_FAT GO:0022403~cell cycle phase 9 10.5 4.0 3.66×10 ⁻⁴ 0.041436 GOTERM_BP_FAT GO:0019899~enzyme binding 11 12.8 4.0 3.66×10 ⁻⁴ 0.041436 GOTERM_BP_FAT GO:0012604~cell cycle phase 9 10.5 4.0 0.001552 0.042316 GOTERM_BP_FAT GO:0010604~positive regulation of macromolecule metabolic process 13 15.1 2.8 0.001754 0.045158 GOTERM_BP_FAT GO:0030324~lung development 5 5.8 9.4 0.001897 0.045184 GOTERM_BP_FAT GO:0006355~regulation of cell cycle 8 9.3 4.5 0.001858 0.045383 <td>GOTERM BP FAT</td> <td>GO:0045449~regulation of transcription</td> <td>26</td> <td>30.2</td> <td>1.9</td> <td>0.001389</td> <td>0.040185</td>	GOTERM BP FAT	GO:0045449~regulation of transcription	26	30.2	1.9	0.001389	0.040185
GOTERM_BP_FAT GO:0009719~response to endogenous stimulus 9 10.5 4.1 0.001351 0.0403 GOTERM_CC_FAT GO:0031974~membran×10-enclosed lumen 19 22.1 2.3 8.24×10 ⁴ 0.040899 GOTERM_BP_FAT GO:0012502~induction of programmed cell death 8 9.3 4.6 0.00156 0.041362 GOTERM_BP_FAT GO:0012899~enzyme binding 11 12.8 4.0 3.66×10 ⁴ 0.041362 GOTERM_BP_FAT GO:0022403~cell cycle phase 9 10.5 4.0 0.001552 0.042316 GOTERM_BP_FAT GO:0006917~induction of apoptosis 8 9.3 4.6 0.001532 0.042984 GOTERM_BP_FAT GO:0010604~positive regulation of macromolecule metabolic process 13 15.1 2.8 0.001754 0.045158 GOTERM_BP_FAT GO:0030324~lung development 5 5.8 9.4 0.001897 0.045184 GOTERM_BP_FAT GO:0006355~regulation of cell cycle 8 9.3 4.5 0.001858 0.045383 GOTERM_BP_FAT GO:0006355~regulation of transcription, DNA-dependent 20 23.3 2.1 0.001853	SP_PIR_KEYWORDS	cell division	6	7.0	5.1	0.006305	0.040278
GOTERM_CC_FATGO:0031974~membran×10-enclosed lumen1922.12.3 8.24×10^4 0.040899GOTERM_BP_FATGO:0012502~induction of programmed cell death89.34.60.001560.041362GOTERM_MF_FATGO:0019899~enzyme binding1112.84.0 3.66×10^4 0.041436GOTERM_BP_FATGO:00022403~cell cycle phase910.54.00.0015520.042316GOTERM_BP_FATGO:0006917~induction of apoptosis89.34.60.0015320.042984GOTERM_BP_FATGO:0010604~positive regulation of macromolecule metabolic process1315.12.80.0017540.045158GOTERM_BP_FATGO:0030324~lung development55.89.40.0018970.045184GOTERM_BP_FATGO:00051726~regulation of cell cycle89.34.50.0018580.045383GOTERM_BP_FATGO:000535~regulation of cell cycle89.34.50.0018580.045383GOTERM_BP_FATGO:000324~lung development55.89.40.0018580.045383GOTERM_BP_FATGO:0006355~regulation of transcription, DNA-dependent2023.32.10.0018530.046432SP_PIR_KEYWORDSchromosomal rearrangement67.04.80.0079130.04655GOTERM_BP_FATGO:0030323~respiratory tube development55.89.10.0021160.049078	GOTERM_BP_FAT	GO:0009719~response to endogenous stimulus	9	10.5	4.1	0.001351	0.0403
GOTERM_BP_FAT GO:0012502~induction of programmed cell death 8 9.3 4.6 0.00156 0.041362 GOTERM_MF_FAT GO:0019899~enzyme binding 11 12.8 4.0 3.66×10 ⁴ 0.041362 GOTERM_BP_FAT GO:0022403~cell cycle phase 9 10.5 4.0 0.001552 0.042316 GOTERM_BP_FAT GO:0006917~induction of apoptosis 8 9.3 4.6 0.001532 0.042984 GOTERM_BP_FAT GO:001604~positive regulation of macromolecule metabolic process 13 15.1 2.8 0.001754 0.045158 GOTERM_BP_FAT GO:0030324~lung development 5 5.8 9.4 0.001897 0.045184 GOTERM_BP_FAT GO:0006355~regulation of cell cycle 8 9.3 4.5 0.001858 0.045383 GOTERM_BP_FAT GO:0006355~regulation of transcription, DNA-dependent 20 23.3 2.1 0.001853 0.046432 SP_PIR_KEYWORDS chromosomal rearrangement 6 7.0 4.8 0.007913 0.04655 GOTERM_BP_FAT GO:0030323~respiratory tube development 5 5.8 9.1 0.002116 0.0490	GOTERM_CC_FAT	GO:0031974~membran×10-enclosed lumen	19	22.1	2.3	8.24×10 ⁻⁴	0.040899
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	GOTERM_BP_FAT	GO:0012502~induction of programmed cell death	8	9.3	4.6	0.00156	0.041362
GOTERM_BP_FAT GO:0022403~cell cycle phase 9 10.5 4.0 0.001552 0.042316 GOTERM_BP_FAT GO:0006917~induction of apoptosis 8 9.3 4.6 0.001532 0.042984 GOTERM_BP_FAT GO:0010604~positive regulation of macromolecule metabolic process 13 15.1 2.8 0.001754 0.045158 GOTERM_BP_FAT GO:0030324~lung development 5 5.8 9.4 0.001897 0.045184 GOTERM_BP_FAT GO:00051726~regulation of cell cycle 8 9.3 4.5 0.001858 0.045383 GOTERM_BP_FAT GO:0006355~regulation of transcription, DNA-dependent 20 23.3 2.1 0.001853 0.046432 SP_PIR_KEYWORDS chromosomal rearrangement 6 7.0 4.8 0.007913 0.04655 GOTERM_BP_FAT GO:0030323~respiratory tube development 5 5.8 9.1 0.002116 0.049078	GOTERM_MF_FAT	GO:0019899~enzyme binding	11	12.8	4.0	3.66×10 ⁻⁴	0.041436
GOTERM_BP_FAT GO:0006917~induction of apoptosis 8 9.3 4.6 0.001532 0.042984 GOTERM_BP_FAT GO:0010604~positive regulation of macromolecule metabolic process 13 15.1 2.8 0.001754 0.045158 GOTERM_BP_FAT GO:0030324~lung development 5 5.8 9.4 0.001897 0.045184 GOTERM_BP_FAT GO:001657~regulation of cell cycle 8 9.3 4.5 0.001858 0.045383 GOTERM_BP_FAT GO:0006355~regulation of transcription, DNA-dependent 20 23.3 2.1 0.001853 0.046432 SP_PIR_KEYWORDS chromosomal rearrangement 6 7.0 4.8 0.007913 0.04655 GOTERM_BP_FAT GO:0030323~respiratory tube development 5 5.8 9.1 0.002116 0.049078	GOTERM_BP_FAT	GO:0022403~cell cycle phase	9	10.5	4.0	0.001552	0.042316
GOTERM_BP_FAT GO:0010004~positive regulation of macromolecule metabolic process 13 15.1 2.8 0.001754 0.045158 GOTERM_BP_FAT GO:0030324~lung development 5 5.8 9.4 0.001897 0.045184 GOTERM_BP_FAT GO:0006355~regulation of cell cycle 8 9.3 4.5 0.001858 0.045383 GOTERM_BP_FAT GO:0006355~regulation of transcription, DNA-dependent 20 23.3 2.1 0.001853 0.046432 SP_PIR_KEYWORDS chromosomal rearrangement 6 7.0 4.8 0.007913 0.04655 GOTERM_BP_FAT GO:0030323~respiratory tube development 5 5.8 9.1 0.002116 0.049078	GOTERM_BP_FAT	GO:0006917~induction of apoptosis	8	9.3	4.6	0.001532	0.042984
GOTERM_BP_FAT GO:0030324~lung development 5 5.8 9.4 0.001897 0.045184 GOTERM_BP_FAT GO:0051726~regulation of cell cycle 8 9.3 4.5 0.001858 0.045383 GOTERM_BP_FAT GO:0006355~regulation of transcription, DNA-dependent 20 23.3 2.1 0.001853 0.046432 SP_PIR_KEYWORDS chromosomal rearrangement 6 7.0 4.8 0.007913 0.04655 GOTERM_BP_FAT GO:0030323~respiratory tube development 5 5.8 9.1 0.002116 0.049078	GOTERM_BP_FAT	macromolecule metabolic process	13	15.1	2.8	0.001754	0.045158
GOTERM_BP_FAT GO:00051/26~regulation of cell cycle 8 9.5 4.5 0.001858 0.045383 GOTERM_BP_FAT GO:0006355~regulation of transcription, DNA-dependent 20 23.3 2.1 0.001853 0.046432 SP_PIR_KEYWORDS chromosomal rearrangement 6 7.0 4.8 0.007913 0.04655 GOTERM_BP_FAT GO:0030323~respiratory tube development 5 5.8 9.1 0.002116 0.049078	GOTERM_BP_FAT	GO:0030324~lung development	5	5.8	9.4	0.001897	0.045184
SP_PIR_KEYWORDSchromosomal rearrangement67.04.80.0079130.04655GOTERM_BP_FATGO:0030323~respiratory tube development55.89.10.0021160.049078	GOTERM BP_FAT	GO:00051/26~regulation of cell cycle GO:0006355~regulation of transcription,	8	23.3	4.5 2.1	0.001858	0.045383
SF_FIK_KE1 WOKDS chromosomal rearrangement 6 /.0 4.8 0.00/913 0.04655 GOTERM_BP_FAT GO:0030323~respiratory tube development 5 5.8 9.1 0.002116 0.049078		DNA-dependent	6	7.0	4.9	0.007012	0.04655
	GOTERM_BP_FAT_	GO:0030323~respiratory tube development	5	5.8	9.1	0.002116	0.049078

