

Supplementary Methods

Assessment of similarities between miRNA target predictions

The similarity between two target prediction results A and B was defined as the union of the two datasets divided by the intersection.

$$\text{Similarity} = \frac{A \cap B}{A \cup B}$$

The range of similarity values is between 0 and 1, with a higher value indicating a higher degree of similarity between two datasets.

Comparison analysis of miRNA target prediction methods

A comparative analysis was carried out to test whether integrating different algorithms is superior to using a single algorithm by itself. The overlap of miRanda, PITA, TargetScan, RNAhybrid, and their integration with experimentally validated miRNA-lncRNA datasets from starBase v.2.0 (1) and DIANA-lncBase (2) was examined. The significance of the enrichment in overlap between individual methods and the validated dataset was calculated by hypergeometric testing. If N is the total number of all possible miRNA-lncRNA interactions, of which K are included in the validated dataset, and the analytical method of interest has a total of M interactions, of which x overlap with the validated dataset, then the P value corresponding to the significance of enrichment can be calculated as follows:

$$P = 1 - \sum_{t=0}^x \frac{\binom{K}{t} \binom{N-K}{M-t}}{\binom{N}{M}}$$

Evaluation of competing activity score

To test whether the competing activity score is a valuable measurement for the evaluation of the strength of competition in lncACTs, we carried out following analysis:

Comparisons between gold standard triplets and 10-fold random lncACTs

PTEN-associated competing triplets (PTENACTs; n = 137) from an extensive ceRNA sub-network that included PTEN, RB1, STAT3, PDGFRA, RUNX1, VEGFA, and their competing miRNAs were identified and experimentally validated in a previous study (3). These were taken as gold standard PTENACTs. For each PTENACT, 10 random competing activity scores were generated by randomly shuffling the expression profiles. PTENACTs competing activity score were significantly higher than random scores across 12 types of cancer (Fig. S4).

Comparisons between gold standard triplets and 10-fold negative triplets

Negative examples were randomly derived from 289 negative miRNA-target interactions. The miRNA target pairs were used as negative training examples for mining miRNA-target interactions (4); for each pair, two candidate RNAs (lncRNAs or mRNAs) were identified as lncACTs if they interacted with a common miRNA. In this step, a threshold P value < 0.05 was used for hypergeometric testing. The gold standard and negative lncACTs were merged into a list ranked by competing activity score in descending order for which dynamic thresholds (ranging from minimum to maximum of competing activity scores) were used as cut-off points. Ranking was determined by calculating sensitivity and

specificity (i.e., frequency of gold standards ranked above or below a given cut-off point, respectively). We plotted receiver operating characteristic (ROC) curves using the competing activity scores of the lncACTs to facilitate the comparison between PTENACTs and 10-fold negative lncACTs (Fig S5). In a ROC curve, the sensitivity (true positive rate) is plotted as a function of 1-specificity (false positive rate) for different thresholds. We found high AUC values (from 0.81 to 0.98) for ROC curves across 12 cancers. These results indicated that competing activity scores can give high levels of precision to distinguish positive lncACTs from negative lncACTs.

Supplementary Figure Legends

Figure S1. Evaluation of accuracy of our coding/lncRNA gene quantification pipeline. For OV data (A) and UCEC data (B), we plotted our recalculated RPKM values against the true RPKM values, calculated by Akrami et al. High linear correlation was observed between recalculated RPKM and true RPKM values for both OV ($R^2=0.92$) and UCEC ($R^2=0.95$) datasets. The R^2 and F-statistic P-values, calculated by robust linear regression analysis, are shown in each figure. Linear fitting lines are indicated in red. X and Y axes were plotted in the log₂ scale.

Figure S2. (A) Venn diagram of the overlap between miRNA-lncRNA interactions predicted using four methods. (B) The similarity between RNAhybrid and PITA results was only 5.13%; the highest similarity was observed between miRanda and TargetScan results at 24.10%. The total number of differentially predicted results is shown on the bottom line. A 5.8-fold difference was observed between the number of results predicted by RNAhybrid (3,502,121) and miRanda (606,081). Similarities between predictions from RNAhybrid and miRanda was 13.07%, while between RNAhybrid and PITA, the IR was only 5.1%. These results indicate a considerable divergence in miRNA-binding sites predicted using the four methods.

Figure S3. Comparison of different miRNA-lncRNA prediction methods overlapping with validated dataset. The integration method hosts the most number of experimentally validated miRNA-lncRNA interactions than other methods. Hypergeometric test indicated that the overlap between integration method and validated dataset has the most significant enrichment P value.

Figure S4. Individual and box plot comparison of competing activity scores between PTENACTs (red points) and random (green points) lncACTs. The scores of PTENACTs were significantly higher than random scores across 12 types of cancers. Significant P values were calculated by the Mann-Whitney U-test

Figure S5. The ROC curves (blue lines) used to distinguish PTENACTs from negative lncACTs, based on the competing activity score. The AUC score is the most frequently used measure for the evaluation of algorithm performance. For example, an AUC score of 1 indicates that every tested gene ranked prior to other genes, whereas a value of 0.5 indicates that the tested genes were randomly ranked throughout the list.

Figure S6. Illustration of lncACT crosstalk network construction. The lncRNAs, miRNAs and coding-genes are colored blue, red and yellow, respectively. Their interactions are indicated by black lines. (A) Illustration of how a single lncACTs is represented. On the left panel, miRNAs can bind to lncRNA and coding gene molecules based on complementary seed sequence. The lncRNAs can compete with coding genes by sharing miRNA binding sites. This kind of competing status between different RNA molecules can be represented as nodes and edges in the network in the right panel. (B) Illustration of how the lncACT network is represented. It was assumed that lncRNAs and mRNAs in one lncACT compete for binding to miRNAs within other lncACTs (left panel). This type of crosstalk can be represented in the network by adding edges of related lncACTs (right panel). The constructed intricate transcriptional regulatory network can aid studies into how intermolecular relationships dictate cellular behavior.

Figure S7. Detailed comparison of disease-associated and other nodes. Based on topological characteristics of the network, disease-associated nodes were found to have a higher degree and betweenness centrality than other nodes.

Figure S8. A genome-wide map of 5,119 functional lncACTs based on Circos-style visualization. Outer circles indicate human chromosomes and genomic locations of lncRNAs (blue), miRNAs (red), and coding genes (yellow) of lncACTs. Lines within the circle denote pairs of miRNA-lncRNA (blue) and miRNA-gene (red) interactions. Detailed maps for each cancer are shown in the bottom panel.

Figure S9. Detailed functional comparison between different methods. (A, B) The GO terms identified by starBaseV2.0 and Linc2GO are listed on the bottom and ranked from left to right, based on the significant P-value. The GO terms identified by our method were mapped to these lists and are indicated as black bars. To investigate functional similarity, we calculated the enrichment score using a slipping window (width=100 terms, step=1 term) along the lists. In each slipping step, the enrichment score was calculated as the number of mapped GO terms/window width. The blue curve of the enrichment score was generated by slipping the window along the list. We found that GO terms identified by our method were enriched on top of the starBaseV2.0 and Linc2GO lists. (C, D) Comparison of enriched KEGG pathways (top ten) with starBaseV2.0 and Linc2GO. Pathways were indicated by red underlines if they were also identified in the top ten pathways of our method. These results indicated that starBaseV2.0 and Linc2GO identified similar functions to our method.

Figure S10. Construction of cancer-specific sub-networks. Each of 10 cancer-specific clusters (left) were converted into a sub-network as follows (right): (a) lncRNA-miRNA-mRNA interactions in the lncACT cluster were identified; (b) lncRNAs, miRNAs, and mRNAs were represented as nodes, and interactions between them were represented as edges; (c) repeated values were merged into single nodes and edges; (d) nodes and edges were used to construct a cancer-specific sub-network. Clusters 4 and 6 were integrated into the same BRCA-specific sub-network.

Figure S11. Detailed information for nine cancer-specific sub-networks. Similar to the global network, sub-networks had a layered organization, with lncRNAs (blue), miRNAs (red), and coding genes (yellow) as nodes.

Figure S12. Degree distribution of nine cancer-specific sub-networks. Similar to the global network, sub-networks presented a scale-free structure.

Figure S13. Kaplan-Meier survival analysis to test whether the HB_module can better distinguish patients than lncRNAs/miRNAs/mRNAs or combinations thereof. Survival curves of classification based on each node of the HB_module (A-N), integration of BRCA2 and miR-20b (O), H19- and BRCA1/2-associated lncACTs (P and Q, respectively), and all lncRNAs, miRNAs, and coding genes in the HB_module (R, S, and T, respectively) were generated. Patients showing no progression or who were still alive at the time of the last follow-up were censored (+). P values were calculated by the log-rank test.

Figure S14. The use of lncACTs to predict the clinical outcomes of cancer patients. The survival analysis revealed that lncACT modules could distinguish patients with different clinical outcomes in (A) BRCA, (B) BLCA, (C) LUSC, (D) LUAD, (E) UCEC and (F) KIRP.

From (A) to (F), the topological graph for each functional module is illustrated in each panel (top). The lncRNAs, miRNAs and coding-genes are colored blue, red and yellow, respectively. The expression heat map is shown on the middle panel. Highly expressed genes are shown in red, low expression genes are shown in green. A corresponding Kaplan-Meier survival plot (bottom) of the two patient subgroups, identified by hierarchical clustering of expression profiles (middle), was generated. Patients that showed no progression or who were still alive at the time of the last follow-up were censored (+). Survival days are shown along the X axis. Overall survival rates are shown along the Y axis.

Figure S15. Kaplan-Meier survival analysis of single nodes in the miR-335-associated network module. The nodes could not distinguish BRCA patients. Patients showing no progression or who were still alive at the time of the last follow-up were censored (+). P values were calculated by the log-rank test.

Figure S16. An overview of the online website framework. (1) A browse module of the database. (2) A flexible gateway to search for relevant lncACTs. (3) Functional annotation tools based on KEGG and GO for lncACTs or lncRNAs. (4) Retrieval of lncACTs based on user-provided expression profiles. (5) A built-in multi-track visualization platform that allows users to browse genome-wide lncACTs. (6) Downloading corresponding datasets. (7) Links to relevant sources of functional data. Downloadable description of the website working principles and user manual are also provided.

Figure S17. Illustration of a potential mechanism to explain the inverse expression patterns of DANCR-miR222-TCEAL1 lncACT.

