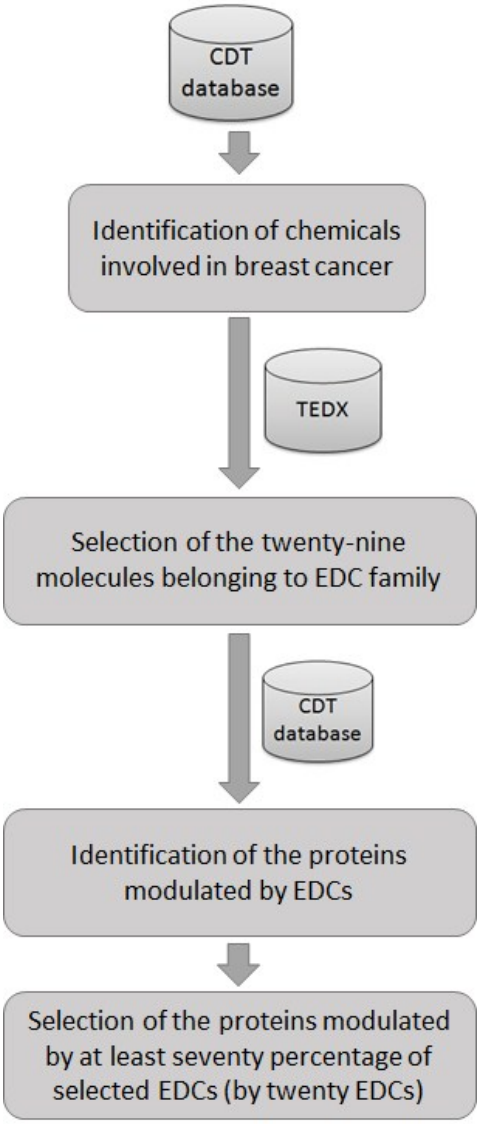
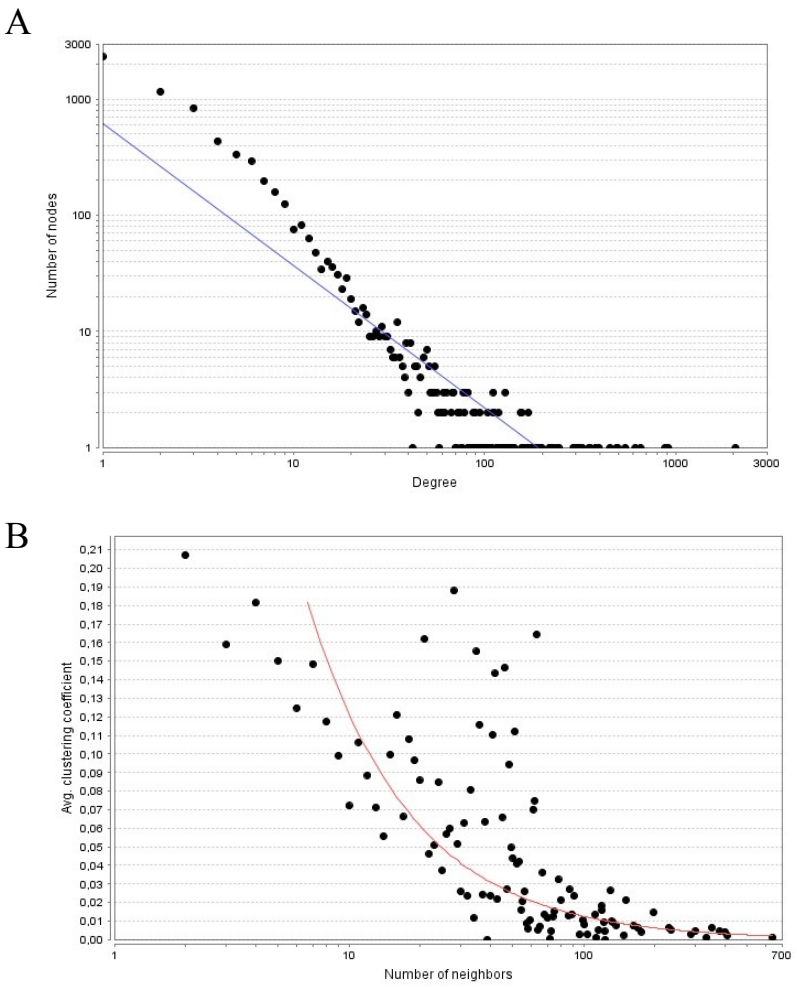
