Figure S1. GO and KEGG analysis of downregulated DEGs. (A) GO analysis of downregulated DEGs. Gene counts are displayed on the x-axis and GO function enrichment on the y-axis. (B) KEGG analysis of downregulated DEGs. Gene counts are displayed on the x-axis and KEGG pathway analysis on the y-axis. KEGG, Kyoto Encyclopedia of Genes and Genomes; GO, Gene Ontology; DEG, differentially expressed gene; MF, molecular function; BP, biological process; CC, cellular component; PPAR, peroxisome proliferator-activated receptor; AMPK, AMP-activated protein kinase; PKG, protein kinase G.

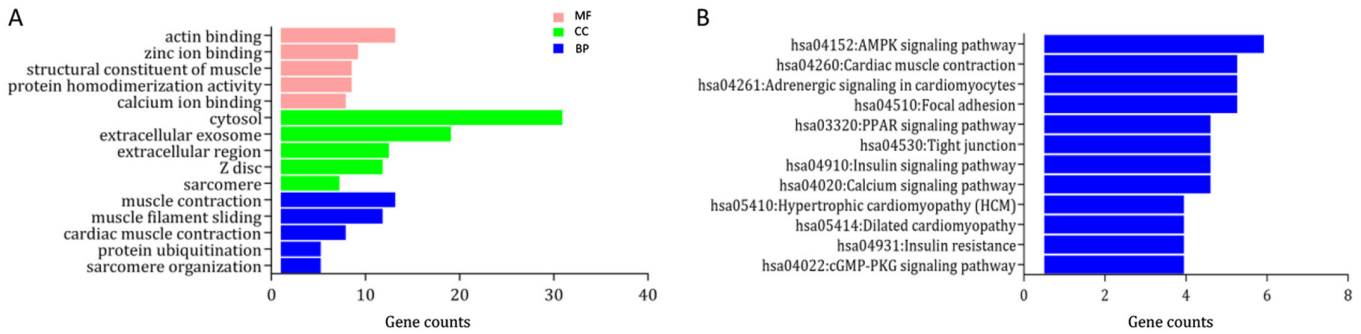

Figure S2. Protein-protein interaction networks of differentially expressed genes visualized by Cytoscape.