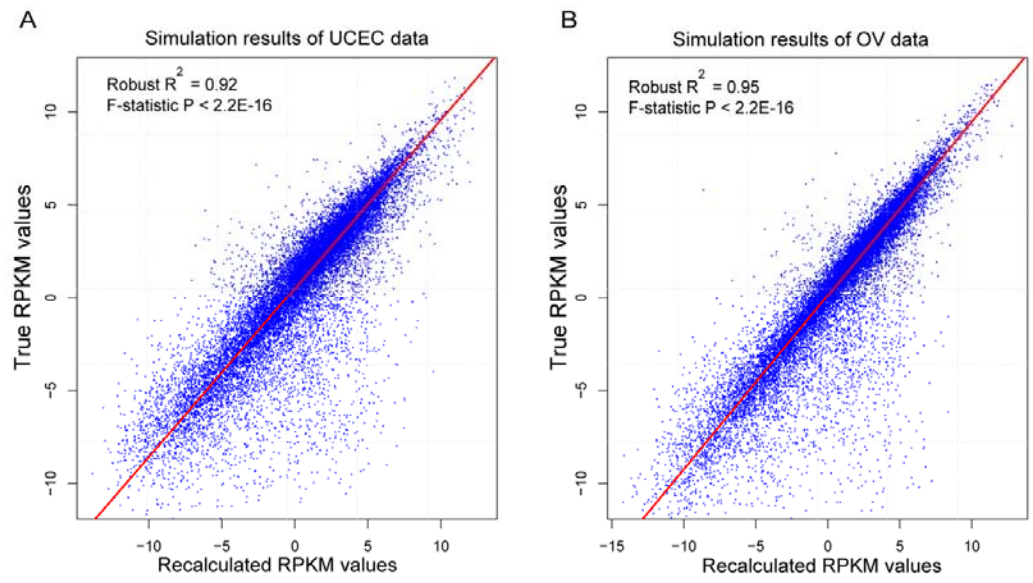


Figure S1

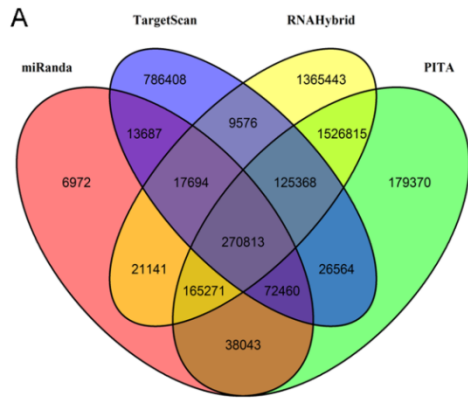


Figure S2

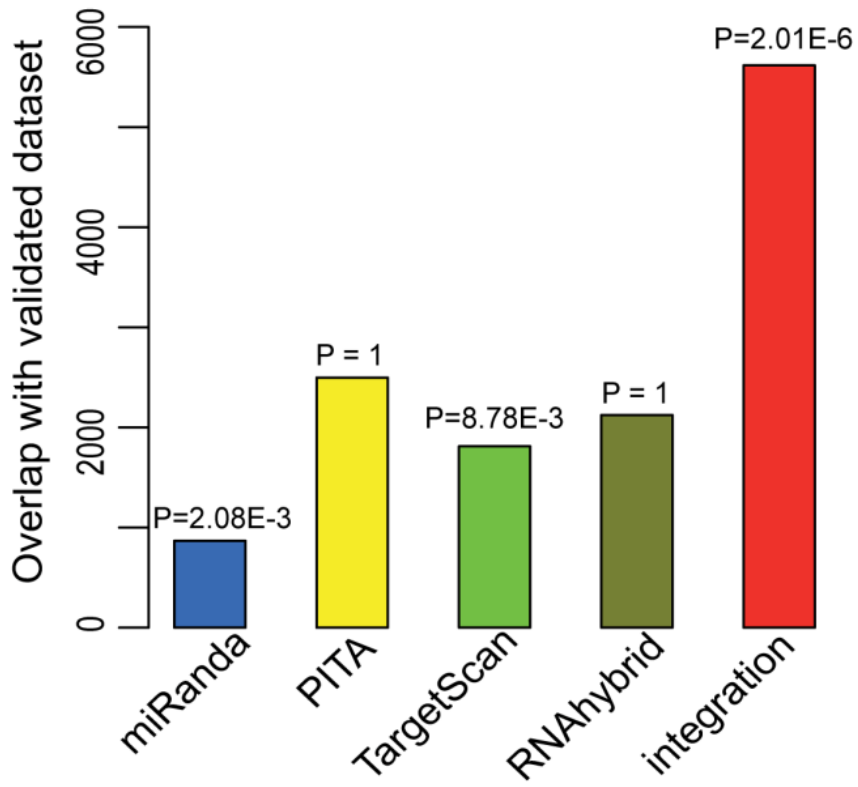


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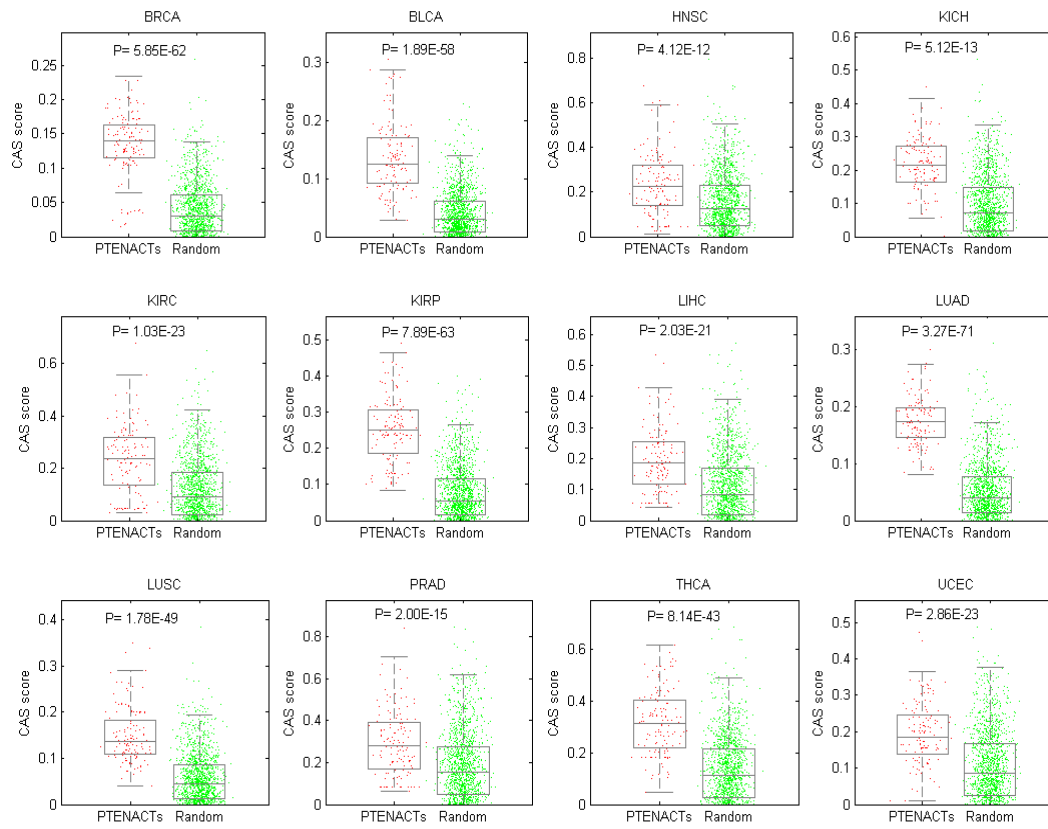


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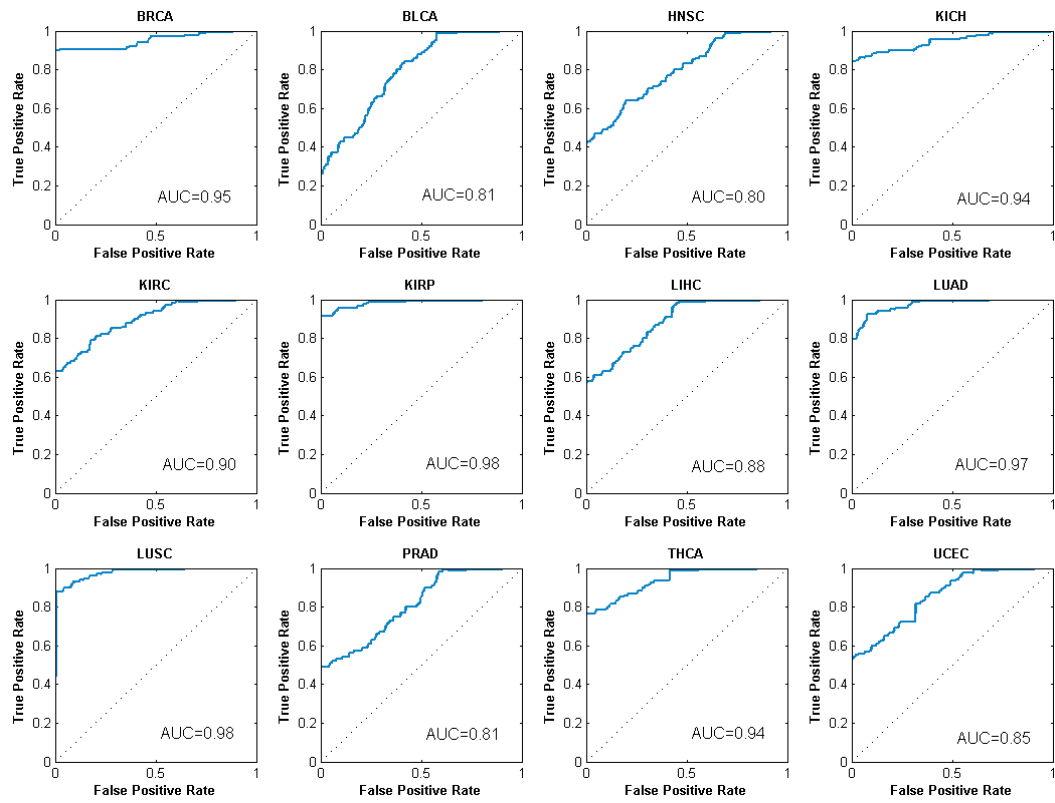


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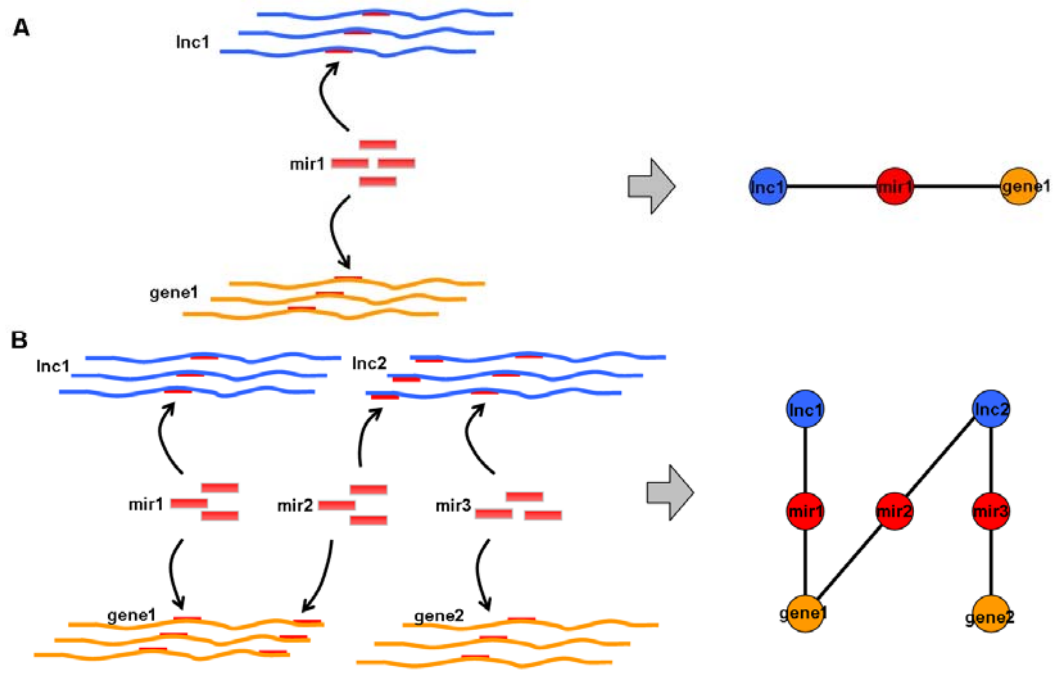


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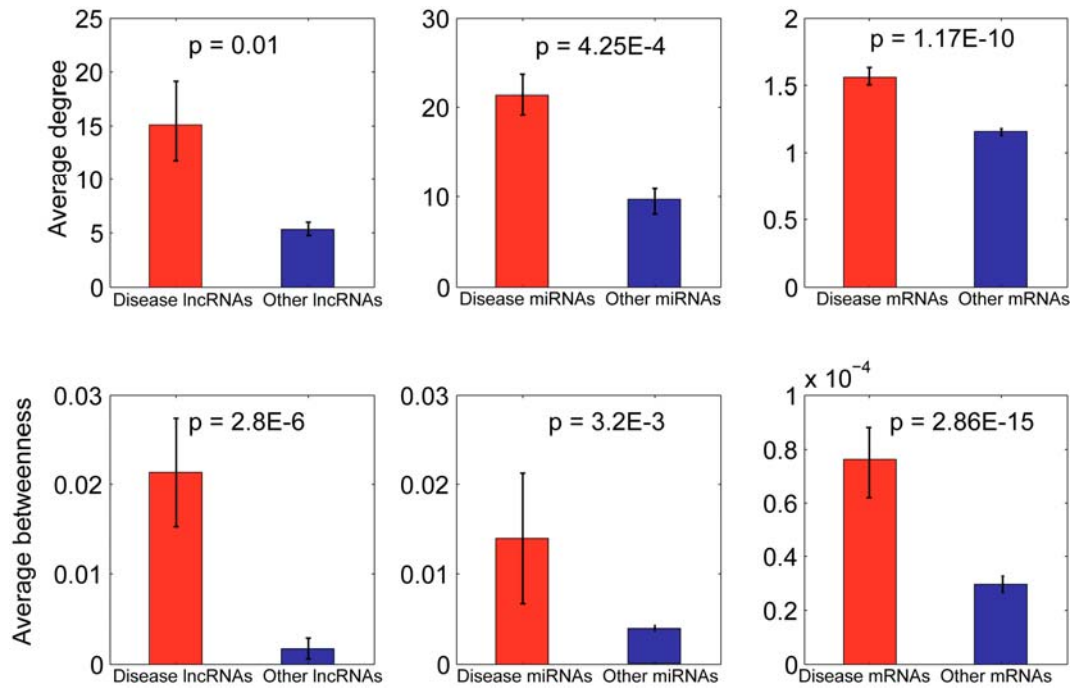


