

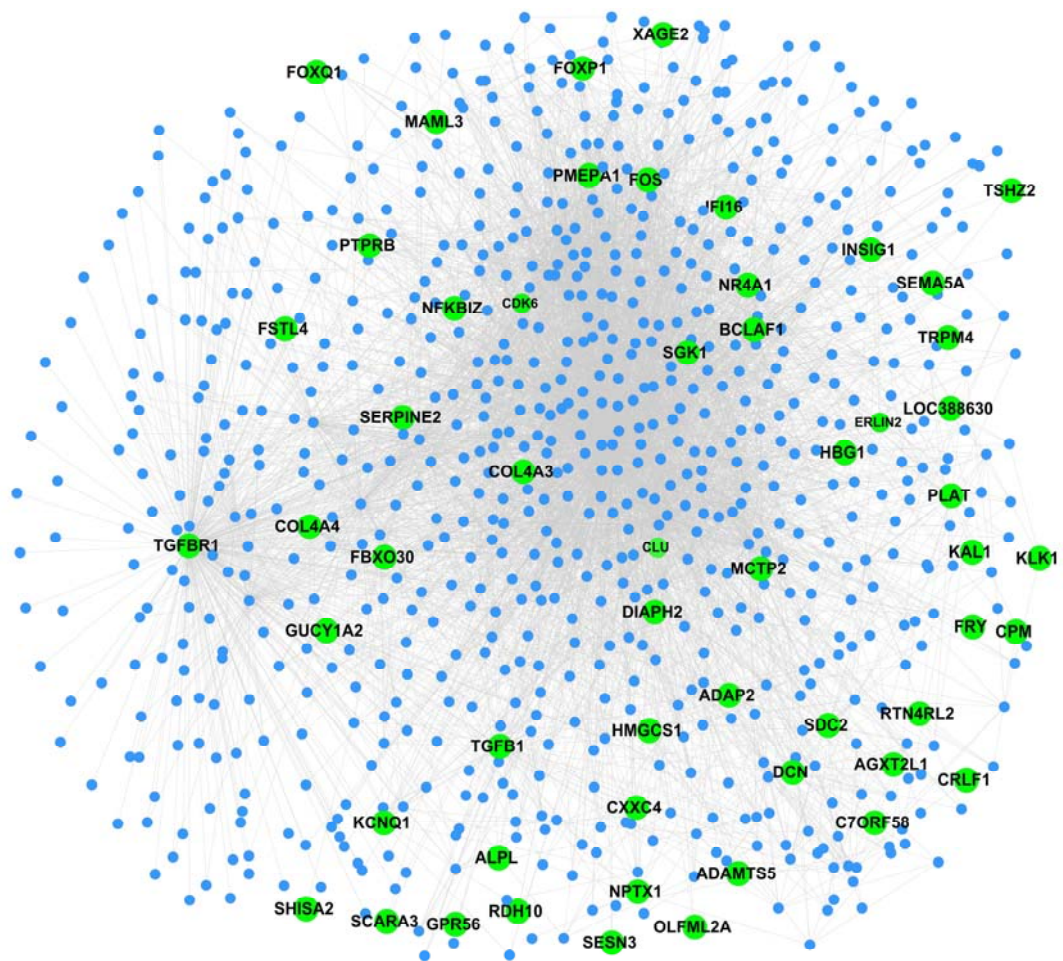
# **Network based analyses of gene expression profile of *LCN2* overexpression in esophageal squamous cell carcinoma**

Bingli Wu<sup>1\*</sup>, Chunquan Li<sup>1,2\*</sup>, Zepeng Du<sup>3</sup>, Qianlan Yao<sup>4</sup>, Jianyi Wu<sup>1</sup>, Li Feng<sup>4</sup>, Pixian Zhang<sup>1</sup>, Shang Li<sup>2</sup>, Liyan Xu<sup>5</sup>, Enmin Li<sup>1</sup>