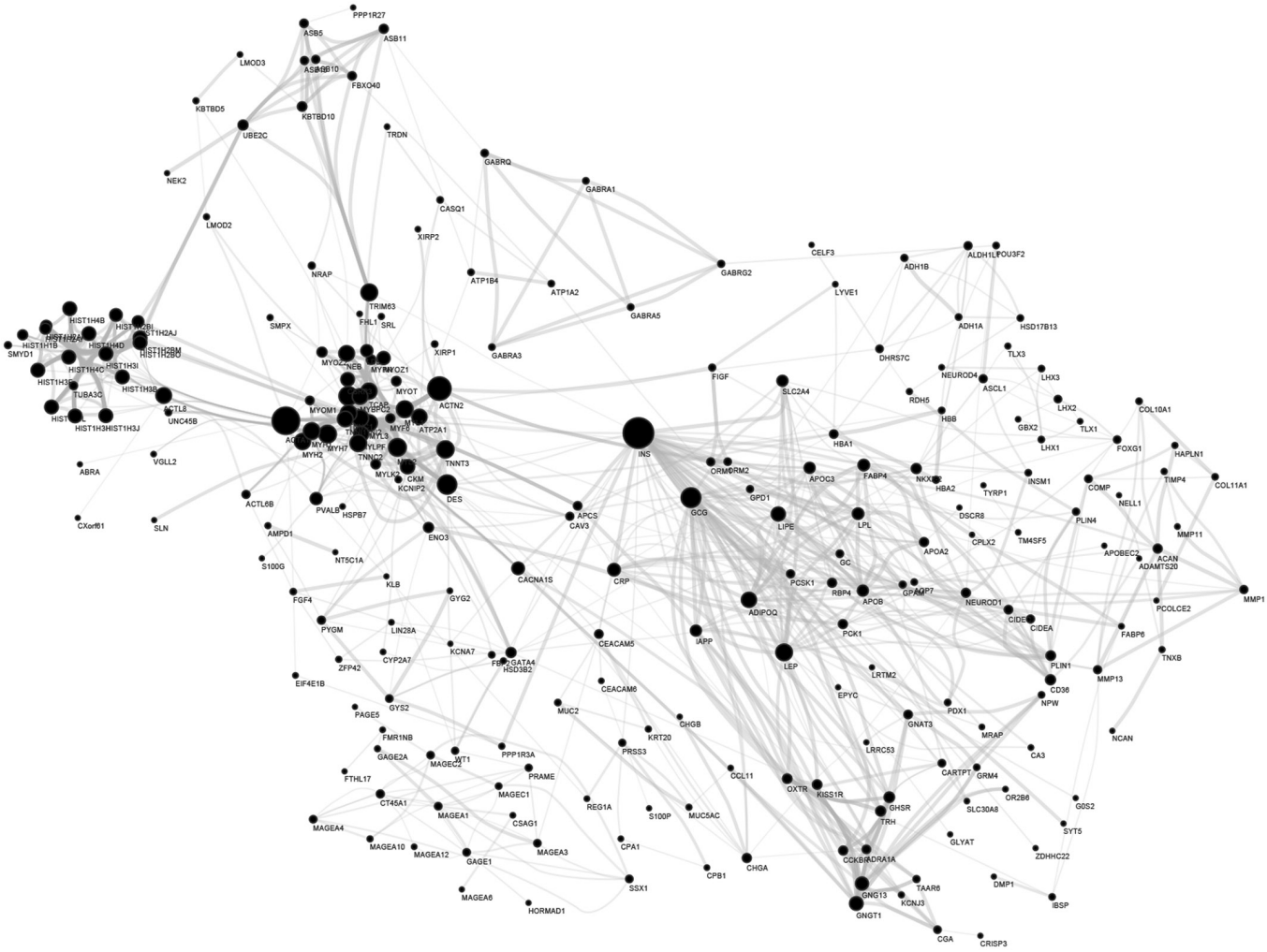

Figure S3. Violin plot of hub gene expression levels in breast cancer and normal tissues. The x-axis represents hub genes and the y-axis represents gene expression. P>0.05. HIST1, histone cluster 1.

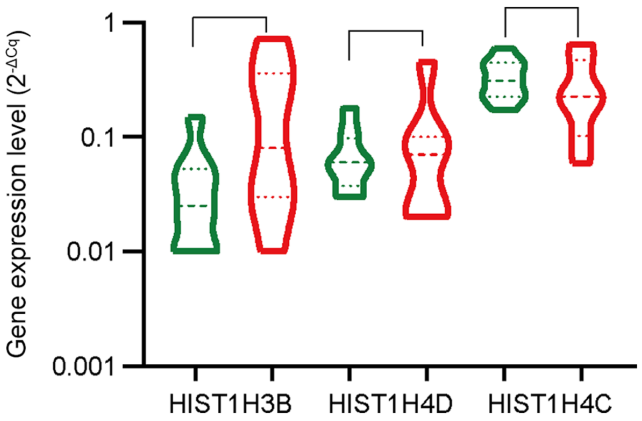

Table SI. The detail number of patients for reverse transcription-quantitative PCR.

No. of patients	Age (year)	Sex	Cancer samples	Adjacent normal samples	Pathological type
677	76	Female	T677		Invasive ductal breast carcinoma
874	64	Female	T874-1	C874-2	Invasive ductal breast carcinoma
581	66	Female	T581-1	C581-2	Invasive ductal breast carcinoma
145	65	Female	T145-1	C145-2	Invasive ductal breast carcinoma
883	58	Female	T883		Invasive ductal breast carcinoma
990	46	Female	T990		Invasive ductal breast carcinoma
926	61	Female	T926		Invasive ductal breast carcinoma

T, tumor tissues; C, normal control tissues.

Table SII. The PCR primer sequences.

Gene	Forward primer	Reverse primer
HIST1H1B	CTAAGGAGCGCAATGGCCTTT	CTTCGGAGTCTTCTTCACTGC
HIST1H2BI	GGCTATGGGGATTATGAACTCCT	CACAGCCGTTTGGATCTCC
HIST1H2BO	GACCCGGCTAAATCTGCTCC	GGCCTTGGTTACGGCTTTC
HIST1H3F	TACTGTCGCCCTCCGTGAAA	CACCAGGTAAGCCTCGCAG
HIST1H3B	ATGGCTCGTACTAAACAGACAGC	TTCCGAATCAGCAACTCGGTC
HIST1H4D	GCGGAAAGGGTCTAGGTAAGG	GCCAGAAATACGCTTGACGC
HIST1H4C	GCAAAGGCGGAAAAGGCTTG	TAGCCGGTTTTGTAATGCCCT
GAPDH	TCTCTGCTCCTCCTGTTCGA	GCGCCCAATACGACCAAATC

HIST1, histone cluster 1.