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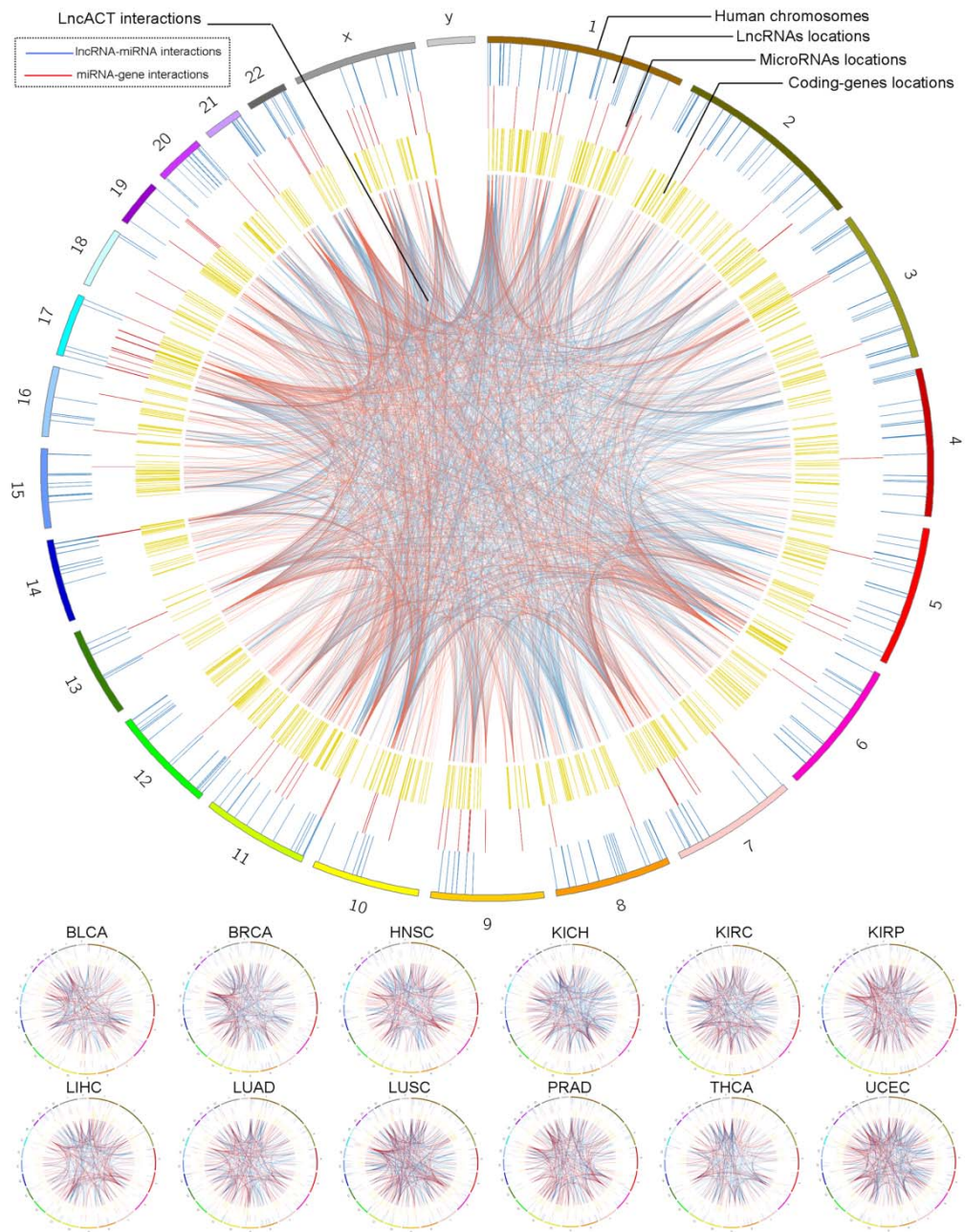


Figure S8

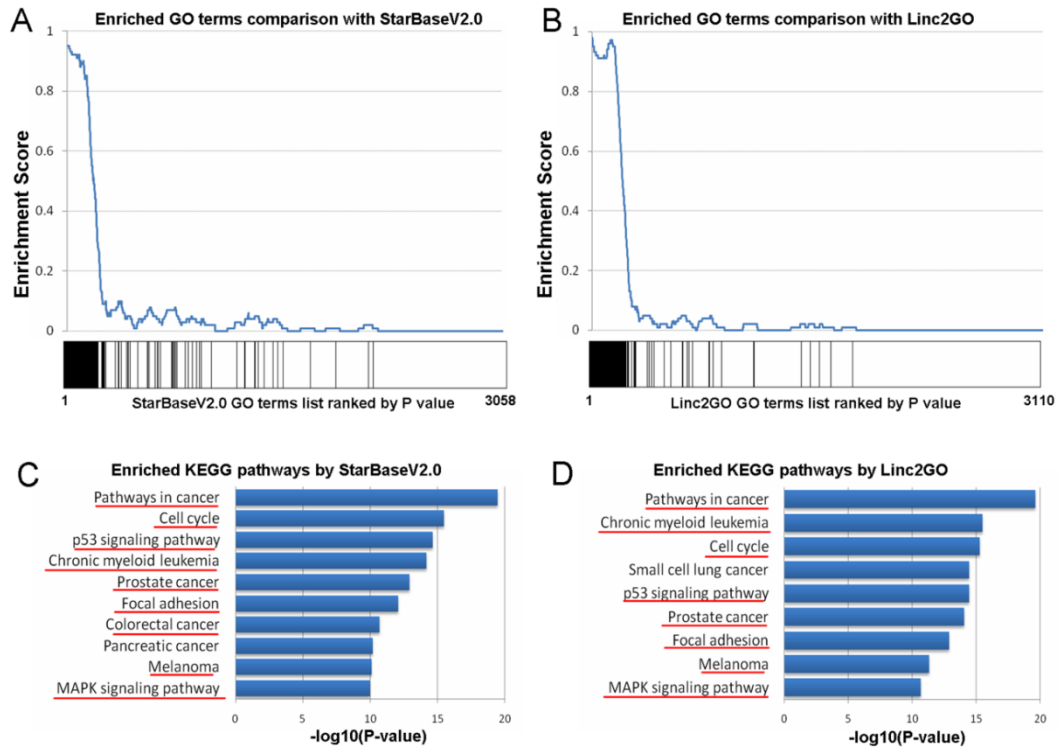


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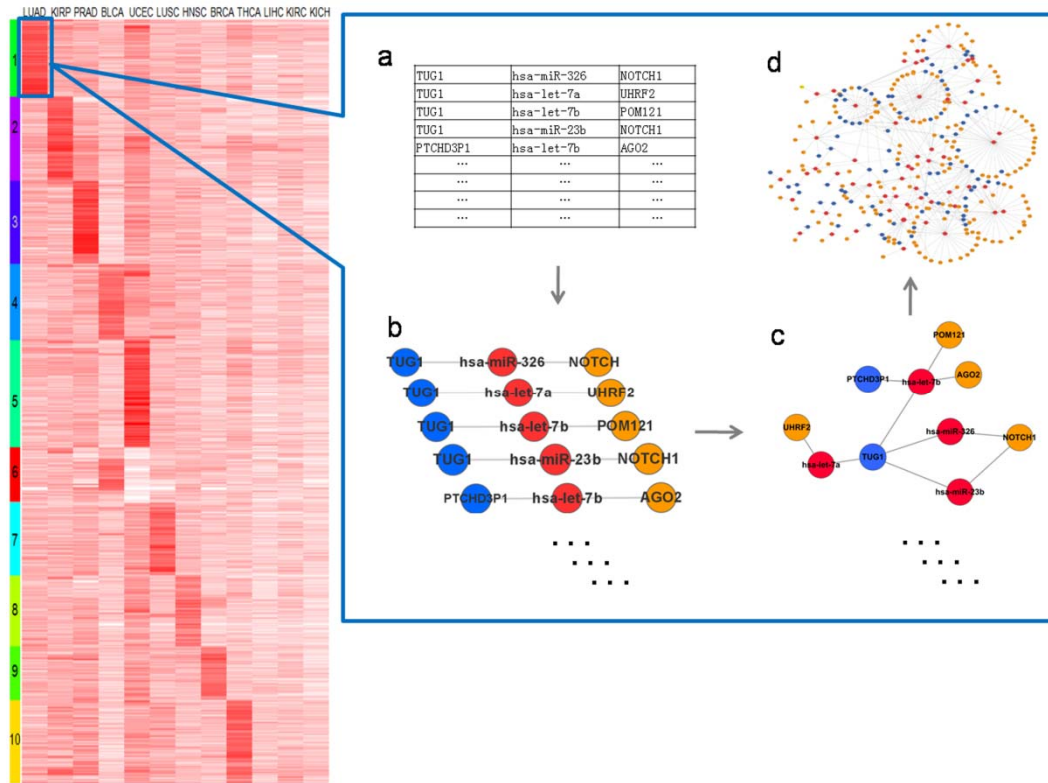


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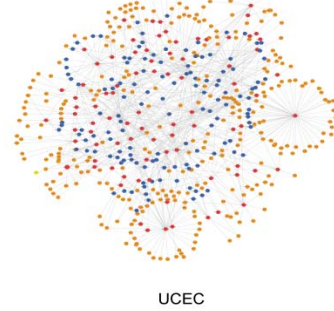
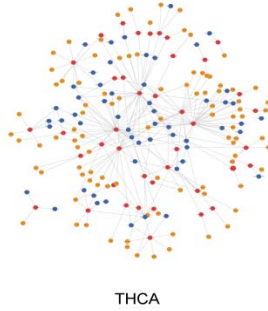
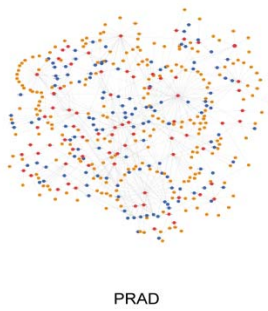
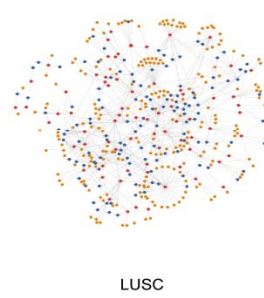
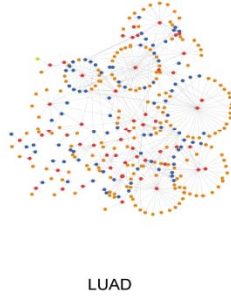
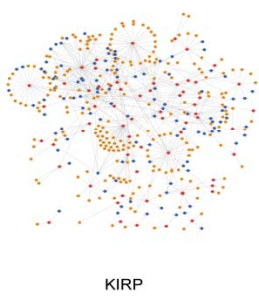
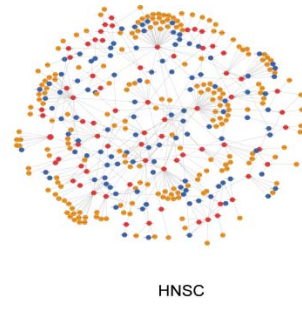
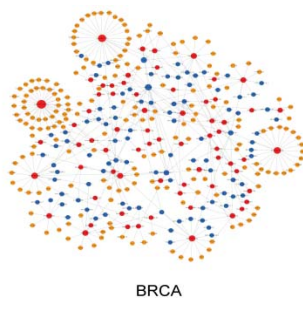
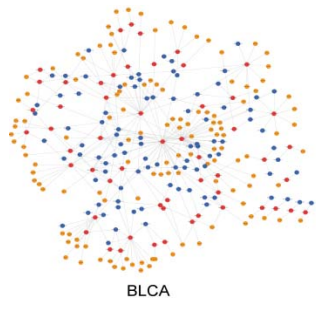


