

Supplemental Information

Highly deregulated lncRNA LOC is associated with overall worse prognosis in Hepatocellular Carcinoma patients

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Figure S1

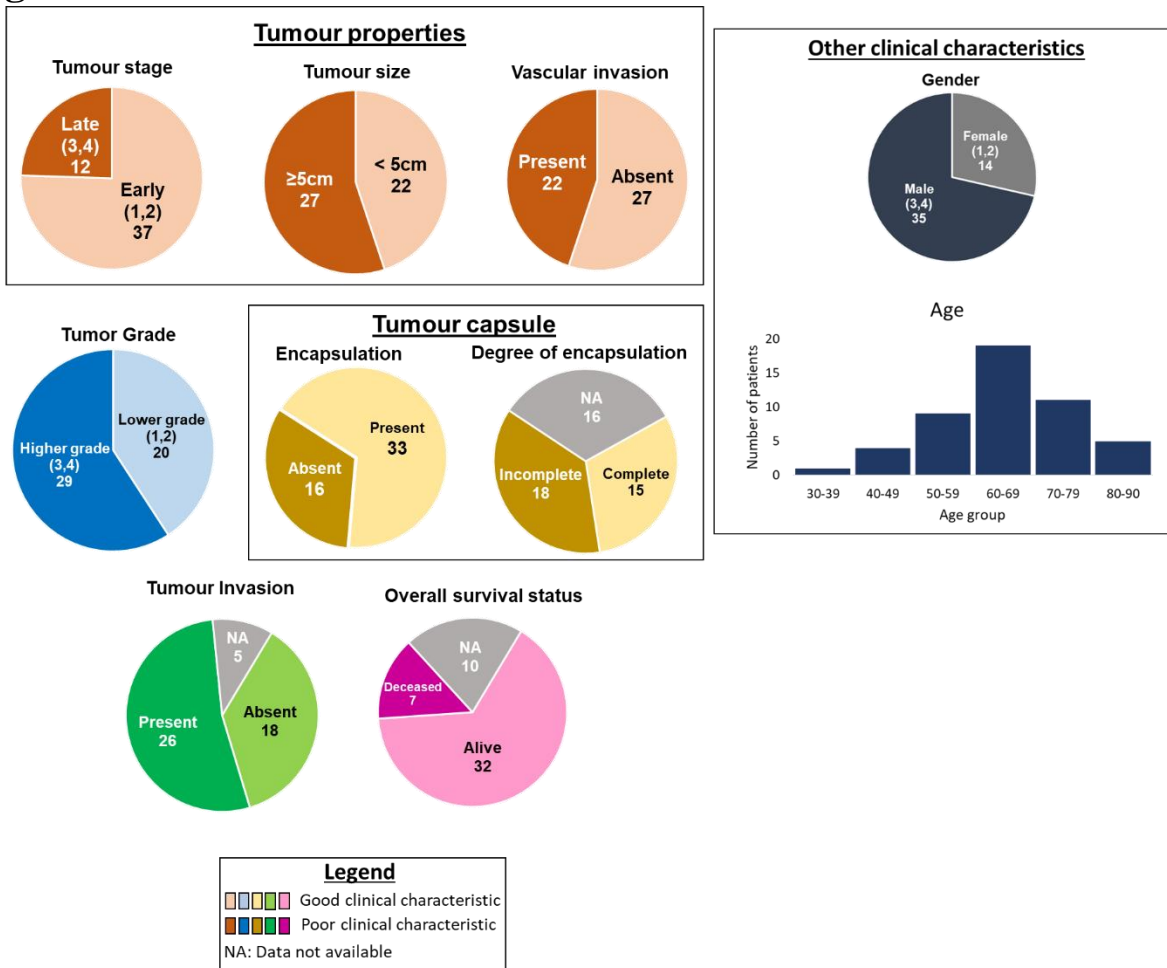


Figure S1 Summary of clinical characteristics in 49 HCC patients

Left panel: The eight clinical characteristics that are used for clinical analysis are further divided into 5 categories (Tumor properties, Tumor grade, Tumor capsule, Tumor invasion and Overall survival status). Within each clinical characteristics, it is further classified into good clinical characteristic and poor clinical characteristic. Dark orange/blue/yellow/green/purple background with white font: Poor clinical characteristic; Light orange/blue/yellow/green/purple background with black font: Good clinical characteristic. Grey background with white font: Data not available.