<sup>1</sup> Department of Biochemistry and Molecular Biology, Shantou University Medical College, Shantou515041, China, <sup>2</sup> College of Medical Informatics, Daqing Campus, Harbin Medical University, Daqing163319, China, <sup>3</sup> Department of Pathology, Shantou Central Hospital, Shantou515041, China, <sup>4</sup> College of Bioinformatics Science and Technology, Harbin Medical University, Harbin150081, China, <sup>5</sup> Institute of Oncologic Pathology, Shantou University Medical College, Shantou515041, China,

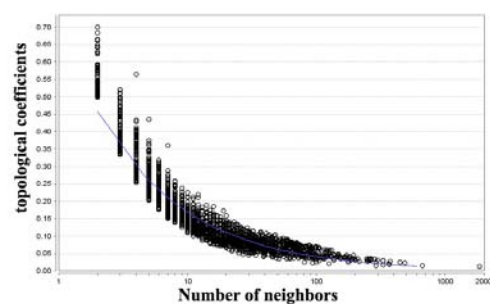
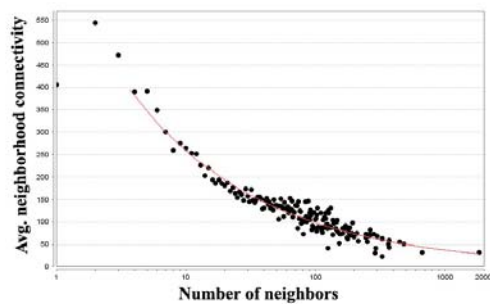
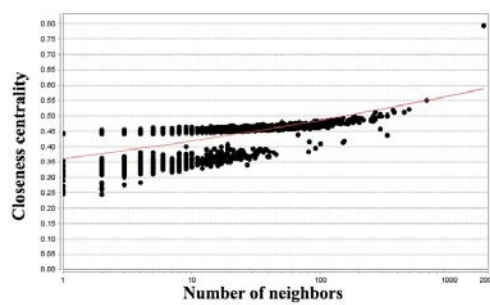
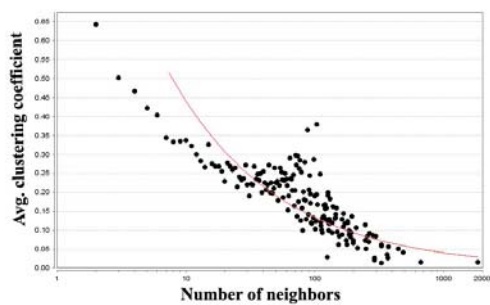
\*These authors contributed equally to this work

Correspondence and requests for materials should be addressed to L.X. ([lyxu@stu.edu.cn](mailto:lyxu@stu.edu.cn)) or E.L. ([nmli@stu.edu.cn](mailto:nmli@stu.edu.cn)) (Fax: +86-754-88900847; Tel: +86-754-88900413)