Supplementary Table 3	F Top five clusters of categories (terms) overrepresented in the list of genes with the
highest in-degree in the	F-network.

Annotation Cluster 1	Enrennent Score. 4.70			E 11		
Category	Term	Count	%	Fold	P-Value	Beniamini
Sangory	10.00	eouni	,,	Enrichment	1 vuide	Denjanini
GOTERM CC FAT	GO:0031981~nuclear lumen	29	21.3	2.7	7.77×10 ⁻⁷	1.83×10 ⁻⁴
GOTERM CC FAT	GO:0031974~membrane-enclosed lumen	32	23.5	2.3	3.76×10 ⁻⁶	2.95×10 ⁻⁴
GOTERM CC FAT	GO:0043233~organelle lumen	31	22.8	23	7.57×10 ⁻⁶	4.47×10^{-4}
GOTERM CC FAT	CO:0070013- intracellular organelle lumen	30	22.0	2.5	1.43×10^{-5}	6.73×10^{-4}
COTERM_CC_FAT		30	14.0	2.5	1.43^10 5.5(10 ⁻⁵	0.73~10
GOTERM_CC_FAT	GO:0005654~nucleoplasm	19	14.0	2.9	5.56×10 ⁻⁵	0.002185
GOTERM_CC_FAT	GO:0005730~nucleolus	14	10.3	2.7	0.001567	0.051489
Annotation Cluster 2	Enrichment Score: 4.55					
6.4	T	C 1	0/	Fold	DX7.1	р · · ·
Category	lerm	Count	%	Enrichment	P v alue	Benjamini
GOTERM BP FAT	GO:0042981~regulation of apontosis	24	17.6	35	1 93×10 ⁻⁷	1.32×10^{-4}
GollEidan_DI_IIII	GO:00/12/01 regulation of programmed cell	21	17.0	5.5	1.95 10	1.52 10
GOTERM_BP_FAT	dooth	24	17.6	3.5	2.31×10 ⁻⁷	1.05×10 ⁻⁴
		24	17.0	2.5	2 4 C 10 ⁻⁷	0.40 10-5
GOTERM_BP_FAT	GO:0010941~regulation of cell death	24	17.6	3.5	2.46×10	8.42×10
GOTERM_BP_FAT	GO:0043065~positive regulation of apoptosis	15	11.0	4.1	1.50×10^{-5}	0.002274
COTEDM DD EAT	GO:0043068~positive regulation of	15	11.0	4.1	1.62×10^{-5}	0.002011
GOTERM_BF_FAT	programmed cell death	15	11.0	4.1	1.02^10	0.002011
GOTERM BP FAT	GO:0010942~positive regulation of cell death	15	11.0	4.1	1.70×10^{-5}	0.001792
GOTERM BP FAT	GO:0043066~negative regulation of anontosis	13	9.6	43	4.30×10^{-5}	0.003671
GollEidan_Di_IIII	CO:0013060- negative regulation of	15	2.0	1.5	1.50 10	0.005071
GOTERM_BP_FAT	negative regulation of	13	9.6	4.3	4.93×10 ⁻⁵	0.003957
		10	0.6	4.0	5.06 10-5	0.000000
GOTERM_BP_FAT	GO:0060548~negative regulation of cell death	13	9.6	4.2	5.06×10 ⁻⁵	0.003839
SP_PIR_KEYWORDS	Apoptosis	12	8.8	4.5	7.96×10 ⁻⁵	0.00117
GOTERM_BP_FAT	GO:0006917~induction of apoptosis	12	8.8	4.4	8.04×10 ⁻⁵	0.005486
	GO:0012502~induction of programmed cell	10	0.0		0.07 10-5	0.005120
GOTERM_BP_FAT	death	12	8.8	4.4	8.2/×10 ⁻	0.005129
GOTERM BP FAT	GO:0008219~cell death	18	13.2	29	1.05×10^{-4}	0.00594
COTERM PD FAT	CO:0016265_dooth	19	12.2	2.9	1.03×10^{-4}	0.005744
GOTERM_BF_FAT		16	13.2	2.9	1.14^10	0.003/44
GOTERM_BP_FAT	GO:0012501~programmed cell death	16	11.8	3.1	1.84×10	0.008655
GOTERM_BP_FAT	GO:0006915~apoptosis	15	11.0	2.9	5.28×10 ⁻⁴	0.019335
GOTERM_BP_FAT	GO:0006916~anti-apoptosis	8	5.9	4.6	0.001785	0.041964
Annotation Cluster 3	Enrichment Score: 4.17					
Annotation Cluster 3	Enrichment Score: 4.17	Count	0/	Fold	DValue	Doniomini
Annotation Cluster 3 Category	Enrichment Score: 4.17 Term	Count	%	Fold Enrichment	PValue	Benjamini
Annotation Cluster 3 Category	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of	Count	%	Fold Enrichment	PValue	Benjamini
Annotation Cluster 3 Category GOTERM_BP_FAT	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression	Count 14	% 10.3	Fold Enrichment 7.8	PValue 2.42×10 ⁻⁸	Benjamini 3.32×10 ⁻⁵
Annotation Cluster 3 Category GOTERM_BP_FAT	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:002268_regulation of callular protain	Count 14	% 10.3	Fold Enrichment 7.8	PValue 2.42×10 ⁻⁸	Benjamini 3.32×10 ⁻⁵
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein mathedia process	Count 14 13	% 10.3 9.6	Fold Enrichment 7.8 3.2	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴	Benjamini 3.32×10 ⁻⁵ 0.021802
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:006447	Count 14 13 7	% 10.3 9.6	Fold Enrichment 7.8 3.2	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴	Benjamini 3.32×10 ⁻⁵ 0.021802
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation	Count 14 13 7	% 10.3 9.6 5.1	Fold Enrichment 7.8 3.2 6.0	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation	Count 14 13 7 5	% 10.3 9.6 5.1 3.7	Fold Enrichment 7.8 3.2 6.0 10.6	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation	Count 14 13 7 5	% 10.3 9.6 5.1 3.7	Fold Enrichment 7.8 3.2 6.0 10.6	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06	Count 14 13 7 5	% 10.3 9.6 5.1 3.7	Fold Enrichment 7.8 3.2 6.0 10.6	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term	Count 14 13 7 5	% 10.3 9.6 5.1 3.7	Fold Enrichment 7.8 3.2 6.0 10.6 Fold	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term	Count 14 13 7 5 Count	% 10.3 9.6 5.1 3.7 %	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding	Count 14 13 7 5 Count 21	% 10.3 9.6 5.1 3.7 % 15.4	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue 1.23×10 ⁻⁹	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding	Count 14 13 7 5 Count 21 22	% 10.3 9.6 5.1 3.7 % 15.4 16.2	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue 1.23×10 ⁻⁹ 1.13×10 ⁻⁶	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term ma-binding GO:0003723~RNA binding IPB012677~Nucleotide-binding_alpha-beta	Count 14 13 7 5 Count 21 22	% 10.3 9.6 5.1 3.7 % 15.4 16.2	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue 1.23×10 ⁻⁹ 1.13×10 ⁻⁶	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait	Count 14 13 7 5 Count 21 22 11	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue 1.23×10 ⁻⁹ 1.13×10 ⁻⁶ 6.63×10 ⁻⁶	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term ma-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR0006044PNA secondifier of CDND 1	Count 14 13 7 5 Count 21 22 11 10	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue 1.23×10 ⁻⁹ 1.13×10 ⁻⁶ 6.63×10 ⁻⁶ 4.15×10 ⁻⁵	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.02522
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term ma-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1	Count 14 13 7 5 Count 21 22 11 10 10	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue 1.23×10 ⁻⁹ 1.13×10 ⁻⁶ 6.63×10 ⁻⁶ 4.15×10 ⁻⁵ 2.25×10 ⁻⁴	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.005973 0.02573
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM	Count 14 13 7 5 Count 21 22 11 10 10	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5	$\begin{array}{c} \textbf{PValue} \\ \hline 2.42 \times 10^{-8} \\ \hline 6.44 \times 10^{-4} \\ 0.001054 \\ 0.001263 \\ \hline \textbf{PValue} \\ \hline 1.23 \times 10^{-9} \\ \hline 1.13 \times 10^{-6} \\ \hline 6.63 \times 10^{-6} \\ \hline 4.15 \times 10^{-5} \\ \hline 3.21 \times 10^{-4} \\ \hline \end{array}$	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.005973 0.026592
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:000417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM	Count 14 13 7 5 Count 21 22 11 10 10 6	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 7.4 4.4	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-6} 4.15×10^{-5} 3.21×10^{-4} 0.001566	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.005973 0.026592 0.13857
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM domain:RRM 2	Count 14 13 7 5 Count 21 22 11 10 6 5	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-6} 4.15×10^{-5} 3.21×10^{-4} 0.001566 0.00573	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.02592 0.13857 0.279738
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM domain:RRM 1	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 7.0	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-6} 4.15×10^{-5} 3.21×10^{-4} 0.001566 0.00573 0.00573	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.026592 0.13857 0.279738 0.279738
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 1 domain:RRM 1 domain:RRM 3	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7 2.2	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue 1.23×10 ⁻⁹ 1.13×10 ⁻⁶ 6.63×10 ⁻⁶ 4.15×10 ⁻⁵ 3.21×10 ⁻⁴ 0.001566 0.00573 0.00573 0.04867	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.0026592 0.13857 0.279738 0.794592
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term ma-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 3	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 7.4 3.7 3.7	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 7.0 8.4	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue 1.23×10 ⁻⁹ 1.13×10 ⁻⁶ 6.63×10 ⁻⁶ 4.15×10 ⁻⁵ 3.21×10 ⁻⁴ 0.001573 0.00573 0.04867	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.005973 0.026592 0.13857 0.279738 0.794592