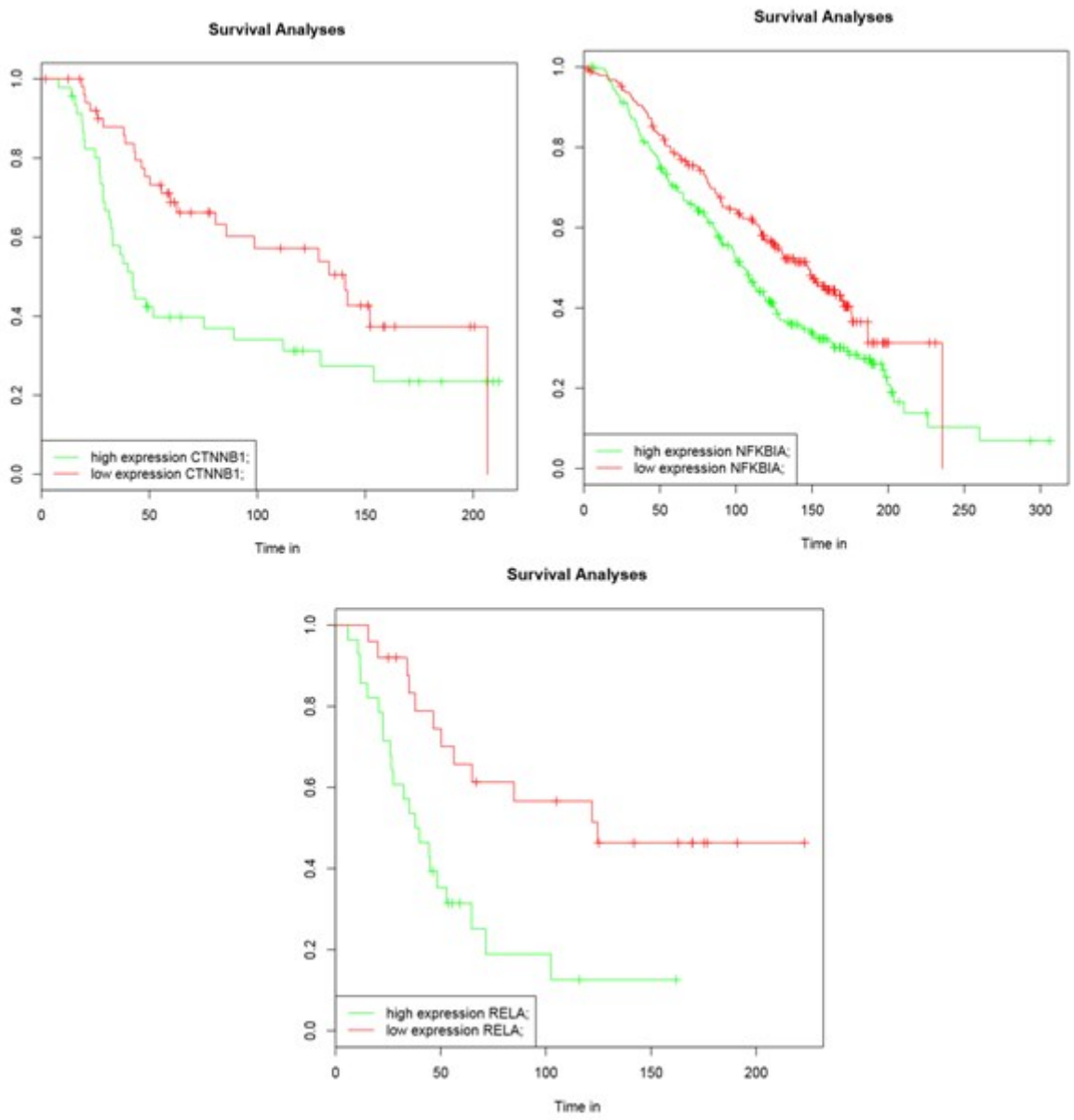
Electronic Supplementary Material (ESI) for Molecular BioSystems.