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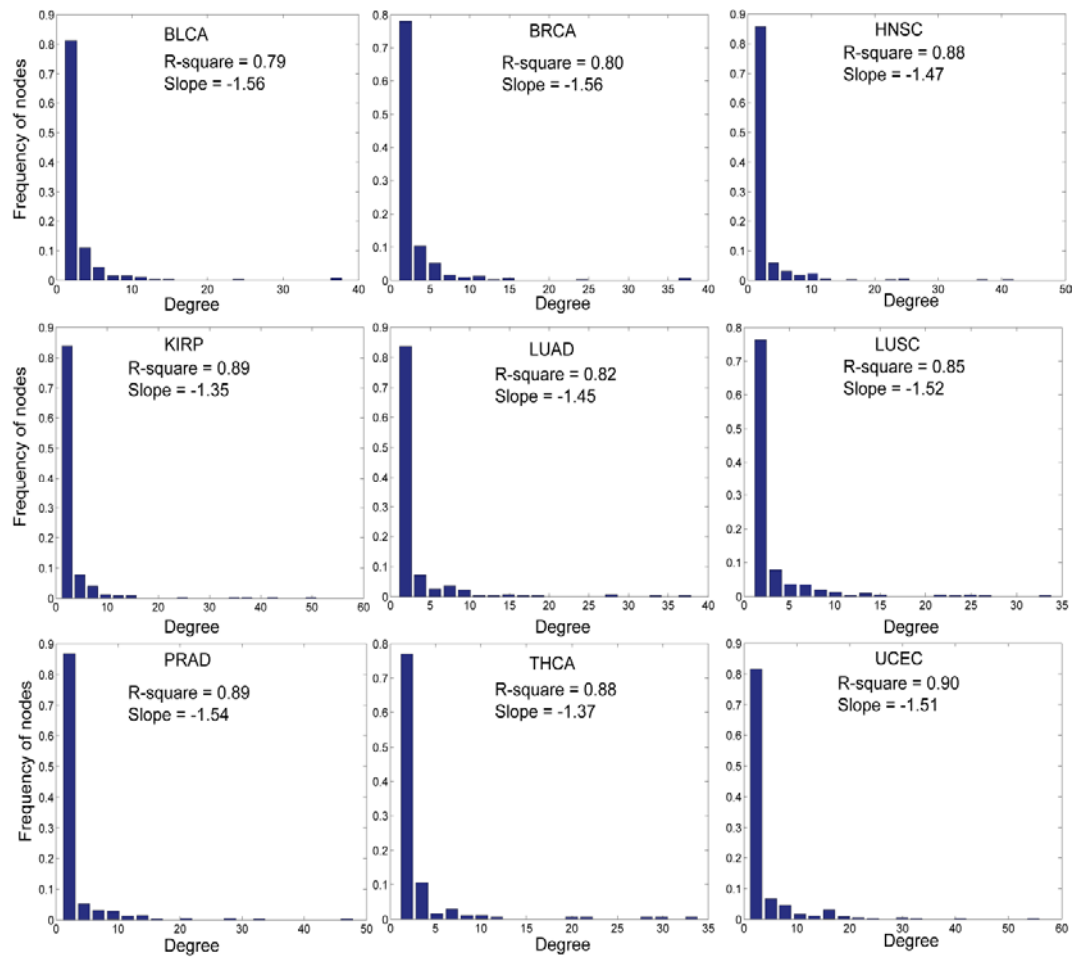


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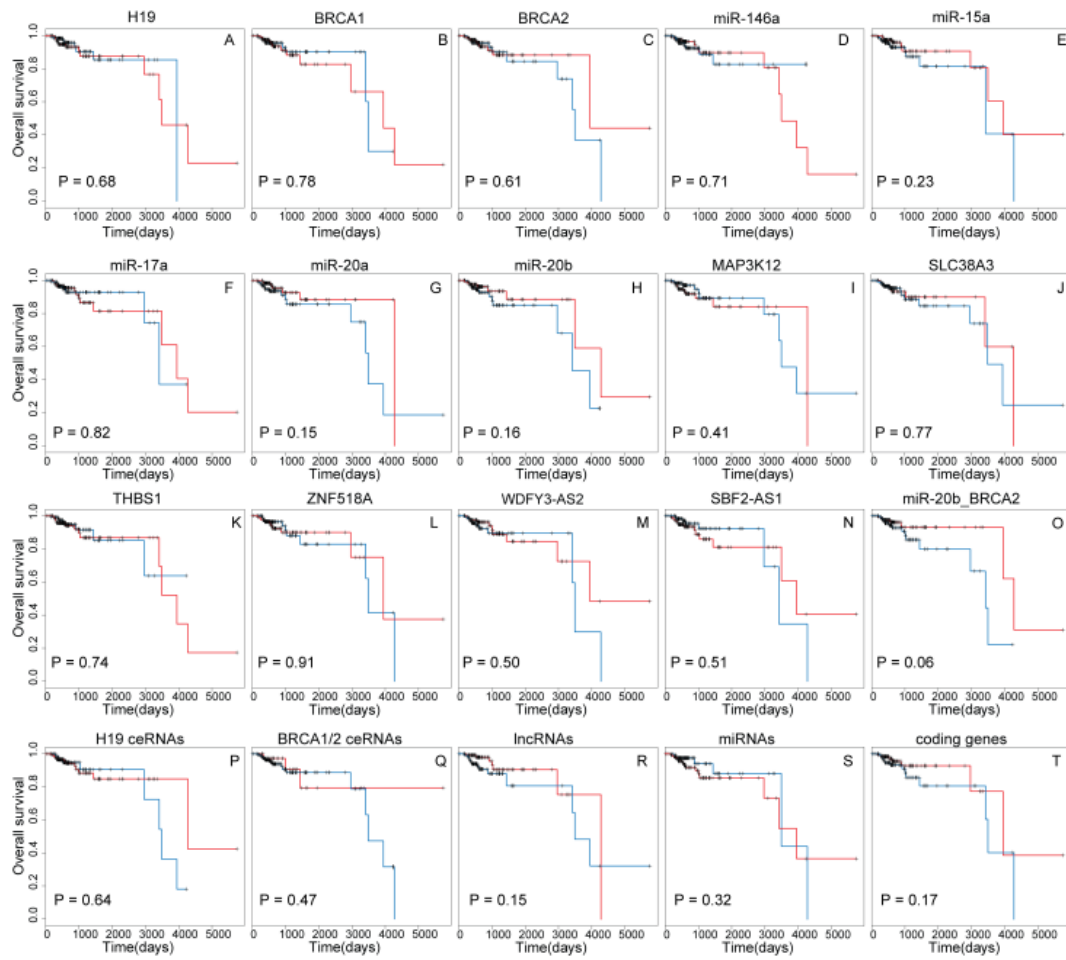


Figure S13

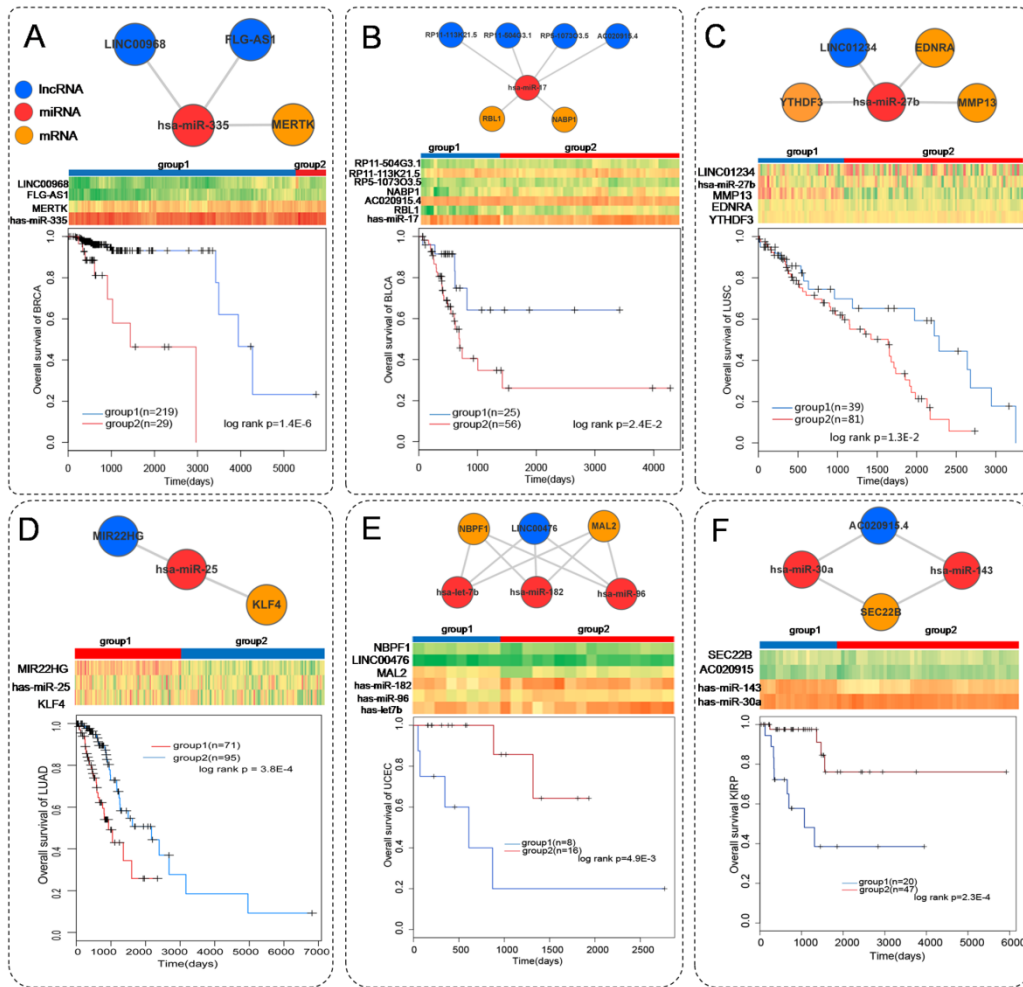


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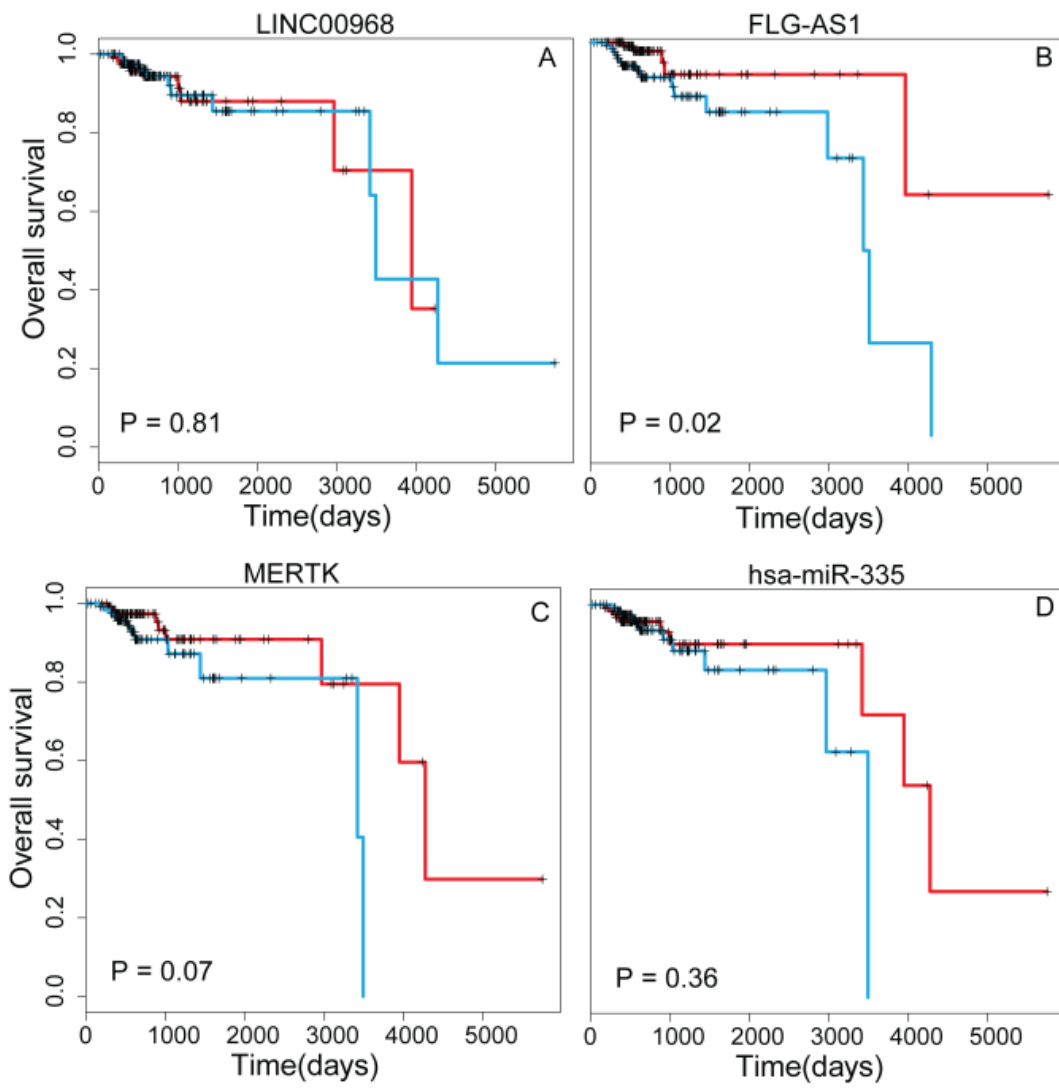


Figure S15

College of Bioinformatics Science and Technology, HBU

LncACTdb: LncRNA-associated Competing Triplets DataBase

Home Search Browse LncACTFun LncACTGet LncACTView Download Links Help

Browse by:

- 1. LncRNAs
- miRNAs
- genes
 - 2. AACS
 - AACS1
 - AACA1
 - ABC6
 - ABC1
 - ABC9
 - ABC11
 - ABC3
 - ABC4
 - ABC11
 - ABC2
 - ABC10
 - ABC11
 - ABC5
 - ABL1
 - ACA2
 - ACAM
 - ACE2
 - ACTL2
 - ACTA2
 - ACT1
 - ACT1
 - ACT1A
 - ACTB
 - ACT1
 - ACT1B
 - ACT1C
 - ACT2A
 - ADAM10