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 3	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7 2.2	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4	$\begin{array}{c} \textbf{PValue} \\ \hline 2.42 \times 10^{-8} \\ \hline 6.44 \times 10^{-4} \\ \hline 0.001054 \\ \hline 0.001263 \\ \hline \textbf{PValue} \\ \hline 1.23 \times 10^{-9} \\ \hline 1.13 \times 10^{-6} \\ \hline 6.63 \times 10^{-6} \\ \hline 4.15 \times 10^{-5} \\ \hline 3.21 \times 10^{-4} \\ \hline 0.001566 \\ \hline 0.00573 \\ \hline 0.00573 \\ \hline 0.04867 \\ \hline \end{array}$	Benjamini 3.32×10^{-5} 0.021802 0.029596 0.011767 Benjamini 1.27×10^{-7} 3.42×10^{-4} 0.001914 0.026592 0.13857 0.279738 0.794592
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 3	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7 2.2	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-6} 4.15×10^{-5} 3.21×10^{-4} 0.00573 0.00573 0.04867	Benjamini 3.32×10^{-5} 0.021802 0.029596 0.011767 Benjamini 1.27×10^{-7} 3.42×10^{-4} 0.001914 0.026592 0.13857 0.279738 0.794592
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61 Term	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 Count Count	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7 2.2 %	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4 Fold Enrichment	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-5} 3.21×10^{-4} 0.00573 0.00573 0.00573 0.04867	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.005973 0.026592 0.13857 0.279738 0.279738 0.794592 Benjamini
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61 Term GO:0007167~enzyme linked receptor protein	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 Count L4	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 7.4 3.7 2.2 % 10.3	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-5} 3.21×10^{-3} 0.00573 0.00573 0.00573 0.04867 PValue	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.026592 0.13857 0.279738 0.279738 0.794592 Benjamini 0.001165
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61 Term GO:0007167~enzyme linked receptor protein signaling pathway	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 Count 14	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 7.4 3.7 2.2 % 10.3	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4 Fold Enrichment 4.8	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-5} 3.21×10^{-4} 0.001566 0.00573 0.04867 PValue 5.97×10^{-6}	Benjamini 3.32×10^{-5} 0.021802 0.029596 0.011767 Benjamini 1.27×10^{-7} 3.42×10^{-4} 0.001914 0.005973 0.279738 0.794592 Benjamini 0.001165
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO INTERPRO SMART UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61 Term GO:0007167~enzyme linked receptor protein signaling pathway GO:0048008~platelet-derived growth factor	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 Count 14 14 5	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7 2.2 % 10.3 2.7	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4 Fold Enrichment 4.8 21.0	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-6} 4.15×10^{-5} 3.21×10^{-4} 0.001566 0.00573 0.04867 PValue 5.97×10^{-6} 1.69×10^{-5}	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.005973 0.026592 0.13857 0.279738 0.794592 Benjamini 0.001165 0.001215
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:003268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM domain:RRM 1 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61 Term GO:0007167~enzyme linked receptor protein signaling pathway GO:0048008~platelet-derived growth factor receptor signaling pathway	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 Count 14 5	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7 2.2 % 10.3 3.7	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4 Fold Enrichment 4.8 31.0	PValue 2.42×10 ⁻⁸ 6.44×10 ⁻⁴ 0.001054 0.001263 PValue 1.23×10 ⁻⁹ 1.13×10 ⁻⁶ 6.63×10 ⁻⁶ 4.15×10 ⁻⁵ 3.21×10 ⁻⁴ 0.001566 0.00573 0.04867 PValue 5.97×10 ⁻⁶ 1.68×10 ⁻⁵	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.026592 0.13857 0.279738 0.794592 Benjamini 0.001165 0.001915
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61 Term GO:0007167~enzyme linked receptor protein signaling pathway GO:0007169~transmembrane recentor protein	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 Count 14 5	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7 2.2 % 10.3 3.7	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 7.0 7.0 8.4 Fold Enrichment 4.8 31.0	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-6} 4.15×10^{-5} 3.21×10^{-4} 0.001566 0.00573 0.00573 0.00573 0.04867 PValue 5.97×10^{-6} 1.68×10^{-5}	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.026592 0.13857 0.279738 0.279738 0.794592 Benjamini 0.001165 0.001915
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE Category GOTERM_BP_FAT GOTERM_BP_FAT	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61 Term GO:0007167~enzyme linked receptor protein signaling pathway GO:0007169~transmembrane receptor protein tyrosine kinase signaling nathway	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 Count 14 5 9	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7 2.2 % 10.3 3.7 6.6	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4 Fold Enrichment 4.8 31.0 4.7	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-5} 3.21×10^{-4} 0.00573 0.00573 0.00573 0.04867 PValue 5.97×10^{-6} 1.68×10^{-5} 6.09×10^{-4}	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.005973 0.026592 0.13857 0.279738 0.279738 0.794592 Benjamini 0.001165 0.001915 0.021154
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO SMART UP_SEQ_FEATURE	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61 Term GO:0007167~enzyme linked receptor protein signaling pathway GO:0007169~transmembrane receptor protein tyrosine kinase signaling pathway GO:0007166~cell surface recent linked	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 Count 14 5 9	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 7.4 3.7 2.2 % 10.3 3.7 6.6	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4 Fold Enrichment 4.8 31.0 4.7	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-5} 3.21×10^{-4} 0.00573 0.00573 0.04867 PValue 5.97×10^{-6} 1.68×10^{-5} 6.09×10^{-4}	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.005973 0.026592 0.13857 0.279738 0.279738 0.794592 Benjamini 0.001165 0.001915 0.021154
Annotation Cluster 3 Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT SP_PIR_KEYWORDS Annotation Cluster 4 Category SP_PIR_KEYWORDS GOTERM_MF_FAT INTERPRO INTERPRO INTERPRO SMART UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE UP_SEQ_FEATURE Category GOTERM_BP_FAT GOTERM_BP_FAT GOTERM_BP_FAT	Enrichment Score: 4.17 Term GO:0010608~posttranscriptional regulation of gene expression GO:0032268~regulation of cellular protein metabolic process GO:0006417~regulation of translation translation regulation Enrichment Score: 4.06 Term rna-binding GO:0003723~RNA binding IPR012677:Nucleotide-binding, alpha-beta plait IPR000504:RNA recognition motif, RNP-1 SM00360:RRM domain:RRM 2 domain:RRM 1 domain:RRM 1 domain:RRM 3 Enrichment Score: 3.61 Term GO:0007167~enzyme linked receptor protein signaling pathway GO:0007169~transmembrane receptor protein signaling pathway GO:0007166~cell surface receptor linked signaling pathway GO:0007166~cell surface receptor linked signaling pathway	Count 14 13 7 5 Count 21 22 11 10 10 6 5 5 3 Count 14 5 9 23	% 10.3 9.6 5.1 3.7 % 15.4 16.2 8.1 7.4 4.4 3.7 2.2 % 10.3 3.7 6.6 16.9	Fold Enrichment 7.8 3.2 6.0 10.6 Fold Enrichment 5.5 3.4 6.6 6.0 4.5 7.1 7.0 8.4 Fold Enrichment 4.8 31.0 4.7 1.5	PValue 2.42×10^{-8} 6.44×10^{-4} 0.001054 0.001263 PValue 1.23×10^{-9} 1.13×10^{-6} 6.63×10^{-6} 4.15×10^{-5} 3.21×10^{-4} 0.001566 0.00573 0.04867 PValue 5.97×10^{-6} 1.68×10^{-5} 6.09×10^{-4} 0.059357	Benjamini 3.32×10 ⁻⁵ 0.021802 0.029596 0.011767 Benjamini 1.27×10 ⁻⁷ 3.42×10 ⁻⁴ 0.001914 0.005973 0.026592 0.13857 0.279738 0.279738 0.794592 Benjamini 0.001165 0.001915 0.021154 0.43637