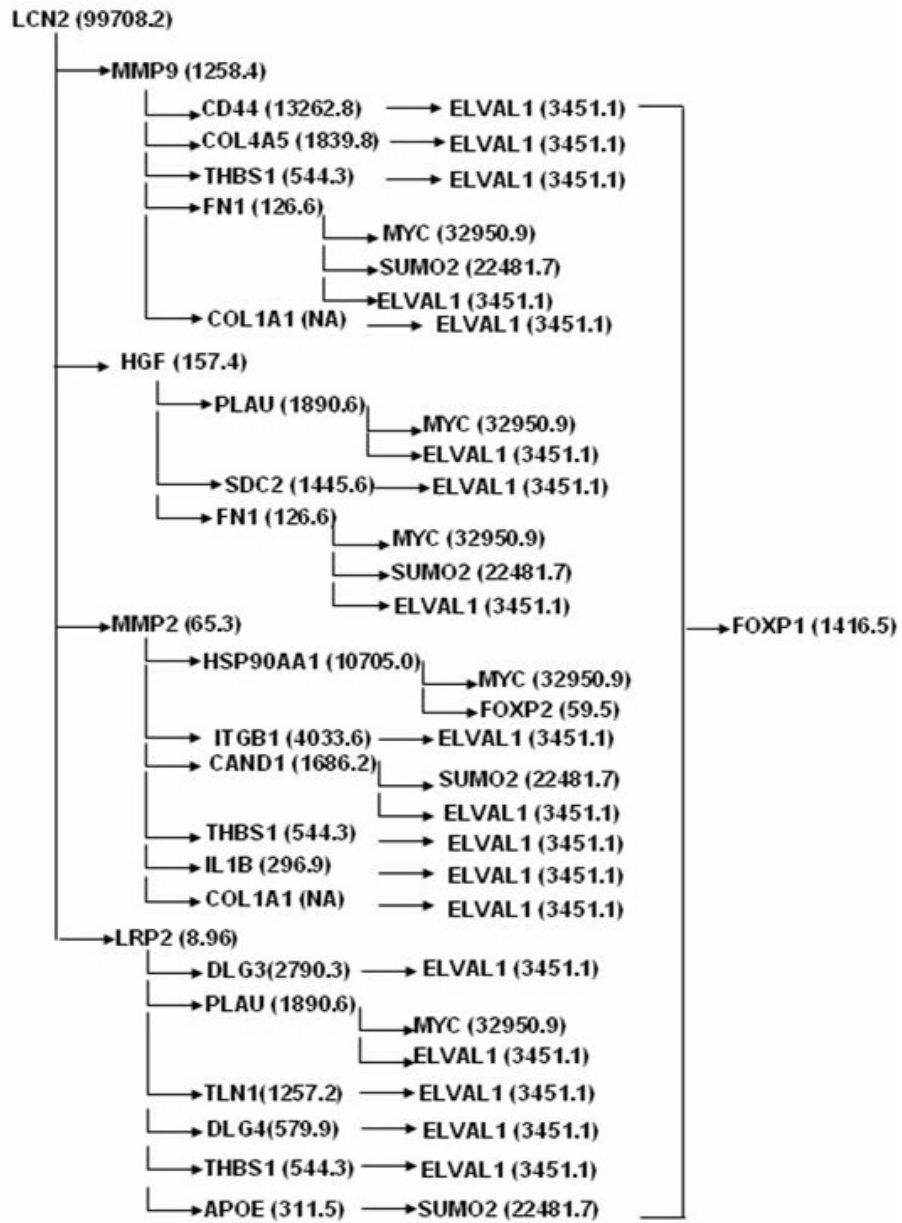


Supplementary Figure S1





Supplementary Figure S3



Supplementary Figure S4

**Supplementary Table S1****Differentially expressed genes with ability to translocate from cytoplasm to nucleus.**

<b>Gene symbol</b>	<b>Full name</b>	<b>Expression trend</b>	<b>Reference of translocation from cytoplasm to nucleus</b>
DACH1	dachshund family transcription factor 1	Upregulated	Wu K, Chen K, Wang C, Jiao X, Wang L, Zhou J, Wang J, Li Z, Addya S, Sorensen PH, Lisanti MP, Quong A, Ertel A, Pestell RG. Cell fate factor DACH1 represses YB-1-mediated oncogenic transcription and translation. <i>Cancer Res.</i> 2014;74(3):829-39.
SMAD9	SMAD family member 9	Upregulated	Heldin CH, Miyazono K, ten Dijke P. TGF-beta signalling from cell membrane to nucleus through SMAD proteins. <i>Nature.</i> 1997;390(6659):465-71.
TP63	tumor protein p63	Upregulated	Munne PM, Gu Y, Tumiati M, Gao P, Koopal S, Uusivirta S, Sawicki J, Wei GH, Kuznetsov SG. TP53 supports basal-like differentiation of mammary epithelial cells by preventing translocation of deltaNp63 into nucleoli. <i>Sci Rep.</i> 2014;4:4663.
CLU	clusterin	Downregulated	Mazzarelli P, Pucci S, Spagnoli LG. CLU and colon cancer. The dual face of CLU: from normal to malignant phenotype. <i>Adv Cancer Res.</i> 2009;105:45-61.
FOXP1	forkhead box P1	Downregulated	Rayoo M, Yan M, Takano EA, Bates GJ, Brown PJ, Banham AH, Fox SB. Expression of the forkhead box transcription factor FOXP1 is associated with oestrogen receptor alpha, oestrogen receptor beta and improved survival in familial breast cancers. <i>J Clin Pathol.</i> 2009;62(10):896-902.
DISC1	disrupted in schizophrenia 1	Downregulated	Zhou X, Chen Q, Schaukowitch K, Kelsoe JR, Geyer MA. Insoluble DISC1-Boymaw fusion proteins generated by DISC1 translocation. <i>Mol Psychiatry.</i> 2010;15(7):669-72.