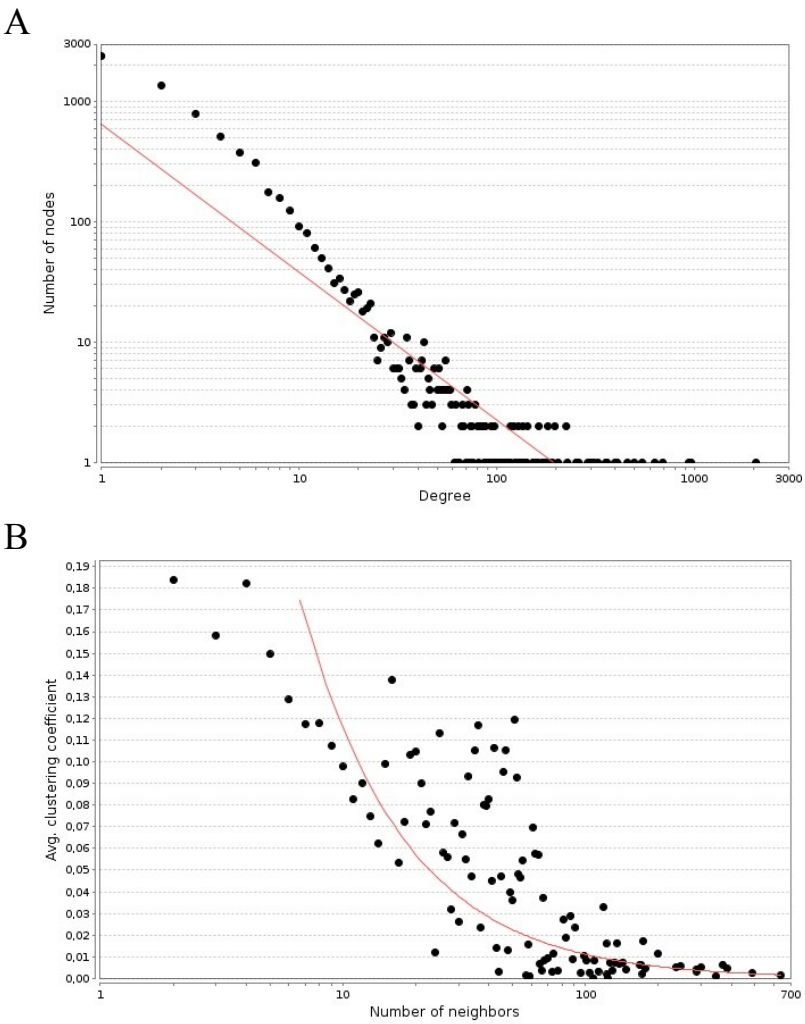
Supplementary Figure 1. Flow-chart of the protocol used to select the endocrine disruptors and the proteins modulated by them in breast cancer. Firstly, we identified all the chemicals involved in breast cancer by CDT database. Secondly, among all the chemicals we selected the twenty-nine molecules belonging to EDC family by TEDX database. Finally, we identified all the proteins modulated by EDCs by CDT database, and among all these proteins we chose only those proteins modulated by at least seventy percentage of selected EDCs (and, hence, by twenty EDCs).