Annotation Cluster 1	Enrichment Score: 3.89					
Category	Term	Count	%	Fold Enrichment	P-Value	Benjamini
GOTERM_BP_FAT	GO:0042981~regulation of apoptosis	17	19.8	3.9	3.72×10 ⁻⁶	0.00181
GOTERM_BP_FAT	GO:0043067~regulation of programmed cell death	17	19.8	3.9	4.23×10 ⁻⁶	0.001371
GOTERM_BP_FAT	GO:0010941~regulation of cell death	17	19.8	3.9	4.43×10 ⁻⁶	0.001078
SP_PIR_KEYWORDS	Apoptosis	10	11.6	5.9	4.67×10 ⁻⁵	0.001212
GOTERM_BP_FAT	GO:0012501~programmed cell death	13	15.1	3.9	8.27×10 ⁻⁵	0.008027
GOTERM_BP_FAT	GO:0043065~positive regulation of apoptosis	11	12.8	4.7	8.72×10 ⁻⁵	0.007693
GOTERM_BP_FAT	GO:0043068~positive regulation of programmed cell death	11	12.8	4.7	9.24×10 ⁻⁵	0.00747
GOTERM_BP_FAT	GO:0010942~positive regulation of cell death	11	12.8	4.7	9.60×10 ⁻⁵	0.007165
GOTERM_BP_FAT	GO:0043066~negative regulation of apoptosis	10	11.6	5.2	1.03×10 ⁻⁴	0.00717
GOTERM_BP_FAT	GO:0043069~negative regulation of programmed cell death	10	11.6	5.2	1.15×10 ⁻⁴	0.007443
GOTERM_BP_FAT	GO:0060548~negative regulation of cell death	10	11.6	5.1	1.17×10 ⁻⁴	0.007128
GOTERM_BP_FAT	GO:0006915~apoptosis	12	14.0	3.7	3.16×10 ⁻⁴	0.014535
GOTERM_BP_FAT	GO:0008219~cell death	13	15.1	3.4	3.76×10 ⁻⁴	0.015817
GOTERM_BP_FAT	GO:0016265~death	13	15.1	3.3	4.01×10 ⁻⁴	0.016137
GOTERM_BP_FAT	GO:0006917~induction of apoptosis	8	9.3	4.6	0.001532	0.042984
GOTERM_BP_FAT	GO:0012502~induction of programmed cell death	8	9.3	4.6	0.00156	0.041362
GOTERM_BP_FAT	GO:0006916~anti-apoptosis	5	5.8	4.5	0.024044	0.238507