3. Quick Search for lncRNA-miRNA-Competing triplets

4. Advanced Search for lncRNA-miRNA-Competing triplets

5. Available Targets

6. DOWNLOAD

- Experimental validated miRNA targets
- Functionally activated lncACTs
- Cancer-associated lncACTs
- Long noncoding RNAs datasource

7. Experimental validated miRNA target characteristics

8. Predicted miRNA target characteristics

Figure S16

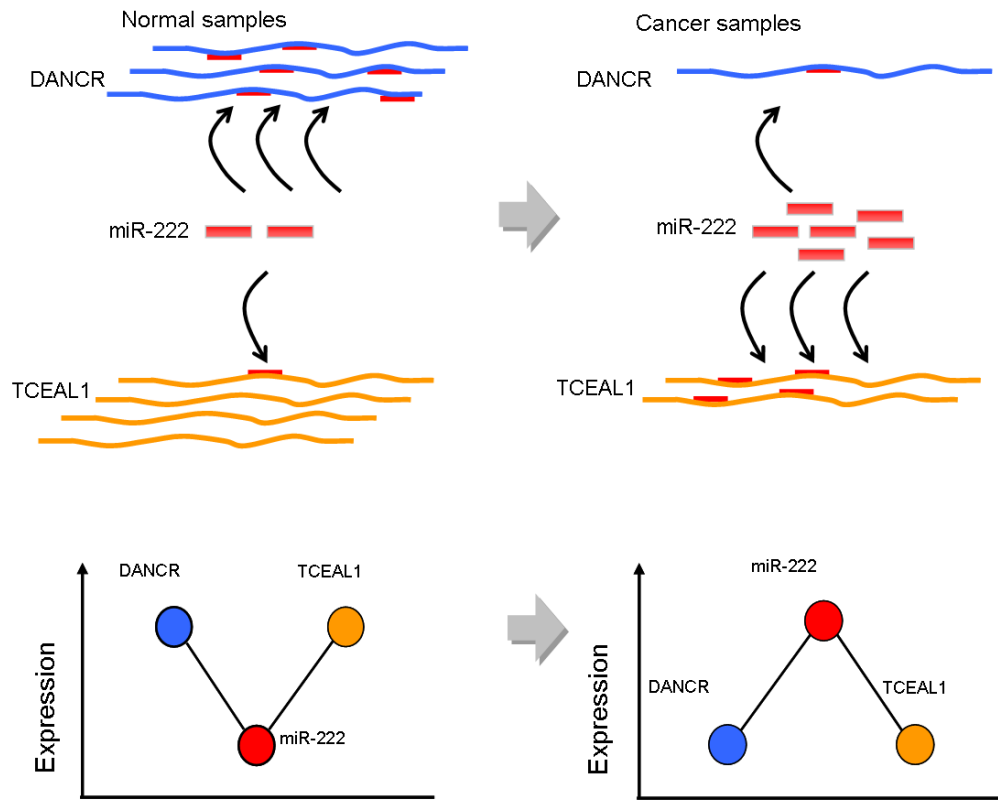


Figure S17

Supplementary Table S1. RNA sequencing data for 12 types of cancer from TCGA

Abbreviations	Cancer names	No.of samples
BLCA	Bladder Urothelial Carcinoma	81
BRCA	Breast invasive carcinoma	248
HNSC	Head and Neck squamous cell carcinoma	158
KICH	Kidney Chromophobe	50
KIRC	Kidney renal clear cell carcinoma	30
KIRP	Kidney renal papillary cell carcinoma	67
LIHC	Liver hepatocellular carcinoma	71
LUAD	Lung adenocarcinoma	166
LUSC	Lung squamous cell carcinoma	120
PRAD	Prostate adenocarcinoma	59
THCA	Thyroid carcinoma	229
UCEC	Uterine Corpus Endometrioid Carcinoma	24

Supplementary Table S2. List of lncRNAs used in this work which identified from TCGA RNA-seq data.

Ensembl ID	lncRNA Name	Ensembl ID	lncRNA Name
ENSG00000093100	XXbac-B461K10.4	ENSG00000237125	HAND2-AS1
ENSG00000100181	TPTEP1	ENSG00000237149	ZNF503-AS2
ENSG00000122043	LINC00544	ENSG00000237152	DLEU7-AS1
ENSG00000124915	DKFZP434K028	ENSG00000237159	CNTFR-AS1
ENSG00000125514	LINC00029	ENSG00000237166	AC007163.3
ENSG00000125804	FAM182A	ENSG00000237187	NR2F1-AS1
ENSG00000126005	MMP24-AS1	ENSG00000237188	RP11-337C18.8
ENSG00000129816	TTY1B	ENSG00000237212	RP11-569G13.2
ENSG00000129845	TTY1	ENSG00000237233	RP11-809M12.1
ENSG00000130600	H19	ENSG00000237248	LINC00987
ENSG00000131007	TTY9B	ENSG00000237250	RP11-193H5.1
ENSG00000131538	TTY6	ENSG00000237267	RP11-181F12.1
ENSG00000131548	TTY6B	ENSG00000237292	RP11-540K16.1
ENSG00000132204	LINC00470	ENSG00000237298	TTN-AS1
ENSG00000132832	LINC01260	ENSG00000237339	RP11-98L5.2
ENSG00000136315	RP11-84C10.2	ENSG00000237361	TUSC8
ENSG00000137808	RP11-809H16.2	ENSG00000237380	HOXD-AS2
ENSG00000142396	ERVK3-1	ENSG00000237399	PITRM1-AS1
ENSG00000145063	FLJ33534	ENSG00000237401	LINC01304
ENSG00000146666	LINC00525	ENSG00000237413	MGC27382
ENSG00000147753	TTY7	ENSG00000237438	CECR7
ENSG00000147761	TTY7B	ENSG00000237461	RP11-554F20.1
ENSG00000149656	LINC00266-1	ENSG00000237463	RP11-280O1.2
ENSG00000151303	AGAP11	ENSG00000237479	AC007557.2
ENSG00000152931	PART1	ENSG00000237484	AP000476.1
ENSG00000153363	LINC00467	ENSG00000237489	LINC00959
ENSG00000157306	THTPA	ENSG00000237499	RP11-356I2.4
ENSG00000163364	LINC01116	ENSG00000237505	PKN2-AS1
ENSG00000163597	SNHG16	ENSG00000237513	RP11-325F22.2
ENSG00000164621	SMAD5-AS1	ENSG00000237517	DGCR5
ENSG00000166770	ZNF667-AS1	ENSG00000237523	LINC00857
ENSG00000167117	LINC00483	ENSG00000237548	TTLL11-IT1
ENSG00000167355	OR51B5	ENSG00000237563	TTY21B
ENSG00000167459	LINC00905	ENSG00000237594	AP000251.3
ENSG00000167912	RP11-25K19.1	ENSG00000237596	RP13-143G15.4
ENSG00000168367	LINC00917	ENSG00000237613	FAM138A
ENSG00000170161	GLIDR	ENSG00000237637	FRY-AS1
ENSG00000170846	AC093323.3	ENSG00000237647	ERICH1-AS1
ENSG00000170919	TPT1-AS1	ENSG00000237654	AP003025.2
ENSG00000171671	SHANK2-AS3	ENSG00000237667	LINC01115
ENSG00000171889	MIR31HG	ENSG00000237675	TEX36-AS1

ENSG00000172250	SERHL	ENSG00000237686	RP5-1120P11.1
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ENSG00000173867	RP11-97O12.7	ENSG00000237742	RP11-624M8.1
ENSG00000174171	RP11-23P13.6	ENSG00000237750	AC007740.1
ENSG00000174365	SNHG11	ENSG00000237753	FLJ42351
ENSG00000174403	C20orf166-AS1	ENSG00000237803	LINC00211
ENSG00000174680	GRIK1-AS1	ENSG00000237807	RP11-400K9.4
ENSG00000175061	LRRC75A-AS1	ENSG00000237836	PHKA2-AS1
ENSG00000175147	TMEM51-AS1	ENSG00000237862	RP1-63G5.7
ENSG00000175611	LINC00476	ENSG00000237870	AC073130.1
ENSG00000175699	LINC00521	ENSG00000237914	RP11-77C3.3
ENSG00000175701	LINC00116	ENSG00000237927	RP3-393E18.2
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ENSG00000176754	LINC00303	ENSG00000237986	CELF2-AS2
ENSG00000176840	MIR7-3HG	ENSG00000238005	RP11-443B7.1
ENSG00000177112	MRV11-AS1	ENSG00000238035	AC138035.2
ENSG00000177133	LINC00982	ENSG00000238039	AF011889.2
ENSG00000177337	DLGAP1-AS1	ENSG00000238045	AC009133.12
ENSG00000177338	LINC00469	ENSG00000238062	SPATA3-AS1
ENSG00000177340	FLJ13224	ENSG00000238078	LINC01352
ENSG00000177369	FLJ40194	ENSG00000238099	RP11-12A2.3
ENSG00000177406	RP11-218M22.1	ENSG00000238113	LINC01410
ENSG00000177410	ZFAS1	ENSG00000238120	CTA-941F9.9
ENSG00000177596	RP11-512C24.3	ENSG00000238121	LINC00426
ENSG00000177640	CASC2	ENSG00000238122	RP11-483I13.2
ENSG00000177738	CTD-2201E18.3	ENSG00000238133	MLK7-AS1
ENSG00000177822	MGC45800	ENSG00000238164	RP3-395M20.8
ENSG00000178193	RP4-682C21.5	ENSG00000238184	CD81-AS1
ENSG00000178248	AP000345.1	ENSG00000238197	PAXBP1-AS1
ENSG00000178457	LINC00314	ENSG00000238198	RP11-31F15.2
ENSG00000178803	ADORA2A-AS1	ENSG00000238217	AC093590.1
ENSG00000178947	LINC00086	ENSG00000238266	LINC00707
ENSG00000178977	LINC00324	ENSG00000238268	RP11-229P13.19
ENSG00000179082	C9orf106	ENSG00000238755	RP11-23D24.2
ENSG00000179136	LINC00670	ENSG00000239219	RP11-379K17.4
ENSG00000179141	MTUS2-AS1	ENSG00000239225	TTY23
ENSG00000179406	LINC00174	ENSG00000239265	CLRN1-AS1
ENSG00000179447	RP5-1027G4.3	ENSG00000239440	RP11-260O18.1

ENSG00000179676	LINC00305	ENSG00000239482	RP11-90K6.1
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ENSG00000180846	CSNK1G2-AS1	ENSG00000239920	AC015691.13
ENSG00000180910	TTY11	ENSG00000239921	RP11-59J16.1
ENSG00000181171	FER1L6-AS1	ENSG00000239922	RP11-71N10.1
ENSG00000181211	HECW1-IT1	ENSG00000240040	AC096579.13
ENSG00000181798	LINC00471	ENSG00000240045	RP11-451G4.2
ENSG00000181995	LINC00301	ENSG00000240050	RP1-93H18.1
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ENSG00000234177	LINC01114	ENSG00000267454	ZNF582-AS1
ENSG00000234186	C16orf82	ENSG00000267465	AC011525.4
ENSG00000234199	LINC01191	ENSG00000267470	ZNF571-AS1
ENSG00000234229	RP11-308N19.4	ENSG00000267506	RP11-13K12.1
ENSG00000234264	DEPDC1-AS1	ENSG00000267532	MIR497HG
ENSG00000234277	CTD-2090I13.1	ENSG00000267535	LINC00868
ENSG00000234323	RP11-308N19.1	ENSG00000267559	RP11-383M4.6
ENSG00000234336	JAZF1-AS1	ENSG00000267575	CTC-459F4.3
ENSG00000234350	AC007405.4	ENSG00000267581	CTC-559E9.4
ENSG00000234352	MIR490	ENSG00000267586	LINC00907
ENSG00000234377	RNF219-AS1	ENSG00000267603	LINC01028