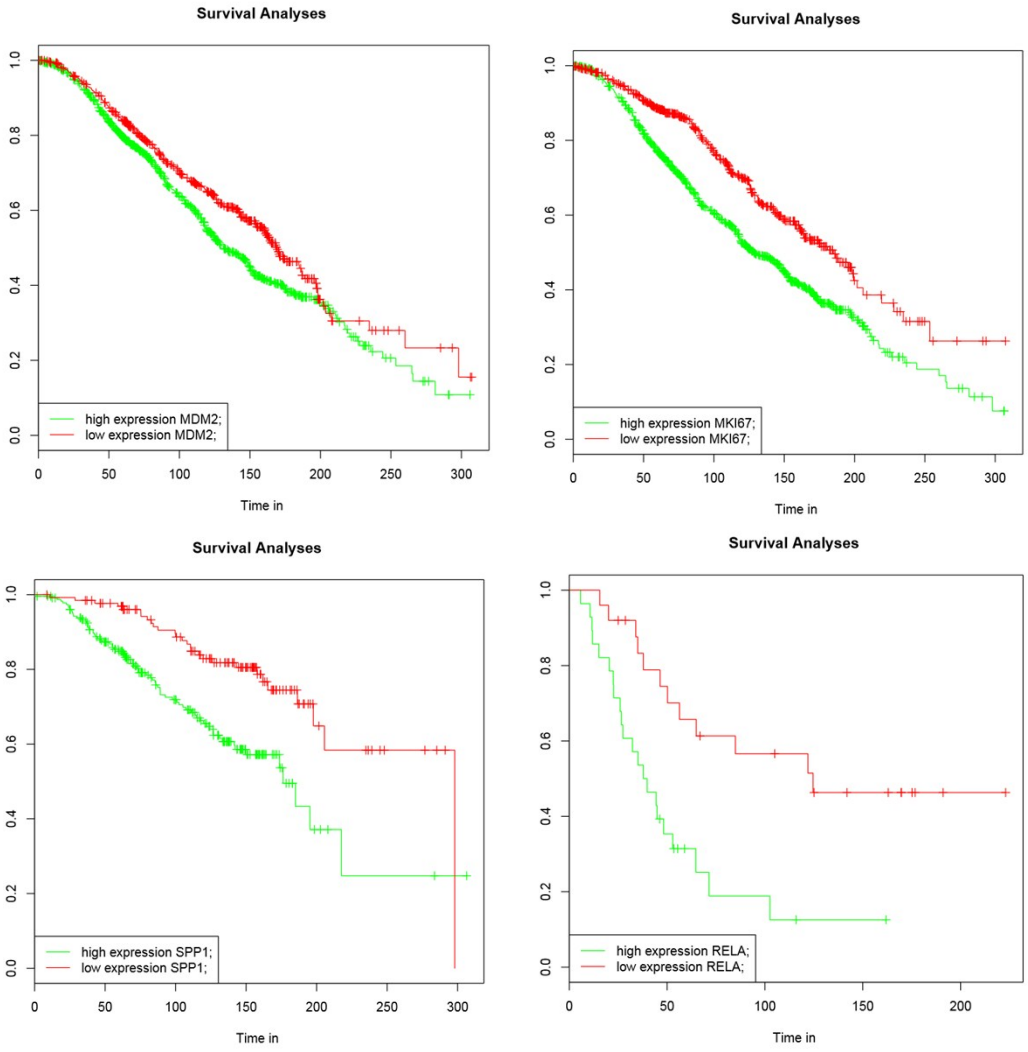
Supplementary Figure 2. Evaluation of topological properties of the network obtained for the proteins modulated by environmental EDCs in Breast Cancer: (A) node degree distribution where the node degree means the number of connections that each node has with others nodes andthe related distribution is the probability of these degrees calculated over the whole network, (B) average clustering coefficient where clustering coefficient means the tendency of the nodes in the network to tend to cluster together. In the graph, we report the average of the clustering coefficients for all nodes in the network.