Right panel: Other clinical characteristics that are not included in the clinical analysis

Figure S2

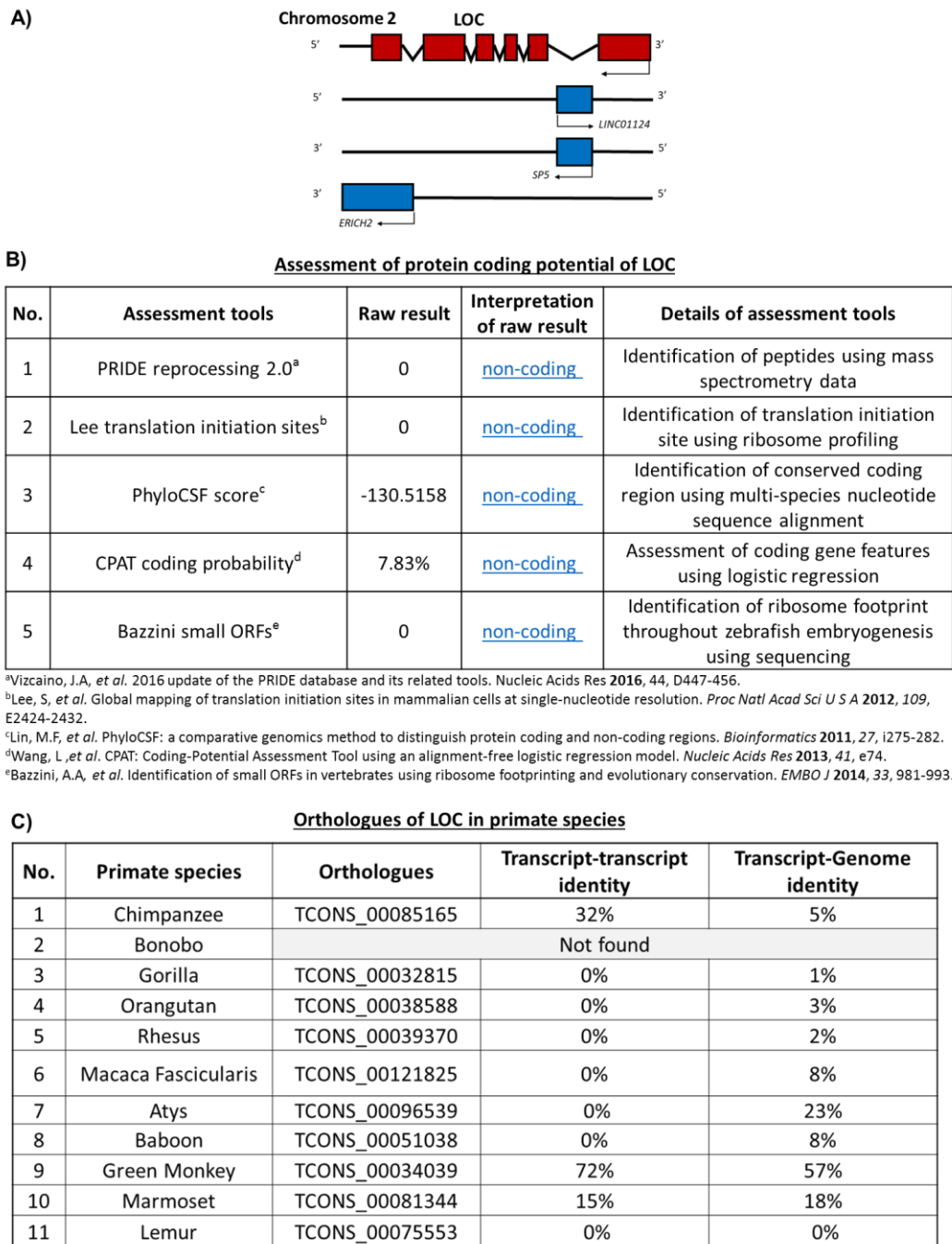


Figure S2 *In silico* analysis of LOC genomic location and sequence conservation

A) Schematic diagram of LOC genomic location. Boxes in red: Exons of LOC; Boxes in blue: Exons of genes; Arrows: Transcription start site; Black lines: Introns

B) Protein coding potential of LOC using five assessment tools. This figure was adapted from Lncipedia (Version 5.2) (<https://lncipedia.org/>).