EGR1	early growth response 1	Downregulated	Yamamoto C, Basaki Y, Kawahara A, Nakashima K, Kage M, Izumi H, Kohno K, Uramoto H, Yasumoto K, Kuwano M, Ono M. Loss of PTEN expression by blocking nuclear translocation of EGR1 in gefitinib-resistant lung cancer cells harboring epidermal growth factor receptor-activating mutations. <i>Cancer Res.</i>

NR4A1	nuclear receptor subfamily 4, group A, member 1	Downregulated	2010;70(21):8715-25. Renaud J, Chiasson K, Bournival J, Rouillard C, Martinoli MG. 17 $\beta$ -estradiol delays 6-OHDA-induced apoptosis by acting on Nur77 translocation from the nucleus to the cytoplasm. <i>Neurotox Res.</i> 2014;25(1):124-34.
FOS	FBJ murine osteosarcoma viral oncogene homolog	Downregulated	Chida K, Nagamori S, Kuroki T. Nuclear translocation of Fos is stimulated by interaction with Jun through the leucine zipper. <i>Cell Mol Life Sci.</i> 1999;55(2):297-302.
CDK6	cyclin-dependent kinase 6	Downregulated	Nagasawa M, Melamed I, Kupfer A, Gelfand EW, Lucas JJ. Rapid nuclear translocation and increased activity of cyclin-dependent kinase 6 after T cell activation. <i>J Immunol.</i> 1997;158(11):5146-54.
RASGRP3	RAS guanyl releasing protein 3 (calcium and DAG-regulated)	Downregulated	Okamura SM, Oki-Idouchi CE, Lorenzo PS. The exchange factor and diacylglycerol receptor RasGRP3 interacts with dynein light chain 1 through its C-terminal domain. <i>J Biol Chem.</i> 2006;281(47):36132-9.
BCLAF1	BCL2-associated transcription factor 1	Downregulated	Lee YY, Yu YB, Gunawardena HP, Xie L, Chen X. BCLAF1 is a radiation-induced H2AX-interacting partner involved in $\gamma$ H2AX-mediated regulation of apoptosis and DNA repair. <i>Cell Death Dis.</i> 2012;3:e359.

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**Supplementary Table S2**  
**Interesting Significant GO terms.**