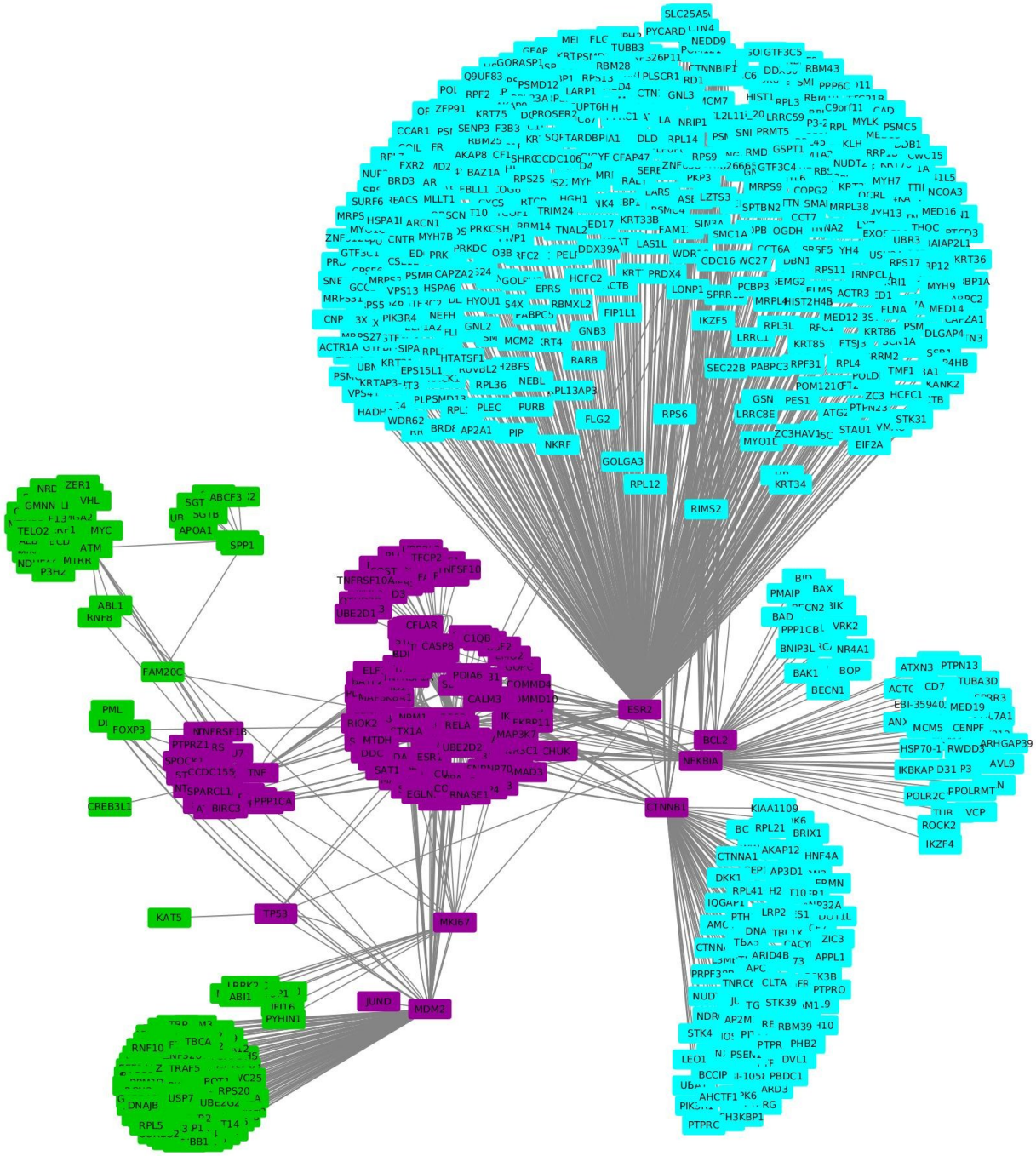
Supplementary Figure 3. Kaplan - Meyer survival curves performed by SynTarget online tool, able to test the effect of genes on survival outcome in cancer (http://www.bioprofiling.de), using public METABRIC Database[23] and GSE25066[24], for CTNNB1, NFKBIA and RELA.



Supplementary Figure 4. Evaluation of topological properties of the network obtained for the proteins modulated by mycotoxins EDCs in Breast Cancer: (A) node degree distribution where the node degree means the number of connections that each node has with others nodes and the related distribution is the probability of these degrees calculated over the whole network, (B) average clustering coefficient where clustering coefficient means the tendency of the nodes in the network to tend to cluster together. In the graph, we report the average of the clustering coefficients for all nodes in the network.