C) Orthologues of LOC in primate species. This figure shows the orthologues of LOC in 10/11 primate species (Adapted from SyntDB)(<http://syntdb.amu.edu.pl/>). Transcript-transcript identity: percentage of sequences that are aligned and identical between exons of LOC and exons of orthologues; Transcript-genome identity: percentage of LOC that are aligned and identical to the syntenic genomic locus.

Table S1 Primer sequences and annealing temperature used in this study

Gene name	Forward primer sequences (5' to 3')	Reverse primer sequences (5' to 3')	Tm (°C)	Purpose
HOTAIR	GGTAGAAAAAGCAACCACGAAGC	ACATAAACCTCTGTCTGTGAGTGCC	58	PCR
Actin	ATGTTTGAGACCTTCACACC	AGGTAGTCAGTCAGGTCCCGGCC	60	PCR/qPCR
LOC101926913	TCACTGTTGCTTCTCTGACCA	AGGGATTGGTGATAATCTTTTCTGA	60	PCR/qPCR

Table S2 Top 28 highly differentially expressed lncRNAs that have at least three clinical association.

No.	LncRNA		Expression in HCC			Clinical phenotypes							
						Tumor properties			Tumor grade	Tumor capsule		Tumor invasion	Survival
						Tumor Stage	Tumor size	Vascular invasion		Tumor capsule	Degree of encapsulation		
seqname	GeneSymbol	p-value	FDR	Fold-Change									
1	NR_110185	LOC101926913	2.11E-09	3.69E-08	7.09	↑		↑				↑	↑
2	NR_038429	RNASEH1-AS1	3.78E-13	3.72E-11	2.66	↑	↑	↑	↑				
3	T377450	G089309	1.72E-05	8.58E-05	2.04	↑			↑	↑			↑
4	NR_125797	ZFPM2-AS1	5.71E-05	2.44E-04	3.57				↑	↑			↑
5	NR_046173	LOC254896	1.63E-04	6.05E-04	2.67		↑		↑			↑	
6	NR_024443	LOC100133920	1.62E-10	4.37E-09	2.62			↑	↑*	↑			
7	T010075	G002110	7.85E-07	5.93E-06	2.46		↑	↑	↑				
8	T318968	G074705	1.35E-02	2.78E-02	-2.06	↓		↓	↓			↓	
9	T340880	G079999	5.53E-11	1.84E-09	-2.09	↓	↓		↓	↓			
10	NR_027300	C3P1	1.86E-06	1.24E-05	-2.27	↓	↓		↓				↓
11	NR_024479	FAM83A-AS1	3.51E-05	1.59E-04	-2.71		↓	↓	↓			↓	
12	NR_046615	ITIH4-AS1	2.05E-05	9.95E-05	-2.00		↓		↓				↓
13	TCONS_00025782	XLOC_012588	4.17E-04	1.38E-03	-2.19		↓		↓	↓			
14	T304533	G071023	4.88E-06	2.85E-05	-2.20	↓	↓		↓				
15	T111422	G026327	7.26E-10	1.50E-08	-2.40		↓		↓			↓	
16	NR_046612	HTR2A-AS1	5.47E-10	1.19E-08	-2.48		↓		↓			↓	
17	ENST00000514791	RP11-434D9.2	4.06E-09	6.50E-08	-2.63		↓	↓	↓				
18	ENST00000560903	RP11-244F12.3	2.17E-10	5.56E-09	-2.64	↓	↓		↓				
19	uc002bxs.3	DQ597539	1.05E-08	1.46E-07	-2.78		↓		↓				↓
20	uc021trn.1	DQ571055	8.44E-10	1.70E-08	-2.79	↓			↓				↓
21	ENST00000608133	RP11-523G9.3	5.05E-08	5.70E-07	-3.55			↓	↓	↓			
22	T099727	G023548	5.68E-11	1.88E-09	-3.83				↓	↓			↓
23	NR_125934	LOC102723766	1.60E-10	4.35E-09	-4.03		↓		↓	↓			
24	ENST00000424701	RP11-298H24.1	1.98E-11	8.03E-10	-4.47		↓		↓			↓	
25	NR_002733	DGCR5	2.13E-06	1.39E-05	-4.61	↓	↓	↓					
26	TCONS_00023434	XLOC_011275	2.08E-07	1.92E-06	-6.21		↓	↓	↓				
27	T074342	G017089	2.17E-12	1.38E-10	-7.48	↓	↓		↓				
28	T099335	G023451	3.86E-11	1.37E-09	-8.61			↓	↓			↓	

Up arrow with red background: Upregulated in tumor tissues compared to adjacent non-tumor tissues; Down arrow with green background: Downregulated in tumor tissues compared to adjacent non-tumor tissues.