upplementary Table 4 Top three clusters of categories (terms) overrepresented in the list of genes with the	e
ighest in-degree in the IS-network.	

Annotation Cluster 2	Enrichment Score: 3.04					
Category	Term	Count	%	Fold Enrichment	P-Value	Benjamini
GOTERM_BP_FAT	GO:0010608~posttranscriptional regulation of gene expression	10	11.6	8.8	1.67×10 ⁻⁶	0.00163
SP_PIR_KEYWORDS	translation regulation	4	4.7	13.4	0.003254	0.021864
GOTERM_BP_FAT	GO:0032268~regulation of cellular protein metabolic process	9	10.5	3.5	0.00359	0.06514
GOTERM_BP_FAT	GO:0006417~regulation of translation	4	4.7	5.4	0.036521	0.30398

Annotation Cluster 3	Enrichment Score: 2.96					
Category	Term	Count	%	Fold Enrichment	P-Value	Benjamini
GOTERM_BP_FAT	GO:0007167~enzyme linked receptor protein signaling pathway	10	11.6	5.4	7.95×10 ⁻⁵	0.008565
GOTERM_BP_FAT	GO:0048008~platelet-derived growth factor receptor signaling pathway	4	4.7	39.0	1.32×10 ⁻⁴	0.007522
GOTERM_BP_FAT	GO:0007169~transmembrane receptor protein tyrosine kinase signaling pathway	7	8.1	5.8	0.001212	0.037377
GOTERM_BP_FAT	GO:0007166~cell surface receptor linked signal transduction	15	17.4	1.5	0.109849	0.568095

Three-node sub-networks

In total there exists sixteen non-equivalent (i.e., non-isomorphic) directed three-node subnetworks. All of them are shown in Supplementary Fig. 2. Three of these sub-networks are disconnected, and thirteen are connected. For all connected sub-networks we summarized data on their occurrence in random graphs as well as in the constructed F-network and IS-network in Supplementary Table 5.



Supplementary Figure 2 | All non-equivalent (i.e., non-isomorphic) directed three-node sub-networks. Sub-networks 1, 2, 4 are disconnected, all other sub-networks are connected.