Supplementary Figure 5. Kaplan - Meyer survival curves performed by SynTarget online tool, able to test the effect of genes on survival outcome in cancer (http://www.bioprofiling.de), using public METABRIC Database[23] and GSE25066[24], for MDM2, MKI67, SPP1 and RELA.



Supplementary Figure 6. First order interaction network obtained by merging two networks related to proteins modulated by environmental and mycotoxins EDCs in breast cancer. We report the nodes of environmental EDCs network are shown in cyan, the nodes of mycotoxins network in green and the nodes linking the two networks in purple.

Supplementary Table 1. Molecular pathways in which seven hub nodes in the network of proteins modulated by environmental EDCs in breast cancer are involved.

MOLECULAR PATHWAYS	Proteins involved in each pathway
Apoptosis	AKT1, BAX, BCL2, NFKBIA, RELA, CASP8, TNF, TP53
Toll-like receptor signaling	AKT1, CXCL8, FOS, JUN, NFKBIA, RELA, CASP8, IL6, TNF
T-cell receptor signaling	AKT1, FOS, JUN, NFKBIA, RELA, IFNG, TNF
Neurotrophin signaling	AKT1, BAX, BCL2, JUN, NFKBIA, RELA, TP53
NOD-like receptor	CXCL8, NFKBIA, RELA, CASP8, IL6, TNF
p53 signaling	BAX, CASP8, CCND1, CDKN2A, TP53
B-cell receptor signaling	AKT1,FOS, JUN, NFKBIA, RELA
Adipocytokine signaling	AKT1, RELA, NFKBIA, TNF
RIG-I-like receptor signaling	CXCL8, NFKBIA, RELA, CASP8, TNF
MAPK signaling	AKT1, FOS, JUN, RELA, TNF, TP53
Focal adhesion	AKT1, BCL2, JUN, CTNNB1, CCND1
Cytosolic DNA-sensing	NFKBIA, IL6, RELA
Wnt signaling	JUN, CTNNB1, CCND1, TP53

Supplementary Table 2. Effect of hub nodes (in two networks obtained for the proteins modulated by environmental and mycotoxin EDCs in breast cancer) on survival outcome by SynTarget online tool. The p-values lower than 0.05 were considered as statistically significant.

	Nodes	Survival Effect	p-value
Environmental EDCs network	high levels of CTNNB1 (all samples)	negative	0.00255
	high levels of RELA (all samples)	negative	0.0467
	high levels of CASP8 (estrogen-responsive samples)	negative	0.0166
	low levels of BCL2 (estrogen-responsive samples)	negative	0.000067
Mycotoxin EDCs network	high levels of MDM2 (all samples)	negative	0.00163
	high levels of MKI67 (all samples)	negative	1.73e-10
	high levels of SPP1 (all samples)	negative	0.000659
	high levels of RELA (all samples)	negative	0.0467
	high levels of MDM2 (estrogen-responsive samples)	negative	0.00154
	high levels of MKI67 (estrogen-responsive samples)	negative	0.00000543
	high levels of SPP1 (estrogen-responsive samples)	negative	0.00157
	high levels of CASP8 (estrogen-responsive samples)	negative	0.0166

Supplementary Table 3. Molecular pathways in which hub nodes in the network of proteins modulated by mycotoxins EDCs in breast cancer are involved.