<b>Significant GO list</b>	<b>Term name</b>	<b>P-Value Corrected with Bonferroni</b>
<b>Immunity-related terms</b>		
GO:0002253	activation of immune response	1.50E-19
GO:0050778	positive regulation of immune response	2.43E-15
GO:0045089	positive regulation of innate immune response	9.95E-11
GO:0002684	positive regulation of immune system process	5.31E-15
GO:0002682	regulation of immune system process	1.36E-22
GO:0045087	innate immune response	2.62E-22
<b>Pathway-related terms</b>		
GO:0017015	regulation of transforming growth factor beta receptor signaling pathway	8.67E-7
GO:0030111	regulation of Wnt receptor signaling pathway	2.33E-5
GO:0030177	positive regulation of Wnt receptor signaling pathway	9.84E-4
GO:0030512	negative regulation of transforming growth factor beta receptor signaling pathway	1.97E-5
GO:0090101	negative regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	1.315E-4
GO:0042059	negative regulation of epidermal growth factor receptor signaling pathway	2.99E-5
GO:0042058	regulation of epidermal growth factor receptor signaling pathway	5.04E-4
GO:0007219	Notch signaling pathway	1.98E-7
GO:0030518	intracellular steroid hormone receptor signaling pathway	8.34E-12
GO:0030521	androgen receptor signaling pathway	9.89E-8
GO:0033143	regulation of intracellular steroid hormone receptor signaling pathway	8.44E-5
<b>Cell cycle related terms</b>		
GO:0000075	cell cycle checkpoint	5.99E-15
GO:0000080	G1 phase of mitotic cell cycle	2.57E-43
GO:0000082	G1/S transition of mitotic cell cycle	1.08E-14
GO:0000086	G2/M transition of mitotic cell cycle	1.24E-4
GO:0000087	M phase of mitotic cell cycle	1.07E-8
GO:0000216	M/G1 transition of mitotic cell cycle	3.42E-5
GO:0000278	mitotic cell cycle	3.15E-25
GO:0006977	DNA damage response, signal transduction by p53 class mediator resulting in cell cycle arrest	1.41E-8
GO:0007050	cell cycle arrest	1.48E-17
GO:0007093	mitotic cell cycle checkpoint	3.16E-15
GO:0007346	regulation of mitotic cell cycle	2.26E-15
GO:0010564	regulation of cell cycle process	8.85E-16



GO:0022402	cell cycle process	8.89E-27
GO:0022403	cell cycle phase	3.11E-23
GO:0031571	mitotic cell cycle G1/S transition DNA damage checkpoint	2.66E-9
GO:0045786	negative regulation of cell cycle	2.38E-18
GO:0045787	positive regulation of cell cycle	2.39E-4
GO:0051436	negative regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle	5.58E-13
GO:0051437	positive regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle	2.63E-13
GO:0051439	regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle	2.25E-13
GO:0051726	regulation of cell cycle	3.31E-26
GO:0071156	regulation of cell cycle arrest	1.12E-13
GO:0071158	positive regulation of cell cycle arrest	7.18E-11
GO:0072474	signal transduction involved in mitotic cell cycle G1/S checkpoint	1.41E-8
GO:0090068	positive regulation of cell cycle	5.10E-11
GO:2000602	regulation of interphase of mitotic cell cycle	1.38E-10
<b>Cellular response-related terms</b>		
GO:0071219	cellular response to molecule of bacterial origin	6.35E-6
GO:0071216	cellular response to biotic stimulus	1.06E-7
<b>Extracellular matrix-related terms</b>		
GO:0030198	extracellular matrix organization	1.72E-5

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## Supplementary Text S1

**1) Closeness centrality** determines how “close” a node is to other nodes in a network by measuring the sum of the shortest distances (geodesic paths) between that node and all other nodes in the network.

**2)** The connectivity of a node is the number of its neighbors. The neighborhood connectivity of a node  $n$  is defined as the average connectivity of all neighbors of  $n$ . The **neighborhood connectivity distribution** gives the average of the neighborhood connectivities of all nodes  $n$  with  $k$  neighbors for  $k = 0, 1, \dots$ .

**3) Topological coefficient** is a relative measure for the extent to which a node shares neighbors with other nodes.

**4) Average clustering coefficient distribution** gives the average of the clustering coefficients for all nodes  $n$  with  $k$  neighbors for  $k = 2, \dots$ . NetworkAnalyzer also computes the network clustering coefficient that is the average of the clustering coefficients for all nodes in the network.