Table SIII. The genes in the most significant cluster.

Gene symbol	Full name	logFC	P-value	Degree
Upregulated				
ACTL8	Actin like 8	7.818285059	$9.78x10^{-40}$	22
HIST1H3B	Histone cluster 1 H3 family member b	5.298670758	$1.07x10^{-38}$	18
HIST1H4C	Histone cluster 1 H4 family member c	4.206544129	$5.81x10^{-28}$	18
HIST1H3J	Histone cluster 1 H3 family member j	4.262544483	$7.01x10^{-55}$	18
HIST1H3F	Histone cluster 1 H3 family member f	4.428397181	$2.74x10^{-28}$	18
HIST1H3H	Histone cluster 1 H3 family member h	4.279640468	$3.31x10^{-66}$	18
HIST1H4D	Histone cluster 1 H4 family member d	4.10449024	$5.60x10^{-41}$	18
HIST1H4B	Histone cluster 1 H4 family member b	4.262544483	$3.88x10^{-23}$	18
HIST1H4L	Histone cluster 1 H4 family member l	4.816953387	$4.25x10^{-13}$	18
HIST1H2BO	Histone cluster 1 H2B family member o	4.44351895	$4.44x10^{-57}$	18
HIST1H3I	Histone cluster 1 H3 family member i	5.341310443	$9.89x10^{-25}$	18
HIST1H2BM	Histone cluster 1 H2B family member m	4.797846435	$5.62x10^{-28}$	18
HIST1H2BI	Histone cluster 1 H2B family member i	4.121811608	$2.22x10^{-21}$	16
HIST1H2AJ	Histone cluster 1 H2A family	4.816953387	$7.95x10^{-33}$	14

	member j			
HIST1H2AI	Histone cluster 1 H2A family member i	4.705190664	$7.92x10^{-58}$	13
HIST1H2AM	Histone cluster 1 H2A family member m	4.002655119	$1.39x10^{-62}$	13
HIST1H1B	Histone cluster 1 H1 family member b	4.812539771	$3.96x10^{-31}$	11
Downregulated				
ACTA1	Actin α1, skeletal muscle	-7.036199218	0	45
ACTN2	Actinin α2	-6.01530596	$1.60x10^{-225}$	37
DES	Desmin	-4.876745382	$4.59x10^{-147}$	29
TTN	Titin	-5.116702703	0	28
MYL2	Myosin light chain 2	-8.02426588	$3.13x10^{-194}$	26
MYH7	Myosin heavy chain 7	-7.840354901	$1.33x10^{-142}$	26
TNNT3	Troponin T3, fast skeletal type	-5.25164149	$1.11x10^{-213}$	25
TNNC1	Troponin C1, slow skeletal and cardiac type	-6.207439976	0	24
TNNC2	Troponin C2, fast skeletal type	-6.415431034	0	24
MYL1	Myosin light chain 1	-7.76586129	$2.35x10^{-66}$	24
MYH1	Myosin heavy chain 1	-4.082528426	$6.13x10^{-116}$	24
TNNI2	Troponin I2, fast skeletal type	-5.011854864	$2.13x10^{-267}$	24
TCAP	Titin-cap	-4.793296142	$9.87x10^{-233}$	23
MYL3	Myosin light chain 3	-6.12393464	0	23

MYH2	Myosin heavy chain 2	-8.601067067	$2.37x10^{-302}$	23
TNNI1	Troponin I1, slow skeletal type	-5.493817731	0	22
NEB	Nebulin	-6.160388081	0	22
MYBPC2	Myosin binding protein C, fast type	-5.742647309	$4.45x10^{-253}$	22
ATP2A1	ATPase sarcoplasmic/endoplasmic reticulum Ca^{2+} transporting 1	-6.246434248	0	21
MYLPF	Myosin light chain, phosphorylatable, fast skeletal muscle	-7.025932089	0	21

Table SIV. The expression levels of hub genes in breast concer vs. normal breast tissues, data from Oncomine.