MOLECULAR PATHWAYS	Proteins involved in each pathway
TNF signaling pathway	AKT1, CCL20, CXCL2, FOS, JUN, NFKBIA, RELA, CASP8, IL3, MMP3, MMP9, PTGS2, TNF
Pathways in cancer	AKT1, BAX, BCL2, CXCL12, CXCL8, FOS, JUN, MDM2, NFKBIA, RELA, CASP8, HIF1A, IGF1, IL6, MMP9, NOS2, PTEN, PTGS2, TP53
Toll-like receptor signaling pathway	AKT1, CXCL8, CXCL9, FOS, JUN, NFKBIA, RELA, CASP8, IL6, SPP1, TNF
Apoptosis	AKT1, ATM, BAX, BCL2, NFKBIA, RELA, CASP8, TNF, TP53
Transcriptionalmisregulation in cancer	ATM, CXCL8, DDIT3, MDM2, RELA, IGF1, IL6, MMP3, MMP9, TP53
NF-kappa B signaling pathway	ATM, BCL2, CXCL12, CXCL8, NFKBIA, RELA, PTGS2, TNF
HIF-1 signalingpathway	AKT1, BCL2, RELA, HIF1A, IGF1, IFNG, IL6, NOS2
p53 signalingpathway	ATM, BAX, MDM2, CASP8, IGF1, PTEN, TP53
FoxOsignalingpathway	AKT1, ATM, MDM2, CAT, IGF1, IL6, PTEN, SOD2
NOD-like receptor signaling pathway	CXCL8, NFKBIA, RELA, CASP8, IL6, TNF
T cell receptor signaling pathway	AKT1, FOS, JUN, NFKBIA, RELA, IFNG, TNF
Sphingolipidsignalingpathway	AKT1, BAX, BCL2, RELA, PTEN, TNF, TP53
Neurotrophinsignalingpathway	AKT1, BAX, BCL2, JUN, NFKBIA, RELA, TP53
Chemokinesignalingpathway	AKT1, CCL20, CXCL12, CXCL2, CXCL8, CXCL9, NFKBIA, RELA
Osteoclastdifferentiation	AKT1, FOS, JUN, NFKBIA, RELA, IFNG, TNF
Ovariansteroidogenesis	CYP1A1, CYP17A1, CYP19A1, IGF1, PTGS2
MicroRNAs in cancer	ATM, ABCB1, BCL2, MDM2, MMP9, PTEN, PTGS2, TP53, VIM
B cell receptor signaling pathway	AKT1, FOS, JUN, NFKBIA, RELA
RIG-I-like receptor signaling pathway	CXCL8, NFKBIA, RELA, CASP8, TNF
PI3K-Akt signalingpathway	AKT1, RELA, BCL2, MDM2, IGF1, IL6, PTEN, SPP1, TP53
Proteoglycans in cancer	AKT1, MDM2, HIF1A, IGF1, MMP9, TNF, TP53
Cytokine-cytokinereceptorinteraction	CCL20, CXCL12, CXCL8, CXCL9, IFNG, IL6, TNF
Steroidhormonebiosynthesis	CYP1A1, CYP17A1, CYP19A1, CYP3A4
mTORsignalingpathway	AKT1, IGF1, PTEN, TNF
MAPK signalingpathway	AKT1, DDIT3, FOS, JUN, RELA, TNF, TP53
Leukocytetransendothelialmigration	CXCL12, CLDN1, CLDN4, MMP9, OCLN
Central carbon metabolism in cancer	AKT1, HIF1A, PTEN, TP53
Epithelial cell signaling in Helicobacter pylori infection	CXCL8, JUN, NFKBIA, RELA
Adipocytokinesignalingpathway	AKT1, RELA, NFKBIA, TNF
Prolactinsignalingpathway	AKT1, FOS, RELA, CYP17A1
Focaladhesion	AKT1, BCL2, JUN, IGF1, PTEN, SPP1
Tight junction	AKT1, CLDN1, CLDN4, OCLN, PTEN
Chemicalcarcinogenesis	CYP1A1, CYP3A4, GSTP1, PTGS2,
Oxytocinsignalingpathway	FOS, JUN, EEF2, PTGS2, RGS2
Estrogensignalingpathway	AKT1, JUN, FOS, MMP9
Cholinemetabolism in cancer	AKT1, FOS, JUN, HIF1A
Thyroidhormonesignalingpathway	AKT1, MDM2, HIF1A, TP53
cAMPsignalingpathway	AKT1, FOS, JUN, NFKBIA, RELA
Glutathionemetabolism	GSTP1, GPX1, GPX2