ENSG00000234380	AP000330.8	ENSG00000267606	AC006116.21
ENSG00000234384	LINC01049	ENSG00000267629	AC138430.4
ENSG00000234423	LINC01250	ENSG00000267640	CTD-2554C21.2
ENSG00000234437	RP1-206D15.3	ENSG00000267665	RP11-13K12.2
ENSG00000234449	RP11-706O15.3	ENSG00000267690	LDLRAD4-AS1
ENSG00000234456	MAGI2-AS3	ENSG00000267696	CTB-151G24.1
ENSG00000234492	RPL34-AS1	ENSG00000267698	AC002116.7
ENSG00000234497	ERICH3-AS1	ENSG00000267709	AC024592.9
ENSG00000234509	AP000253.1	ENSG00000267712	RP11-456O19.4
ENSG00000234572	AC007880.1	ENSG00000267750	AC003102.3
ENSG00000234608	MAPKAPK5-AS1	ENSG00000267761	CTD-2130O13.1
ENSG00000234636	MED14OS	ENSG00000267767	CTC-523E23.4
ENSG00000234661	CHL1-AS1	ENSG00000267779	CTC-360P9.3
ENSG00000234663	AC104820.2	ENSG00000267787	RP11-35G9.5
ENSG00000234665	RP11-262H14.3	ENSG00000267827	CTC-471J1.8
ENSG00000234684	SDCBP2-AS1	ENSG00000267858	AC016629.8
ENSG00000234688	RP1-293L6.1	ENSG00000267943	CTD-2620I22.3
ENSG00000234690	AC073283.4	ENSG00000268006	PTOV1-AS1
ENSG00000234696	GPR50-AS1	ENSG00000268038	AC011516.2
ENSG00000234736	FAM170B-AS1	ENSG00000268049	CTD-2619J13.9
ENSG00000234741	GAS5	ENSG00000268061	NAPA-AS1
ENSG00000234754	C1orf140	ENSG00000268119	CTD-2561J22.5
ENSG00000234771	RP11-395P17.3	ENSG00000268218	AC137932.4
ENSG00000234773	CTD-2666L21.1	ENSG00000268230	CTD-2619J13.8
ENSG00000234787	LINC00458	ENSG00000268240	RP11-678G14.4
ENSG00000234807	LINC01135	ENSG00000268262	CTC-246B18.8
ENSG00000234810	RP11-466L17.1	ENSG00000268362	CTD-2017D11.1
ENSG00000234817	RP3-400B16.1	ENSG00000268364	SMC5-AS1
ENSG00000234828	RP11-526A4.1	ENSG00000268388	FENDRR
ENSG00000234840	LINC01239	ENSG00000268460	DKFZp434J0226
ENSG00000234855	RP11-453E2.2	ENSG00000268516	CTD-3138B18.5
ENSG00000234859	AC003958.2	ENSG00000268530	CTC-273B12.5
ENSG00000234880	LINC00163	ENSG00000268573	RP11-158H5.7
ENSG00000234883	MIR155HG	ENSG00000268575	RP1-283E3.8
ENSG00000234899	SOX9-AS1	ENSG00000268621	AC006262.5
ENSG00000234902	AC007879.2	ENSG00000268649	MIR296
ENSG00000234912	SNHG20	ENSG00000268654	MIMT1
ENSG00000234945	GTF3C2-AS1	ENSG00000268658	LINC00664
ENSG00000234962	LINC00700	ENSG00000268751	SCGB1B2P
ENSG00000234986	XX-C2158C12.1	ENSG00000268818	CITF22-62D4.1
ENSG00000234996	RP11-480I12.7	ENSG00000268894	PLCE1-AS1
ENSG00000235016	RP11-493K19.3	ENSG00000268895	A1BG-AS1
ENSG00000235023	AP001626.2	ENSG00000269086	CTC-523E23.5
ENSG00000235026	DPP10-AS1	ENSG00000269107	RP11-15H20.7

ENSG00000235033	RP11-61I13.3	ENSG00000269110	CTC-513N18.7
ENSG00000235049	LINC00940	ENSG00000269235	HCCAT3
ENSG00000235054	RP5-1166F10.1	ENSG00000269243	CTD-2231E14.8
ENSG00000235106	LINC00094	ENSG00000269289	CTB-92J24.3
ENSG00000235118	AC010731.4	ENSG00000269293	ZSCAN16-AS1
ENSG00000235123	DSCAM-AS1	ENSG00000269386	RAB11B-AS1
ENSG00000235139	AC003984.1	ENSG00000269416	LINC01224
ENSG00000235142	RP1-60O19.1	ENSG00000269535	CTD-2525I3.6
ENSG00000235172	LINC01366	ENSG00000269604	AC005523.2
ENSG00000235244	RP11-761E20.1	ENSG00000269609	RPARP-AS1
ENSG00000235257	ITGA9-AS1	ENSG00000269640	CTD-2521M24.9
ENSG00000235295	FLJ41941	ENSG00000269696	AC007228.11
ENSG00000235304	LINC01281	ENSG00000269749	AC005614.5
ENSG00000235381	RP11-477D19.2	ENSG00000269793	AC006115.3
ENSG00000235387	LINC00961	ENSG00000269834	CTD-3018O17.3
ENSG00000235408	SNORA71B	ENSG00000269893	SNHG8
ENSG00000235412	TTY4B	ENSG00000269959	SPACA6P-AS
ENSG00000235437	LINC01278	ENSG00000269994	RP11-276H19.2
ENSG00000235453	TOPORS-AS1	ENSG00000270002	RP11-93H12.4
ENSG00000235475	LINC01372	ENSG00000270066	SCARNA2
ENSG00000235480	RP11-363D14.1	ENSG00000270246	SNORD109A
ENSG00000235481	UBE2R2-AS1	ENSG00000270279	RP4-806M20.5
ENSG00000235513	RP4-756G23.5	ENSG00000270362	HMG3-AS1
ENSG00000235527	HIPK1-AS1	ENSG00000270547	LINC01235
ENSG00000235532	LINC00402	ENSG00000270574	RP11-171I2.2
ENSG00000235535	RP11-532N4.2	ENSG00000270580	RP11-1186N24.5
ENSG00000235560	AC002310.12	ENSG00000270641	TSIX
ENSG00000235563	RP11-334A14.8	ENSG00000270726	AJ271736.10
ENSG00000235584	AC008268.1	ENSG00000271086	NAMA
ENSG00000235590	GNAS-AS1	ENSG00000271147	RP4-769N13.6
ENSG00000235597	LINC01102	ENSG00000271270	TMCC1-AS1
ENSG00000235609	AF127936.7	ENSG00000271430	RP3-368A4.5
ENSG00000235621	LINC00494	ENSG00000271593	RP11-335E6.4
ENSG00000235641	LINC00484	ENSG00000271758	RP11-35J10.5
ENSG00000235652	RP11-545I5.3	ENSG00000271762	RP11-213H15.4
ENSG00000235665	LINC00298	ENSG00000271816	BMS1P4
ENSG00000235699	CXorf51B	ENSG00000271826	PLS3-AS1
ENSG00000235703	LINC00894	ENSG00000271853	RP1-178F15.5
ENSG00000235706	DICER1-AS1	ENSG00000271880	RP11-96C23.5
ENSG00000235726	AC010148.1	ENSG00000271894	RP11-482H16.1
ENSG00000235733	RP3-522P13.3	ENSG00000272005	RP11-91J19.4
ENSG00000235740	RP11-436I24.1	ENSG00000272009	RP1-313I6.12
ENSG00000235770	LINC00607	ENSG00000272030	RP1-178F15.4
ENSG00000235831	BHLHE40-AS1	ENSG00000272053	RP11-367G6.3

ENSG00000235862	RP11-338C15.5	ENSG00000272084	RP5-1126H10.2
ENSG00000235884	LINC00941	ENSG00000272097	RP11-421M1.8
ENSG00000235885	AC023115.2	ENSG00000272140	RP11-574K11.29
ENSG00000235897	TM4SF19-AS1	ENSG00000272142	RP11-428J1.5
ENSG00000235903	CPB2-AS1	ENSG00000272154	AC005754.7
ENSG00000235914	MACROD2-AS1	ENSG00000272168	CASC15
ENSG00000235947	EGOT	ENSG00000272180	RP11-481J13.1
ENSG00000235954	TTC28-AS1	ENSG00000272259	RP11-305P22.9
ENSG00000235958	UBOX5-AS1	ENSG00000272298	RP11-386M24.8
ENSG00000235989	MORC2-AS1	ENSG00000272328	RP4-594A5.1
ENSG00000235994	RP3-470B24.5	ENSG00000272329	RP11-65L19.4
ENSG00000235997	AC109642.1	ENSG00000272446	RP1-225E12.3
ENSG00000236013	RP3-332B22.1	ENSG00000272485	RP11-284J1.1
ENSG00000236017	ASMTL-AS1	ENSG00000272508	RP11-96C23.14
ENSG00000236065	RP1-117O3.2	ENSG00000272549	RP11-351J23.2
ENSG00000236088	COX10-AS1	ENSG00000272568	CTB-113D17.1
ENSG00000236107	AC010127.3	ENSG00000272610	MAGI1-IT1
ENSG00000236133	LINC01069	ENSG00000272620	AFAP1-AS1
ENSG00000236144	AD000090.2	ENSG00000272657	AP000320.7
ENSG00000236200	KDM4A-AS1	ENSG00000272679	RP11-216L13.18
ENSG00000236268	LINC01361	ENSG00000272736	RP11-799N11.1
ENSG00000236301	MRGPRG-AS1	ENSG00000272780	RP11-822E23.8
ENSG00000236306	LINC01241	ENSG00000272801	RP1-170O19.23
ENSG00000236333	TRHDE-AS1	ENSG00000272815	RP11-219A15.4
ENSG00000236340	AC000099.1	ENSG00000272884	RP11-104H15.10
ENSG00000236366	RP11-440G9.1	ENSG00000272888	AC013394.2
ENSG00000236383	LINC00854	ENSG00000272902	RP11-299H21.1
ENSG00000236384	LINC00479	ENSG00000272917	RP11-705C15.5
ENSG00000236404	VLDLR-AS1	ENSG00000272944	CTD-2308L22.1
ENSG00000236423	LINC01134	ENSG00000272949	RP11-514P8.8
ENSG00000236432	AC097662.2	ENSG00000272975	MYHAS
ENSG00000236438	FAM157A	ENSG00000273000	KB-1572G7.2
ENSG00000236445	LINC00608	ENSG00000273018	CTD-2303H24.2
ENSG00000236449	AC018890.6	ENSG00000273065	RP11-58E21.5
ENSG00000236466	RP11-795J1.1	ENSG00000273066	RP11-216L13.19
ENSG00000236467	RP11-443A13.5	ENSG00000273112	RP11-25K21.6
ENSG00000236532	AL035610.2	ENSG00000273125	RP11-115H18.1
ENSG00000236548	STL	ENSG00000273184	RP11-212P7.3
ENSG00000236653	AC005235.1	ENSG00000273189	CTD-3148I10.15
ENSG00000236656	RP11-144L1.4	ENSG00000273299	CTB-13L3.1
ENSG00000236671	PRKG1-AS1	ENSG00000273311	DGCR11
ENSG00000236678	LINC00347	ENSG00000273313	RBAKDN
ENSG00000236700	LINC01010	ENSG00000273328	RP11-141M3.6
ENSG00000236719	OVAAL	ENSG00000273345	CTD-2410N18.4

ENSG00000236740	RP11-411K7.1	ENSG00000273409	RP11-480C22.1
ENSG00000236751	LINC01186	ENSG00000273432	RP5-1165K10.2
ENSG00000236753	MKLN1-AS	ENSG00000273471	RP13-1039J1.4
ENSG00000236780	AC078941.1	ENSG00000198788	MUC2
ENSG00000236790	LINC00299	ENSG00000206082	LINC01002
ENSG00000236810	TCEB3-AS1	ENSG00000218839	FAM138C
ENSG00000236830	CBR3-AS1	ENSG00000225489	RP11-390F4.3
ENSG00000236850	BMS1P20	ENSG00000225706	PTPRD-AS1
ENSG00000236854	AL121656.5	ENSG00000227917	RP11-143M1.3
ENSG00000236859	NIFK-AS1	ENSG00000230724	LINC01001
ENSG00000236908	RP5-1063M23.2	ENSG00000233296	AC092159.2
ENSG00000236914	RP11-1008C21.2	ENSG00000233630	FAM138F
ENSG00000236963	LINC01141	ENSG00000236404	VLDLR-AS1
ENSG00000236990	RP11-433J20.1	ENSG00000237613	FAM138A
ENSG00000237021	RP3-486I3.7	ENSG00000240859	AC093627.10
ENSG00000237037	NDUFA6-AS1	ENSG00000247095	MIR210HG
ENSG00000237048	TTY12	ENSG00000251661	RP11-326C3.11
ENSG00000237069	TTY23B	ENSG00000254815	RP11-496I9.1
ENSG00000237070	AC005550.3	ENSG00000263724	DLGAP1-AS3
ENSG00000237094	RP4-669L17.10	ENSG00000272485	RP11-284J1.1

Supplementary Table S3. List of GO terms enriched in 10 clusters (Top 10 terms for each cluster are listed).