Supplementary Table 5 | Aggregate information on number of connected three-node sub-networks of each type in the F- and IS-networks and in generated random graphs. Sub-network types are given in accordance with Supplementary Fig. 2. For random graphs interquartile intervals [Q1, Q3] for numbers of sub-networks are specified. If an observed number of a sub-network does not belong to the interquartile interval, the conventional estimate of the p-value¹ is additionally presented below the interquartile interval.

Tuna	IS-network			<i>F-network</i>			
Туре	Observed	Erdős–Rényi	Fixed out-degree	Observed	Erdős–Rényi	Fixed out-degree	
3	22913	[17109, 17282] <10 ⁻⁴	[12907, 13610] <10 ⁻⁴	30757	[21178, 21374] <10 ⁻⁴	[16479, 17208] <10 ⁻⁴	
5	24917	[34268, 34521] <10 ⁻⁴	[23734, 29111]	32654	[42418, 42695] <10 ⁻⁴	[30554, 36626]	
6	18	[4, 12] 0.10	[2, 8] 0.017	41	[5, 16] 0.0026	[3, 11] <10 ⁻⁴	
7	7293634	[17110, 17286] <10 ⁻⁴	[7289687, 7293494] 0.23	7732631	[21182, 21377] <10 ⁻⁴	[7732075, 7736051]	
8	1948	[6, 10] <10 ⁻⁴	[2587, 3269] 0.016	2448	[9, 13] <10 ⁻⁴	[3049, 3739] 0.025	
9	0	[0, 0]	[0, 0]	0	[0, 0]	[0, 1]	
10	1773	[4, 12] <10 ⁻⁴	[928, 4389]	5333	[5, 16] <10 ⁻⁴	[1341, 4969] 0.22	
11	0	[0, 0]	[0, 0]	2	[0, 0] <10 ⁻⁴	[0, 1] 0.067	
12	0	[2, 4] 0.065	[1, 3] 0.21	0	[2, 5] 0.025	[1, 4] 0.12	
13	0	[0, 0]	[0, 1]	2	[0, 0] <10 ⁻⁴	[0, 1] 0.18	
14	53	[0, 0] <10 ⁻⁴	[7, 216]	248	[0, 0] <10 ⁻⁴	[16, 228] 0.22	
15	0	[0, 0]	[0, 0]	0	[0, 0]	[0, 0]	
16	0	[0, 0]	[0, 0]	0	[0, 0]	[0, 0]	

Histograms supporting p-values

Histograms supporting specified p-values associated with the three-node network motif depicted in Fig. 2a (sub-network type 6 in accordance with Supplementary Fig. 2) are presented in Supplementary Fig. 3.



Supplementary Figure 3 | Histograms supporting specified p-values associated with the network motif shown in Fig. 2a (sub-network type 6 in accordance with Supplementary Fig. 2). Bars for which the value is equal to or greater than the number of occurrence observed in the constructed networks (i.e., bars contributing to p-value) are colored in orange. Panels a, b correspond to the model of random graph generation with the fixed out-degrees, and panels c, d correspond to the Erdős–Rényi model. Panels a, c correspond to the F-network, and panels b, d correspond to the IS-network.

For the network motif depicted in Fig. 2b (sub-network type 14 in accordance with Supplementary Fig. 2) in case of the F-network the Erdős–Rényi model generated 9,983 random graphs with no occurrence of this sub-network and 17 random graphs with one occurrence; no graphs with at least two occurrences were generated. The numbers for the IS-network were similar (9,988 and 12; no graphs with at least two occurrences).

For the network motif depicted in Fig. 2c (sub-network type 3 in accordance with Supplementary Fig. 2) the number of occurrence was 30,757 for the F-network and 22,913 for the IS-network (see Supplementary Table 5). These numbers exceed the number of occurrence in all generated random graphs. For the Erdős–Rényi model histograms for random graphs are presented in Supplementary Fig. 4. For the model with the fixed out-degrees the difference was even more striking (maximum observed numbers of occurrence in random graphs were 18,568 and 14,846 for the F-network and for the IS-network, respectively).



Supplementary Figure 4 | Histograms supporting specified p-values associated with the network motif shown in Fig. 2c (sub-network type 3 in accordance with Supplementary Fig. 2) for the Erdős–Rényi model. Panel a corresponds to the F-network, and panel b corresponds to the IS-network.

In case of the Erdős–Rényi model random graph core size exceeded 5,000 for all the generated graphs (both for the F-network and the IS-network). Histograms for the core size of random graphs generated by the model with the fixed out-degrees are presented in Supplementary Fig. 5.



Supplementary Figure 5 | Histograms supporting specified p-values associated with the network core size (the model with the fixed out-degrees). Panel a corresponds to the F-network, and panel b corresponds to the IS-network. Bars for which the value is equal to or less than the core size in the constructed networks (i.e., bars contributing to p-value) are colored in orange.

The core of the F-network

Genes forming the core of the F-network and intergenic interaction between these genes induced by the intragenic miRNAs are presented in Supplementary Fig. 6.



Supplementary Figure 6 | The core of the F-network. The nodes are genes, and the nodes (genes) A and B are connected by a directed edge (A - | B) if gene A hosts a miRNA that targets gene B.

Boxplots for the expression levels of genes in the collection of cell lines

For the analyzed collection of 675 cell lines, boxplots illustrating the data on higher expression levels and lower expression variance of genes comprising the network core (compared to the median values) are presented in Supplementary Fig. 7, 8.



Supplementary Figure 7 | Boxplots for expression levels. Boxplots are shown for the complete set of genes (ca. 26 thousand), for the genes comprising the core of the F-network, and for the genes comprising the core of the IS-network. The data is presented for the lower quartile (Q1), median, and upper quartile (Q3) of expression levels (RPKM) in the collection of cell lines.



Supplementary Figure 8 | **Boxplots for expression variance.** Boxplots are shown for the complete set of genes (ca. 26 thousand), for the genes comprising the core of the F-network, and for the genes comprising the core of the IS-network. To increase readability, we set maximum value for the Y axis to three, cutting outliers for the complete set of genes (the outliers have IQR of log₂-scaled RPKM up to 10.6).