Table S3A Genes that are upregulated in cells which overexpressed LOC but downregulated in cells with LOC-knockdown

No.	Gene information		LOC overexpression			LOC knockdown			Correlation of LOC with gene in patient tissues	Pathways/Gene enrichment				
			Expression		FC	Expression		FC		PCC	GTPase activity			Nucleoside-triphosphatase regulator activity
	Seqname	GeneName	LOC	Ctrl		siLOC	siCtrl		GTPase binding		GTPase activator activity	GTPase regulator activity		
1	ENSG00000185304	RGPD2	0.24	0.05	4.58	0.00	0.10	-16.81	-0.63	[Redacted]	[Redacted]	[Redacted]	[Redacted]	[Redacted]
2	ENSG00000164691	TAGAP	0.36	0.14	2.47	0.05	0.14	-2.72						
3	ENSG00000145087	STXBP5L	0.24	0.09	2.44	0.10	0.24	-2.36						
4	ENSG00000167037	SGSM1	1.44	0.66	2.17	0.15	0.38	-2.54						
5	ENSG00000108961	RANGRF	0.12	0.00	19.16	0.00	0.14	-24.72						
6	ENSG00000074966	TXK	0.60	0.28	2.09	0.00	0.10	-16.81						
7	ENSG00000163220	S100A9	0.30	0.14	2.07	0.05	0.14	-2.72						
8	ENSG00000204475	NCR3	0.36	0.00	55.49	0.05	0.29	-5.33						
9	ENSG00000197272	IL27	0.18	0.00	28.24	0.00	0.19	-32.63						
10	ENSG00000267849	AL133262.1	0.18	0.00	28.24	0.00	0.10	-16.81						
11	ENSG00000256591	RP11-286N22.8	0.18	0.00	28.24	0.00	0.10	-16.81						
12	ENSG00000172425	TTC36	0.18	0.00	28.24	0.05	0.43	-7.93						
13	ENSG00000203546	RP11-176H8.1	0.18	0.00	28.24	0.10	0.24	-2.36						
14	ENSG00000157322	CLEC18A	0.18	0.00	28.24	0.19	0.43	-2.16						
15	ENSG00000268098	AP000688.1	0.12	0.00	19.16	0.00	0.10	-16.81						