Cluster	GO Term	Definition	P-value	FDR
cluster1	GO:0042981	regulation of apoptosis	6.10E-09	1.20E-05
cluster1	GO:43067	regulation of programmed cell death	8.00E-09	7.90E-06
cluster1	GO:0010941	regulation of cell death	8.80E-09	5.80E-06
cluster1	GO:0012501	programmed cell death	1.30E-08	6.60E-06
cluster1	GO:0008219	cell death	1.40E-08	5.60E-06
cluster1	GO:0016265	death	1.70E-08	5.50E-06
cluster1	GO:0006915	apoptosis	3.50E-08	9.90E-06
cluster1	GO:0051329	interphase of mitotic cell cycle	9.50E-08	2.40E-05
cluster1	GO:0051325	interphase	1.30E-07	2.90E-05
cluster1	GO:0051329	positive regulation of molecular function	2.50E-07	4.90E-05
cluster2	GO:0007049	cell cycle	2.10E-11	4.50E-08
cluster2	GO:0042127	regulation of cell proliferation	1.20E-10	1.30E-07
cluster2	GO:0042981	regulation of apoptosis	3.00E-09	2.10E-06
cluster2	GO:0043067	regulation of programmed cell death	3.90E-09	2.10E-06
cluster2	GO:0010941	regulation of cell death	4.30E-09	1.90E-06
cluster2	GO:0010033	response to organic substance	7.00E-09	2.50E-06
cluster2	GO:0009719	response to endogenous stimulus	1.20E-08	3.80E-06
cluster2	GO:0010604	positive regulation of macromolecule metabolic process	1.70E-08	4.60E-06
cluster2	GO:0043066	negative regulation of apoptosis	1.90E-08	4.60E-06
cluster2	GO:0043069	negative regulation of programmed cell death	2.50E-08	5.30E-06
cluster3	GO:0010604	positive regulation of macromolecule metabolic process	3.50E-11	3.60E-08
cluster3	GO:0051329	interphase of mitotic cell cycle	2.10E-10	1.50E-07
cluster3	GO:0043067	regulation of programmed cell death	3.00E-10	1.60E-07
cluster3	GO:0010941	regulation of cell death	3.40E-10	1.40E-07
cluster3	GO:0042981	regulation of apoptosis	8.00E-10	2.80E-07
cluster3	GO:0031328	positive regulation of cellular biosynthetic process	5.40E-09	1.60E-06
cluster3	GO:0009891	positive regulation of biosynthetic process	7.80E-09	2.00E-06
cluster3	GO:0043069	negative regulation of programmed cell death	1.20E-08	2.70E-06
cluster3	GO:0051726	regulation of cell cycle	1.20E-08	2.40E-06
cluster3	GO:0060548	negative regulation of cell death	1.20E-08	2.30E-06
cluster4	GO:0042981	regulation of apoptosis	1.10E-05	1.70E-02
cluster4	GO:0043067	regulation of programmed cell death	1.30E-05	1.00E-02
cluster4	GO:0010941	regulation of cell death	1.40E-05	7.10E-03
cluster4	GO:0051329	interphase of mitotic cell cycle	3.40E-05	1.20E-02
cluster4	GO:0051325	interphase	4.10E-05	1.20E-02
cluster4	GO:0007049	cell cycle	5.60E-05	1.40E-02
cluster4	GO:0043065	positive regulation of apoptosis	6.30E-05	1.30E-02
cluster4	GO:0043068	positive regulation of programmed cell death	6.90E-05	1.30E-02

cluster4	GO:0010942	positive regulation of cell death	7.20E-05	1.20E-02
cluster4	GO:0043488	regulation of mRNA stability	1.30E-04	1.80E-02
cluster5	GO:0042127	regulation of cell proliferation	7.90E-14	1.60E-10
cluster5	GO:0051325	interphase	1.40E-11	1.40E-08
cluster5	GO:0012501	programmed cell death	1.50E-11	1.00E-08
cluster5	GO:0007049	cell cycle	6.00E-11	3.10E-08
cluster5	GO:0043067	regulation of programmed cell death	6.30E-11	2.60E-08
cluster5	GO:0010941	regulation of cell death	7.10E-11	2.40E-08
cluster5	GO:0000082	G1/S transition of mitotic cell cycle	7.50E-11	2.20E-08
cluster5	GO:0010604	positive regulation of macromolecule metabolic process	9.10E-11	2.30E-08
cluster5	GO:0051329	interphase of mitotic cell cycle	1.10E-10	2.40E-08
cluster5	GO:0051726	regulation of cell cycle	1.60E-10	3.30E-08
cluster6	GO:0045944	positive regulation of transcription from RNA polymerase II promoter	3.80E-07	6.10E-04
cluster6	GO:0006974	response to DNA damage stimulus	4.10E-07	3.30E-04
cluster6	GO:0045893	positive regulation of transcription, DNA-dependent	6.40E-07	3.40E-04
cluster6	GO:0051254	positive regulation of RNA metabolic process	7.30E-07	2.90E-04
cluster6	GO:0010629	negative regulation of gene expression	1.50E-06	4.70E-04
cluster6	GO:0045934	negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	1.90E-06	4.90E-04
cluster6	GO:0007049	cell cycle	1.90E-06	4.30E-04
cluster6	GO:0010033	response to organic substance	1.90E-06	3.70E-04
cluster6	GO:0006357	regulation of transcription from RNA polymerase II promoter	2.20E-06	3.80E-04
cluster6	GO:0051172	negative regulation of nitrogen compound metabolic process	2.30E-06	3.60E-04
cluster7	GO:0045597	positive regulation of cell differentiation	6.70E-15	1.40E-11
cluster7	GO:0042127	regulation of cell proliferation	1.70E-14	1.80E-11
cluster7	GO:0051094	positive regulation of developmental process	7.60E-14	5.30E-11
cluster7	GO:0009890	negative regulation of biosynthetic process	1.00E-12	5.30E-10
cluster7	GO:0031327	negative regulation of cellular biosynthetic process	2.80E-12	1.20E-09
cluster7	GO:0043067	regulation of programmed cell death	4.40E-12	1.50E-09
cluster7	GO:0010941	regulation of cell death	4.90E-12	1.50E-09
cluster7	GO:0045934	negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	5.90E-12	1.50E-09
cluster7	GO:0010558	negative regulation of macromolecule biosynthetic process	6.90E-12	1.60E-09
cluster7	GO:0051172	negative regulation of nitrogen compound metabolic process	8.40E-12	1.80E-09
cluster8	GO:0042981	regulation of apoptosis	1.10E-17	2.50E-14
cluster8	GO:0043067	regulation of programmed cell death	1.60E-17	1.90E-14

cluster8	GO:0010941	regulation of cell death	1.90E-17	1.40E-14
cluster8	GO:0042127	regulation of cell proliferation	9.30E-16	5.00E-13
cluster8	GO:0010604	positive regulation of macromolecule metabolic process	4.20E-15	1.90E-12
cluster8	GO:0043066	negative regulation of apoptosis	3.10E-14	1.20E-11
cluster8	GO:0043069	negative regulation of programmed cell death	4.40E-14	1.40E-11
cluster8	GO:0060548	negative regulation of cell death	4.70E-14	1.30E-11
cluster8	GO:0051726	regulation of cell cycle	1.90E-12	4.90E-10
cluster8	GO:0045597	positive regulation of cell differentiation	2.00E-12	4.70E-10
cluster9	GO:0042127	regulation of cell proliferation	3.20E-15	6.50E-12
cluster9	GO:0008285	negative regulation of cell proliferation	6.10E-11	6.10E-08
cluster9	GO:0019220	regulation of phosphate metabolic process	3.80E-09	2.60E-06
cluster9	GO:0051174	regulation of phosphorus metabolic process	3.80E-09	2.60E-06
cluster9	GO:0051338	regulation of transferase activity	3.90E-09	2.00E-06
cluster9	GO:0043067	regulation of programmed cell death	8.40E-09	3.40E-06
cluster9	GO:0042325	regulation of phosphorylation	8.70E-09	2.90E-06
cluster9	GO:0010941	regulation of cell death	9.10E-09	2.60E-06
cluster9	GO:0048545	response to steroid hormone stimulus	1.10E-08	2.70E-06
cluster9	GO:0043549	regulation of kinase activity	1.10E-08	2.40E-06
cluster10	GO:0010604	positive regulation of macromolecule metabolic process	3.60E-11	5.90E-08
cluster10	GO:0051254	positive regulation of RNA metabolic process	5.40E-10	4.40E-07
cluster10	GO:0010628	positive regulation of gene expression	6.30E-10	3.40E-07
cluster10	GO:0043067	regulation of programmed cell death	1.20E-09	4.70E-07
cluster10	GO:0010941	regulation of cell death	1.30E-09	4.10E-07
cluster10	GO:0042325	regulation of phosphorylation	1.80E-09	5.00E-07
cluster10	GO:0007049	cell cycle	2.00E-09	4.70E-07
cluster10	GO:0006357	regulation of transcription from RNA polymerase II promoter	2.40E-09	4.80E-07
cluster10	GO:0045935	positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	2.60E-09	4.80E-07
cluster10	GO:0045893	positive regulation of transcription, DNA-dependent	2.80E-09	4.60E-07

Supplementary Table S4. List of KEGG pathways enriched in 10 clusters (Top 10 pathways for each cluster are listed).

Cluster	Pathway	Definition	P-value	FDR
cluster1	path:05215	Prostate cancer	3.10E-10	3.40E-08
cluster1	path:05220	Chronic myeloid leukemia	3.90E-08	2.10E-06
cluster1	path:05200	Pathways in cancer	5.20E-08	1.90E-06
cluster1	path:05214	Glioma	5.80E-08	1.60E-06
cluster1	path:05218	Melanoma	2.10E-07	4.60E-06
cluster1	path:04110	Cell cycle	2.80E-07	5.10E-06
cluster1	path:05210	Colorectal cancer	1.20E-06	1.90E-05
cluster1	path:05223	Non-small cell lung cancer	1.50E-06	2.10E-05
cluster1	path:05211	Renal cell carcinoma	1.70E-06	2.10E-05
cluster1	path:05222	Small cell lung cancer	9.10E-06	1.00E-04
cluster2	path:05200	Pathways in cancer	1.80E-12	2.20E-10
cluster2	path:05218	Melanoma	5.50E-11	3.30E-09
cluster2	path:05220	Chronic myeloid leukemia	1.30E-10	5.10E-09
cluster2	path:05214	Glioma	1.60E-09	4.80E-08
cluster2	path:05219	Bladder cancer	2.00E-09	4.90E-08
cluster2	path:05212	Pancreatic cancer	8.90E-09	1.80E-07
cluster2	path:05215	Prostate cancer	1.50E-08	2.60E-07
cluster2	path:05223	Non-small cell lung cancer	3.50E-08	5.40E-07
cluster2	path:04115	p53 signaling pathway	4.50E-08	6.00E-07
cluster2	path:05222	Small cell lung cancer	6.20E-08	7.50E-07
cluster3	path:05200	Pathways in cancer	5.60E-11	7.00E-09
cluster3	path:05215	Prostate cancer	9.60E-07	4.00E-05
cluster3	path:04110	Cell cycle	1.20E-06	3.60E-05
cluster3	path:04115	p53 signaling pathway	3.60E-06	9.00E-05
cluster3	path:05220	Chronic myeloid leukemia	9.00E-06	1.90E-04
cluster3	path:05214	Glioma	1.10E-04	1.90E-03
cluster3	path:05218	Melanoma	2.50E-04	3.40E-03
cluster3	path:04510	Focal adhesion	8.80E-04	9.10E-03
cluster3	path:04360	Axon guidance	9.00E-04	8.60E-03
cluster3	path:04010	MAPK signaling pathway	1.50E-03	1.20E-02
cluster4	path:05200	Pathways in cancer	8.40E-07	7.40E-05
cluster4	path:05215	Prostate cancer	2.20E-06	9.50E-05
cluster4	path:05218	Melanoma	3.70E-06	1.10E-04
cluster4	path:04110	Cell cycle	4.90E-06	1.10E-04
cluster4	path:05214	Glioma	1.70E-05	3.00E-04
cluster4	path:05212	Pancreatic cancer	4.10E-05	6.10E-04
cluster4	path:04520	Adherens junction	6.40E-05	8.10E-04
cluster4	path:05223	Non-small cell lung cancer	7.10E-05	7.80E-04
cluster4	path:05219	Bladder cancer	2.10E-04	2.10E-03
cluster4	path:05220	Chronic myeloid leukemia	4.50E-04	3.90E-03
cluster5	path:05200	Pathways in cancer	2.40E-17	2.80E-15