Expression levels of core genes in tissue specimens

Analysis of expression levels of core genes in tissue specimens obtained from breast and colorectal cancer patients utilized the microarray series used as training datasets for construction of prognostic gene signatures: GSE17705 for breast cancer patients and GSE39582 for colorectal cancer patients. The series were analyzed separately. Probesets with no associated Gene Symbols were excluded from the analysis. If multiple probesets were associated with the same gene, only the one with the highest median expression level was retained. The Affymetrix Human Genome U133 Plus 2.0 Array that was used for gene expression profiling in GSE39582 series contained probesets for all core genes. The Affymetrix Human Genome U133A Array that was used in GSE17705 series contained probesets for 17 out of 21 genes comprising the core of the F-network, including 10 out of 12 genes comprising the core of the IS-network.

Ranking of genes by median expression level, as well as by the third (higher) or by the first (lower) quartile, demonstrated that core genes have high or at least medium expression levels. All genes comprising the core of the IS-network belonged to the upper half of the ranking (binomial test p-value 9.8×10^{-4} and 2.4×10^{-4} for the breast cancer patients and colorectal cancer patients, respectively). Moreover, in the case of colorectal cancer, 11 out of 12 genes (or even all 12 genes for ranking by the first quartile) belonged to the upper quarter (binomial test p-value 2.2×10^{-6}). In the case of breast cancer, 6 out of 10 IS-core genes with known expression levels belonged to the upper quarter (binomial test p-value 0.020). Similarly, in the core of the F-network, all the genes except one — *PDE4D* for breast cancer and *NR6A1* for colorectal cancer — belonged to the upper half of gene ranking by median expression level, as well as by the first or the third quartile (binomial test p-value 1.4×10^{-4} and 1.0×10^{-5} for breast and colorectal tissue specimens, respectively). Although expression levels for different genes cannot be directly compared in case of microarray expression quantification, these data strongly indicate that the core genes were generally highly expressed in the analyzed tissue specimens.

Analysis of expression variances, quantified as the third quartile to the first quartile ratio of expression levels in linear scale, demonstrated that the core genes tended to have lower variance in comparison to the median values. Note that with respect to ranking, this quantification of expression variance is equivalent to the interquartile range of log-scaled expression levels. To exclude the influence of non-expressed and poorly expressed genes on the analysis results, we focused only on genes from the upper half of genes ranking by the first quartile of expression levels. These genes were ranked by expression variances, and the enrichment of the network cores by the genes from the upper quarter of this ranking was assessed. For the colorectal cancer tissue specimens, the statistical significance of the enrichment was slightly violated (binomial test p-value 0.054 and 0.10 for the core of the IS-network and the core of the F-network, respectively). Moreover, in case of breast cancer, only two and four genes from the core of the IS-network and the F-network and the F-network, respectively). Moreover, in case of breast cancer, only two and four genes from the core of the IS-network and the F-network and the F-network py expression variance.

Datasets utilized for construction of prognostic gene signatures for colorectal cancer patients

Datasets utilized for construction of prognostic gene signatures for colorectal cancer patients are presented in Supplementary Table 6.

Supplementary Table 6 | Datasets utilized for construction of prognostic gene signatures for colorectal cancer patients.

Dataset accession	Dataset type		Patients		
		Total	Recurrence within 3 years	No recurrence and follow-up of at least 4 years	
GSE39582	Training	519	124	245	
GSE37892	Filtration	129	32	48	
GSE17536	Filtration	144	31	58	
GSE14333	Validation	225	41	85	

Prognostic gene triples

The classifiers based on the identified triples of genes from the core of the constructed network had the following parameters.

For the triple *HNRNPK*, *PANK3*, *SMC4* weights w were -0.142, -0.496 and 1.219, respectively, and the value of ρ was -0.193.

For the triple *MCM7*, *PANK3*, *SMC4* weights w were 0.061, -0.457 and 1.101, respectively, and the value of ρ was -0.169.

For the triple *MAP2K4*, *PANK3*, *SMC4* weights w were -0.452, -0.402 and 1.030, respectively, and the value of ρ was -0.141.

For the triple *FASTKD2*, *PANK1*, *HUWE1* weights w were -0.623, -0.417 and 0.282, respectively, and the value of ρ was -0.044.

For breast cancer, among 680 considered triples of genes from the core of the F-network, 250 passed thresholds on sensitivity and specificity for the training dataset. The first filtration dataset kept 163 triples, and finally after the filtration based on the second filtration dataset 17 triples remained. Out of these 17 triples, four included genes only from the core of the IS-network.

For colorectal cancer, among 1330 considered triples of genes from the core of the Fnetwork, 194 triples satisfied the thresholds for the training dataset, 150 triples survived the first filtration, but only 3 triples survived filtration based on the second filtration dataset (two of these three triples included only genes from the core of the IS-core). Interestingly, filtration based solely on the second filtration set (without filtration based on the first dataset) provided almost the same result, keeping 4 triples.

In spite of relatively low thresholds used for filtration, both for breast cancer and colorectal cancer all triples that survived the filtration confirmed their prognostic potential as for the validation dataset they gave AUC value of at least 0.6.

Interplay of the IS-network core and Myc

The interplay between the genes forming the core of the IS-network and a number of well-studied transcription factors (including p53, Myc family, Fos family, Jun family) was analyzed based on published papers. The sources were found in PubMed and Google Scholar using search requests of the form "G and T", where G and T were a gene from the network core and a transcription factor, respectively (or, more precisely, gene symbols associated with the gene and the transcription factor). The analysis showed that in contrast with other studied transcription factors, the Myc family has a remarkable functional connection with the core of the IS-network.

Myc family proteins activate transcription of $MCM7^{2,3}$ and $RCL1^{4,5}$ genes and inhibit expression of $CTDSP1^6$ and $ABCF1^7$ genes. For EIF4H and HNRNPK, binding of N-myc at their promoters has been shown, as well as N-myc-dependent expression of intronic miRNAs of these genes⁸. Furthermore, products of the *EIF4H* and *HNRNPK* genes enhance translation of c-Myc

mRNA^{9,10}. For the genes *SMC4*, *MCM7*, *FASTKD2*, and *HUWE1*, a direct protein-protein interaction with c-Myc or N-Myc has been reported¹¹⁻¹⁴.

Additionally, Myc regulates expression of intronic miRNAs that induce intergenic interactions of the core genes represented by edges of the network. Specifically, it activates expression of the mir-15b/16-2 cluster¹⁵, the mir-25/93/106b cluster³, mir-7-1¹⁶, and mir-590⁸, and inhibits expression of mir-26b⁶, mir-101¹⁷, and mir-877⁸. Furthermore, miR-16-5p, miR-25-3p and miR-98-5p target c-Myc^{18,19}, miR-103 targets the c-Myc activators c-Myb and *DVL1*, thereby reducing c-Myc expression²⁰, and miR-101-3p targets N-Myc^{18,19,21}.