16	ENSG00000126860	EVI2A	0.12	0.00	19.16	0.00	0.10	-16.81
17	ENSG00000185760	KCNQ5	0.12	0.00	19.16	0.05	0.24	-4.46
18	ENSG00000149403	GRIK4	0.12	0.00	19.16	0.29	0.76	-2.57
19	ENSG00000147003	TMEM27	0.36	0.05	6.81	0.10	0.24	-2.36
20	ENSG00000267710	AC006116.20	0.24	0.05	4.58	0.00	0.29	-48.44
21	ENSG00000242950	ERVW-1	0.24	0.05	4.58	0.05	0.19	-3.59
22	ENSG00000159409	CELF3	0.18	0.05	3.47	0.00	0.10	-16.81
23	ENSG00000082074	FYB	0.18	0.05	3.47	0.00	0.10	-16.81
24	ENSG00000187753	C9orf153	0.18	0.05	3.47	0.15	0.33	-2.23
25	ENSG00000186952	TMEM232	0.48	0.14	3.28	0.24	0.52	-2.12
26	ENSG00000163632	C3orf49	0.30	0.09	3.03	0.05	0.29	-5.33
27	ENSG00000203867	RBM20	1.44	0.47	3.02	0.00	0.14	-24.72
28	ENSG00000119725	ZNF410	0.84	0.28	2.92	0.24	0.62	-2.50
29	ENSG00000150636	CCDC102B	0.84	0.28	2.92	0.39	0.95	-2.42
30	ENSG00000124529	HIST1H4B	0.42	0.14	2.88	0.00	0.10	-16.81
31	ENSG00000183479	TREX2	0.96	0.38	2.51	0.15	0.33	-2.23
32	ENSG00000165794	SLC39A2	0.60	0.24	2.50	0.05	0.29	-5.33
33	ENSG00000163519	TRAT1	0.36	0.14	2.47	0.19	0.52	-2.64
34	ENSG00000119608	PROX2	0.36	0.14	2.47	0.24	0.52	-2.12
35	ENSG00000181781	ODF3L2	0.24	0.09	2.44	0.15	0.71	-4.73
36	ENSG00000100505	TRIM9	0.24	0.09	2.44	0.05	0.19	-3.59
37	ENSG00000237289	CKMT1B	1.62	0.66	2.44	0.29	0.67	-2.25
38	ENSG00000136250	AOAH	0.12	0.05	2.35	0.00	0.10	-16.81
39	ENSG00000164304	CAGE1	0.12	0.05	2.35	0.05	0.24	-4.46
40	ENSG00000233024	PKD1P1	0.12	0.05	2.35	0.05	0.14	-2.72
41	ENSG00000188620	HMX3	0.66	0.28	2.30	0.00	0.10	-16.81
42	ENSG00000212670	AL161915.1	0.66	0.28	2.30	0.10	0.62	-6.04
43	ENSG00000072952	MRVI1	0.54	0.24	2.25	0.05	0.14	-2.72
44	ENSG00000178226	PRSS36	3.60	1.61	2.24	0.44	1.05	-2.37
45	ENSG00000122711	SPINK4	0.84	0.38	2.20	0.10	0.29	-2.82
46	ENSG00000162482	AKR7A3	0.72	0.33	2.15	0.24	0.90	-3.65
47	ENSG00000196648	GOLGA6L9	0.60	0.28	2.09	0.24	0.57	-2.31
48	ENSG00000183396	TMEM89	0.30	0.14	2.07	0.00	0.14	-24.72

49	ENSG00000258643	BCL2L2-PABPN1	0.30	0.14	2.07	0.05	0.14	-2.72	
50	ENSG00000189350	FAM179A	1.08	0.52	2.07	0.05	0.24	-4.46	

Table shows the expression and fold change (FC) of genes that are upregulated in LOC-overexpressing cells but downregulated in LOC-knockdown cells, Pearson correlation coefficient (PCC) of each gene in HCC patient tissues as well as pathways involved by the genes. The black box indicates the pathways that are involved by each gene.

Table S3B Genes that are downregulated in cells which overexpressed LOC but upregulated in cells with LOC-knockdown

No.	Gene information		LOC overexpression			LOC knockdown			Correlation of LOC with gene in patient tissues	Pathways/Gene enrichment				
			Expression		FC	Expression		FC		Cellular detoxification		Oxygen transport		Drug transport
	Seqname	GeneName	LOC	Ctrl		siLOC	siCtrl			PCC	Cellular detoxification	Cellular oxidant detoxification	Oxygen transport	
1	ENSG00000042062	FAM65C	0.00	0.28	-43.89	0.49	0.24	2.02	-0.62					
2	ENSG00000170509	HSD17B13	0.00	0.33	-51.04	0.10	0.00	17.19	-0.66					
3	ENSG00000213931	HBE1	0.06	0.42	-6.48	0.88	0.38	2.28						
4	ENSG00000196565	HBG2	0.00	0.19	-29.60	0.49	0.05	9.20						
5	ENSG00000213316	LTC4S	0.00	0.14	-22.45	0.15	0.05	2.84						
6	ENSG00000112077	RHAG	0.06	0.14	-2.23	0.34	0.10	3.43						
7	ENSG00000171798	KNDC1	0.30	0.61	-2.02	0.24	0.00	41.48						
8	ENSG00000213901	SLC23A3	0.48	0.99	-2.05	1.12	0.43	2.59						
9	ENSG00000187492	CDHR4	0.18	0.38	-2.06	0.15	0.05	2.84						
10	ENSG00000116544	DLGAP3	0.18	0.38	-2.06	0.29	0.10	2.95						
11	ENSG00000237452	AC074212.3	0.06	0.14	-2.23	0.24	0.10	2.47						
12	ENSG00000120215	MLANA	0.06	0.14	-2.23	0.15	0.05	2.84						
13	ENSG00000186583	SPATC1	0.06	0.14	-2.23	0.29	0.10	2.95						
14	ENSG00000177340	AC024940.1	0.06	0.14	-2.23	0.29	0.10	2.95						
15	ENSG00000103489	XYLT1	0.06	0.14	-2.23	0.29	0.05	5.57						
16	ENSG00000185668	POU3F1	0.06	0.14	-2.23	0.29	0.05	5.57						
17	ENSG00000165194	PCDH19	0.06	0.14	-2.23	0.10	0.00	17.19						
18	ENSG00000143502	SUSD4	0.06	0.14	-2.23	0.10	0.00	17.19						
19	ENSG00000158560	DYNC111	0.60	1.37	-2.27	0.19	0.05	3.75						