cluster5	path:05220	Chronic myeloid leukemia	1.40E-13	8.50E-12
cluster5	path:05218	Melanoma	7.40E-13	3.00E-11
cluster5	path:04110	Cell cycle	2.00E-12	6.10E-11
cluster5	path:05215	Prostate cancer	3.30E-12	8.00E-11
cluster5	path:05219	Bladder cancer	1.20E-11	2.40E-10
cluster5	path:05214	Glioma	2.00E-11	3.40E-10
cluster5	path:05223	Non-small cell lung cancer	4.10E-10	6.10E-09
cluster5	path:05222	Small cell lung cancer	1.50E-09	2.10E-08
cluster5	path:05212	Pancreatic cancer	1.70E-09	2.10E-08
cluster6	path:05210	Colorectal cancer	2.90E-09	2.70E-07
cluster6	path:04110	Cell cycle	3.10E-08	1.50E-06
cluster6	path:05220	Chronic myeloid leukemia	1.30E-07	4.20E-06
cluster6	path:05200	Pathways in cancer	2.30E-07	5.60E-06
cluster6	path:04115	p53 signaling pathway	6.20E-07	1.20E-05
cluster6	path:05223	Non-small cell lung cancer	1.10E-06	1.80E-05
cluster6	path:05212	Pancreatic cancer	1.00E-05	1.40E-04
cluster6	path:05214	Glioma	3.90E-05	4.70E-04
cluster6	path:05215	Prostate cancer	5.00E-05	5.40E-04
cluster6	path:05218	Melanoma	8.50E-05	8.10E-04
cluster7	path:05200	Pathways in cancer	3.90E-12	4.10E-10
cluster7	path:04110	Cell cycle	3.00E-11	1.60E-09
cluster7	path:05212	Pancreatic cancer	1.20E-09	4.10E-08
cluster7	path:05215	Prostate cancer	1.70E-09	4.60E-08
cluster7	path:05220	Chronic myeloid leukemia	2.00E-09	4.20E-08
cluster7	path:05219	Bladder cancer	1.40E-06	2.50E-05
cluster7	path:05222	Small cell lung cancer	5.90E-06	8.90E-05
cluster7	path:05210	Colorectal cancer	5.90E-06	8.90E-05
cluster7	path:04115	p53 signaling pathway	7.40E-06	9.70E-05
cluster7	path:04350	TGF-beta signaling pathway	8.20E-06	9.60E-05
cluster8	path:05200	Pathways in cancer	5.50E-18	5.90E-16
cluster8	path:05215	Prostate cancer	8.40E-12	4.50E-10
cluster8	path:05222	Small cell lung cancer	3.80E-11	1.40E-09
cluster8	path:05220	Chronic myeloid leukemia	7.80E-11	2.10E-09
cluster8	path:04115	p53 signaling pathway	2.30E-10	4.90E-09
cluster8	path:05210	Colorectal cancer	4.20E-10	7.60E-09
cluster8	path:05218	Melanoma	4.90E-09	7.50E-08
cluster8	path:04510	Focal adhesion	2.00E-08	2.60E-07
cluster8	path:05212	Pancreatic cancer	6.00E-08	7.10E-07
cluster8	path:04110	Cell cycle	1.20E-07	1.30E-06
cluster9	path:05200	Pathways in cancer	6.60E-13	7.40E-11
cluster9	path:04110	Cell cycle	9.10E-08	5.10E-06
cluster9	path:05215	Prostate cancer	1.60E-07	6.20E-06
cluster9	path:05212	Pancreatic cancer	2.00E-07	5.70E-06
cluster9	path:05219	Bladder cancer	3.00E-07	6.60E-06

cluster9	path:04115	p53 signaling pathway	1.30E-06	2.50E-05
cluster9	path:05220	Chronic myeloid leukemia	3.10E-06	4.90E-05
cluster9	path:05222	Small cell lung cancer	8.00E-06	1.10E-04
cluster9	path:05218	Melanoma	1.50E-04	1.80E-03
cluster9	path:05223	Non-small cell lung cancer	2.30E-04	2.60E-03
cluster10	path:05200	Pathways in cancer	4.20E-17	3.70E-15
cluster10	path:05212	Pancreatic cancer	2.30E-11	1.00E-09
cluster10	path:05215	Prostate cancer	2.50E-11	7.40E-10
cluster10	path:05220	Chronic myeloid leukemia	9.00E-09	2.00E-07
cluster10	path:04110	Cell cycle	2.60E-08	4.60E-07
cluster10	path:05222	Small cell lung cancer	3.10E-08	4.50E-07
cluster10	path:05214	Glioma	3.40E-06	4.30E-05
cluster10	path:05210	Colorectal cancer	3.40E-06	3.80E-05
cluster10	path:05211	Renal cell carcinoma	7.70E-06	7.50E-05
cluster10	path:05218	Melanoma	8.60E-06	7.50E-05

Supplementary Table S5. Univariate Cox analysis of lncRNAs/miRNAs/mRNAs in the lncACT network module of *BRCA*

Variable	HR (95% CI)	Coefficient	P-value
H19	1.17 (0.82–1.67)	0.16	3.74E-01
hsa-miR-20a	0.93 (0.60–1.44)	-0.08	7.36E-01
hsa-miR-20b	0.67 (0.49–0.90)	-0.40	8.00E-03
THBS1	1.03 (0.65–1.62)	0.03	9.05E-01
MAP3K12	0.85 (0.56–1.31)	-0.16	4.66E-01
ZNF518A	0.50 (0.25–1.02)	-0.69	5.66E-02
SLC38A3	0.92 (0.73–1.15)	-0.09	4.65E-01
hsa-miR-15a	0.59 (0.30–1.14)	-0.53	1.18E-01
hsa-miR-146a	0.98 (0.69–1.40)	-0.02	9.19E-01
BRCA1	1.11 (0.72–1.71)	0.10	6.46E-01
BRCA2	0.65 (0.43–0.99)	-0.43	4.43E-02
SBF2-AS1	0.60 (0.26–1.39)	-0.51	2.35E-01
has-miR-17	0.93 (0.67–1.31)	-0.07	6.92E-01
WDFY3-AS2	1.20 (0.79–1.81)	0.18	3.88E-01
HB_module	2.45 (1.60–3.76)	0.90	3.73E-05

Singificant P value ($P < 0.05$) was represented as bold.

The network module of all variables in the table was tested in the last line.

Supplementary Table S6. Univariate Cox analysis of lncRNAs/miRNAs/mRNAs in the miR-335-associated lncACT network module of BRCA

Variable	HR (95% CI)	Coefficient	P value
has-miR-335	1.27 (0.93–1.75)	0.24	1.36E–01
MERTK	1.46 (0.95–2.23)	0.38	8.09E–02
FLG-AS1	1.29 (0.97–1.71)	0.25	7.85E–02
LINC00968	1.22 (0.95–1.57)	0.20	1.25E–01
Network module	1.95 (1.17–3.25)	0.67	1.04E–02

Significant P value ($P < 0.05$) was represented as bold.

The network module of all variables in the table was tested in the last line.

Supplementary Table S7. List of KEGG pathways enriched among miR-335 targets (P<0.05).

Pathway	Pathway name	P-Value
path:04060	Cytokine-cytokine receptor interaction	5.49E-05
path:04020	Calcium signaling pathway	1.41E-04
path:04062	Chemokine signaling pathway	2.20E-04
path:04010	MAPK signaling pathway	2.45E-04
path:04640	Hematopoietic cell lineage	3.10E-04
path:04710	Circadian rhythm - mammal	4.78E-04
path:04512	ECM-receptor interaction	5.28E-04
path:04610	Complement and coagulation cascades	7.50E-04
path:05200	Pathways in cancer	1.50E-03
path:04970	Salivary secretion	1.85E-03
path:04920	Adipocytokine signaling pathway	2.76E-03
path:04972	Pancreatic secretion	3.64E-03
path:03320	PPAR signaling pathway	3.83E-03
path:05144	Malaria	4.03E-03
path:04360	Axon guidance	5.44E-03
path:05412	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	6.96E-03
path:04670	Leukocyte transendothelial migration	7.52E-03
path:05150	Staphylococcus aureus infection	9.48E-03
path:04350	TGF-beta signaling pathway	1.29E-02
path:05219	Bladder cancer	1.46E-02
path:05146	Amoebiasis	1.51E-02
path:05140	Leishmaniasis	1.80E-02
path:04514	Cell adhesion molecules (CAMs)	2.35E-02
path:04510	Focal adhesion	2.41E-02
path:04310	Wnt signaling pathway	2.55E-02
path:04720	Long-term potentiation	3.02E-02
path:00120	Primary bile acid biosynthesis	3.14E-02
path:05214	Glioma	3.59E-02
path:04630	Jak-STAT signaling pathway	3.67E-02
path:05020	Prion diseases	3.87E-02
path:04910	Insulin signaling pathway	4.36E-02
path:04744	Phototransduction	4.56E-02

Table S8. List of GO terms enriched among miR-335 targets ($P < 1.0E-3$).

GO Term	Name	P-Value
GO:0006695	cholesterol biosynthetic process	5.03E-06
GO:0007267	cell-cell signaling	2.64E-05
GO:0045669	positive regulation of osteoblast differentiation	5.21E-05
GO:0007160	cell-matrix adhesion	6.50E-05
GO:0030335	positive regulation of cell migration	8.32E-05
	positive regulation of transcription from RNA polymerase II promoter	
GO:0045944	promoter	1.14E-04
GO:0045907	positive regulation of vasoconstriction	2.90E-04
GO:0008285	negative regulation of cell proliferation	2.98E-04
GO:0009887	organ morphogenesis	3.70E-04
GO:0001503	ossification	4.78E-04
GO:0007586	digestion	4.83E-04
GO:0060346	bone trabecula formation	5.97E-04
GO:0051894	positive regulation of focal adhesion assembly	5.97E-04
	positive regulation of canonical Wnt receptor signaling pathway	
GO:0090263	pathway	8.26E-04
GO:0007411	axon guidance	8.76E-04
GO:0042423	catecholamine biosynthetic process	8.85E-04
GO:0001502	cartilage condensation	8.85E-04
GO:0016525	negative regulation of angiogenesis	8.91E-04
GO:0030182	neuron differentiation	9.16E-04
GO:0051046	regulation of secretion	9.31E-04

Supplementary Table S9. Univariate Cox analysis of lncRNAs/miRNAs/mRNAs and their combinations in the lncACT network across different diseases.

Disease	Variable	HR (95% CI)	Coefficient	P-value
BLCA	hsa-miR-17	1.21 (0.85–1.72)	0.19	2.88E–01
	RBL1	1.49 (1.00–2.20)	0.40	4.90E–02
	AC020915.4	0.89 (0.43–1.86)	–0.11	7.61E–01
	NABP1	1.09 (0.85–1.41)	0.09	4.86E–01
	RP5-1073O3.5	1.52 (0.85–2.72)	0.42	1.58E–01
	RP11-113K21.5	0.82 (0.52–1.31)	–0.20	4.10E–01
	RP11-504G3.1	1.79 (0.96–3.33)	0.58	6.66E–02
	Network module	1.71 (1.11–2.62)	0.53	1.42E–02
LUSC	hsa-miR-27b	0.78 (0.48–1.25)	–0.25	3.01E–01
	MMP13	0.95 (0.89–1.02)	–0.05	1.52E–01
	EDNRA	1.02 (0.84–1.25)	0.02	8.34E–01
	YTHDF3	1.30 (0.91–1.85)	0.26	1.43E–01
	LINC01234	0.98 (0.90–1.05)	–0.02	5.24E–01
	Network module	4.55 (1.59–12.95)	1.51	4.61E–03
LUAD	hsa-miR-25	1.23 (0.88–1.73)	0.21	2.21E–01
	KLF4	1.18 (0.99–1.40)	0.16	6.54E–02
	MIR22HG	0.84 (0.63–1.12)	–0.18	2.28E–01
	Network module	2.95 (1.37–6.34)	1.08	5.65E–03
UCEC	hsa-let-7b	0.66 (0.38–1.14)	–0.42	1.34E–01
	hsa-miR-96	0.43 (0.17–1.04)	–0.85	6.20E–02
	hsa-miR-182	0.58 (0.30–1.11)	–0.55	1.02E–01
	MAL2	1.79 (0.91–3.49)	0.58	8.99E–02
	LINC00476	0.54 (0.24–1.25)	–0.61	1.51E–01
	NBPF1	3.88 (1.00–15.03)	1.36	5.00E–02
	Network module	1.52 (1.12–2.07)	0.42	7.38E–03
KIRP	hsa-miR-30a	0.18 (0.06–0.56)	–1.72	2.93E–03
	hsa-miR-143	2.39 (1.34–4.26)	0.87	3.13E–03
	AC020915.4	0.39 (0.13–1.14)	–0.94	8.54E–02
	SEC22B	0.92 (0.30–2.75)	–0.09	8.74E–01
	Network module	2.20 (1.46–3.31)	0.79	1.73E–04

Singificant P value ($P < 0.05$) was represented as bold.

The network module was tested in the last line of each cancer, respectively.

Table S10. Known lncACTs involving protein-coding genes and lncRNA in our framework.

LncRNAs	Coding-genes	References
PVT1	CDH1	(5)
PVT1	TP53	(5)
PVT1	RUNX1	(5)
H19	HMGA2	(6) (7)
H19	MYCN	(8)
LINC00152	THBS1	(8)
HOTAIR	HER2	(9)

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