The described interplay between the core of the IS-network and the Myc family of transcription factors is summarized in Supplementary Fig. 9.



Supplementary Figure 9 | Interplay of the IS-network core and Myc family of transcription factors.

Cross-validation of the identified triples of genes on the training datasets

Results of 3-fold cross-validation of the identified triples of genes on the training datasets are summarized in Supplementary Table 7. For each triple 10,000 cross-validation runs were performed, preserving initial proportion of classes in folds.

In case of 10-fold cross-validation variation of the characteristics was expectedly higher, primarily due to a very small number of patients with recurrence in test fold, which resulted in a very coarse discretization. Yet, the results were highly consistent with the results of 3-fold cross-validation and additionally proved the absence of overfitting. Specifically, lower quartiles of sensitivity and specificity obtained by 10,000 cross-validation runs were at least 50% for all the triples, and lower quartiles for AUC was at least 0.6. Moreover, median AUC was 0.697 for the colorectal cancer triple, 0.7 for two breast cancer triples, and 0.733 for the third breast cancer triple.

Supplementary Table 7 | **Results of 3-fold cross-validation on the training dataset.** For each characteristic the table presents its median value and interquartile range.

Triple	Pathology	Cross-validation results			
		Sensitivity	Specificity	AUC	
HNRNPK, PANK3,	Breast cancer	64.3%	62.3%	0.697	
SMC4		[50.0%, 71.4%]	[56.6%, 67.9%]	[0.654, 0,739]	
MCM7, PANK3,	Breast cancer	57.1%	64.2%	0.690	
SMC4		[50.0%, 71.4%]	[60.4%, 69.8%]	[0.644, 0.733]	
MAP2K4, PANK3,	Breast cancer	64.3%	66.0%	0.726	
SMC4		[57.1%, 71.4%]	[62.3%, 69.8%]	[0.686, 0,768]	
FASTKD2, PANK1,	Colorectal cancer	61.0%	65.4%	0.693	
HUWE1		[56.1%, 65.9%]	[61.7%, 69.1%]	[0.665, 0.721]	

Supplementary references

- 1. Ewens, W. J. On estimating P values by the Monte Carlo method. Am. J. Hum. Genet. 72, 496–498 (2003).
- 2. Shohet, J. M. et al. Minichromosome maintenance protein MCM7 is a direct target of the MYCN transcription factor in neuroblastoma. *Cancer Res.* 62, 1123–1128 (2002).
- 3. Zhao, Z. N. et al. TSA suppresses miR-106b-93-25 cluster expression through downregulation of MYC and inhibits proliferation and induces apoptosis in human EMC. *PLoS One* 7, e45133 (2012).
- 4. Ciribilli, Y., Singh, P., Inga, A. & Borlak, J. c-Myc targeted regulators of cell metabolism in a transgenic mouse model of papillary lung adenocarcinoma. *Oncotarget* 7, 65514–65539 (2016).
- 5. Tworkowski, K. A. et al. Adenovirus E1A targets p400 to induce the cellular oncoprotein Myc. *Proc. Natl. Acad. Sci. U S A* **105**, 6103–6108 (2008).
- 6. Chang, T. C. at al. Widespread microRNA repression by Myc contributes to tumorigenesis. *Nat. Genet.* **40**, 43–50 (2008).
- Porro, A. et al. Direct and coordinate regulation of ATP-binding cassette transporter genes by Myc factors generates specific transcription signatures that significantly affect the chemoresistance phenotype of cancer cells. J. Biol. Chem. 285, 19532–19543 (2010).
- 8. Shohet, J. M. et al. A genome-wide search for promoters that respond to increased MYCN reveals both new oncogenic and tumor suppressor microRNAs associated with aggressive neuroblastoma. *Cancer Res.* **71**, 3841–3851 (2011).
- 9. Vaysse, C. *et al.* Key contribution of eIF4H-mediated translational control in tumor promotion. *Oncotarget* **6**, 39924–39940 (2015).
- 10. Evans, J. *et al.* Members of the poly (rC) binding protein family stimulate the activity of the c-myc internal ribosome entry segment in vitro and in vivo. *Oncogene* **22**, 8012–8020 (2003).
- 11. Murakami-Tonami, Y. *et al.* Inactivation of SMC2 shows a synergistic lethal response in MYCN-amplified neuroblastoma cells. *Cell Cycle* **13**, 1115–1131 (2014).
- 12. Dominguez-Sola, D, *et al.* Non-transcriptional control of DNA replication by c-Myc. *Nature* **448**, 445–451 (2007).
- 13. Ewing, R. M. et al. Large-scale mapping of human protein-protein interactions by mass spectrometry. Mol. Syst. Biol. 3, 89 (2007).
- 14. Adhikary, S. et al. The ubiquitin ligase HectH9 regulates transcriptional activation by Myc and is essential for tumor cell proliferation. *Cell* **123**, 409–421 (2005).
- 15. Mestdagh, P. *et al.* MYCN/c-MYC-induced microRNAs repress coding gene networks associated with poor outcome in MYCN/c-MYC-activated tumors. *Oncogene* **29**, 1394–1404 (2010).
- 16. Chou, Y. T. *et al.* EGFR promotes lung tumorigenesis by activating miR-7 through a Ras/ERK/Myc pathway that targets the Ets2 transcriptional repressor ERF. *Cancer Res.* **70**, 8822–8831 (2010).
- 17. Wang, L. *et al.* c-Myc-mediated epigenetic silencing of MicroRNA-101 contributes to dysregulation of multiple pathways in hepatocellular carcinoma. *Hepatology* **59**, 1850–1863 (2014).
- 18. Vlachos, I. S. *et al.* DIANA-TarBase v7.0: indexing more than half a million experimentally supported miRNA:mRNA interactions. *Nucleic Acids Res.* **43 (Database issue)**, D153–D159 (2015).
- 19. Chou, C. H. et al. miRTarBase 2016: updates to the experimentally validated miRNA-target interactions database. *Nucleic Acids Res.* 44 (D1), D239–D247 (2016).
- 20. Kfir-Erenfeld, S. *et al.* miR-103 inhibits proliferation and sensitizes hemopoietic tumor cells for glucocorticoidinduced apoptosis. *Oncotarget* **8**, 472–489 (2017).
- 21. Buechner, J. *et al.* Tumour-suppressor microRNAs let-7 and mir-101 target the proto-oncogene MYCN and inhibit cell proliferation in MYCN-amplified neuroblastoma. *Br. J. Cancer* **105**, 296–303 (2011).