20	ENSG00000154710	RABGEF1	0.12	0.28	-2.29	0.24	0.10	2.47
21	ENSG00000171860	C3AR1	0.12	0.28	-2.29	0.15	0.05	2.84
22	ENSG00000162426	SLC45A1	0.12	0.28	-2.29	0.19	0.05	3.75
23	ENSG00000198576	ARC	0.18	0.42	-2.31	0.34	0.05	6.47
24	ENSG00000008128	CDK11A	0.18	0.47	-2.57	0.78	0.19	4.00
25	ENSG00000155530	LRGUK	0.24	0.71	-2.90	0.19	0.05	3.75
26	ENSG00000248592	TMEM110- MUSTN1	0.06	0.19	-2.94	0.34	0.14	2.33
27	ENSG00000177494	ZBED2	0.06	0.19	-2.94	0.24	0.05	4.66
28	ENSG00000227921	AL353791.1	0.06	0.19	-2.94	0.24	0.00	41.48
29	ENSG00000104901	DKKL1	0.06	0.19	-2.94	0.29	0.00	49.57
30	ENSG00000100027	YPEL1	0.18	0.66	-3.58	0.63	0.29	2.19
31	ENSG00000153237	CCDC148	0.06	0.24	-3.64	0.54	0.24	2.22
32	ENSG00000183153	GJD3	0.12	0.52	-4.16	0.49	0.19	2.51
33	ENSG00000176732	PFN4	0.18	0.80	-4.34	0.15	0.00	25.28
34	ENSG00000259224	SLC35G6	0.06	0.28	-4.35	0.15	0.00	25.28
35	ENSG00000188389	PDCD1	0.00	0.14	-22.45	0.39	0.14	2.66
36	ENSG00000186231	KLHL32	0.00	0.14	-22.45	0.15	0.05	2.84
37	ENSG00000131771	PPP1R1B	0.00	0.14	-22.45	0.10	0.00	17.19
38	ENSG00000268941	MGC4294	0.00	0.14	-22.45	0.10	0.00	17.19
39	ENSG00000153902	LGI4	0.00	0.14	-22.45	0.24	0.00	41.48
40	ENSG00000105251	SHD	0.00	0.14	-22.45	0.24	0.00	41.48
41	ENSG00000137101	CD72	0.00	0.19	-29.60	0.10	0.00	17.19
42	ENSG00000160951	PTGER1	0.00	0.24	-36.74	0.83	0.33	2.46
43	ENSG00000102539	MLNR	0.00	0.24	-36.74	0.54	0.14	3.64
44	ENSG00000105261	OVOL3	0.00	0.24	-36.74	0.19	0.05	3.75
45	ENSG00000171747	LGALS4	0.00	0.28	-43.89	0.29	0.05	5.57
46	ENSG00000232671	RP11-126K1.2	0.00	0.28	-43.89	0.10	0.00	17.19
47	ENSG00000189269	C22orf43	0.00	0.47	-72.48	0.29	0.10	2.95

Table shows the expression and fold change (FC) of genes that are downregulated in LOC-overexpressing cells but upregulated in LOC-knockdown cells, pearson correlation coefficient (PCC) of each gene in HCC patient tissues as well as pathways involved by the genes. The black box indicates the pathways that are involved by each gene. Blue box: LOC-downregulated genes that are correlated with LOC expression in patient tissues samples.