Gene	Rank	P-value	Fold-change	Reporter
HIST1H1B	353 (in top 2%)	2.01×10^{-35}	6.210	A_23_P250385
HIST1H2AJ	122 (in top 1%)	4.57×10^{-29}	3.987	A_24_P394511
HIST1H2AM	130 (in top 1%)	6.34×10^{-44}	3.079	A_23_P259547
HIST1H2BI	229 (in top 2%)	5.03×10^{-25}	3.440	A_23_P111043
HIST1H2BO	314 (in top 2%)	3.16×10^{-23}	2.885	A_23_P59069
HIST1H3B	196 (in top 1%)	4.42×10^{-26}	4.710	A_23_P93258
HIST1H3F	129 (in top 1%)	9.73×10^{-29}	2.941	A_23_P30799
HIST1H3H	78 (in top 1%)	1.47×10^{-46}	3.433	A_23_P333484
HIST1H4C	354 (in top 3%)	6.78×10^{-6}	3.658	IMAGE_1461138
HIST1H4D	1,420 (in top 8%)	3.20×10^{-13}	3.762	A_23_P395374

HIST1, histone cluster 1.

Table SV. The survival of hub genes in breast cancer patients, data from PrognoScan.

Gene	COX P-value	HR (95% CI)	Cohort	Endpoint	Dataset
HIST1H2AJ	0.002962	2.53 (1.37-4.66)	Stockholm	Overall Survival	GSE1456-GPL96
HIST1H2AM	0.019590	1.68 (1.09-2.59)	Stockholm	Overall Survival	GSE1456-GPL96
HIST1H2BI	0.019661	1.76 (1.09-2.82)	Stockholm	Overall Survival	GSE1456-GPL96
HIST1H2BO	0.016204	1.46 (1.07-2.00)	Stockholm	Overall Survival	GSE1456-GPL96
HIST1H3H	0.049099	1.32 (1.00-1.75)	Stockholm	Overall Survival	GSE1456-GPL96
HIST1H4C	0.012216	2.07 (1.17-3.64)	Duke	Overall Survival	GSE3143
HIST1H2BI	0.043480	1.63 (1.01-2.63)	Stockholm	Relapse Free Survival	GSE1456-GPL96
HIST1H2BO	0.048887	1.37 (1.00-1.87)	Stockholm	Relapse Free Survival	GSE1456-GPL96
HIST1H3H	0.026703	1.25 (1.03-1.51)	GUYT	Relapse Free Survival	GSE6532-GPL570
HIST1H4D	0.031189	2.04 (1.07-3.88)	GUYT	Relapse Free Survival	GSE6532-GPL570
HIST1H1B	0.021894	1.48 (1.06-2.07)	Mainz	Distant Metastasis	GSE11121

				Free Survival	
HIST1H3H	0.026703	1.25 (1.03-1.51)	GUYT	Distant Metastasis Free Survival	GSE6532-GPL570
HIST1H3F	0.000753	1.83 (1.29-2.60)	Mainz	Distant Metastasis Free Survival	GSE11121
HIST1H3B	0.000020	1.56 (1.27-1.91)	Mainz	Distant Metastasis Free Survival	GSE11121
HIST1H4C	0.000046	3.86 (2.02-7.41)	Mainz	Distant Metastasis Free Survival	GSE11121
HIST1H4D	0.031189	2.04 (1.07-3.88)	GUYT	Distant Metastasis Free Survival	GSE6532-GPL570

CI, confidence interval.

Table SVI. Associations between *HIST1H1B* expression and clinicopathological features in breast cancer, based on The Cancer Genome Atlas data.

Clinicopathological feature	Covariates	n	Median	P-value
Age (years)	<60	583	5.36	<0.001[a]
	≥60	508	3.83	
ER Status	Positive	592	4.07	<0.001[a]
	Negative	177	7.99	
PR Status	Positive	515	4.02	<0.001[a]
	Negative	251	7.32	
HER2 Status	Positive	109	6.88	0.003[a]
	Negative	646	4.57	
Stage	I-II	800	4.66	0.997
	III-IV	269	4.67	
T	T1-T2	674	5.15	0.032[a]
	T3-T4	174	4.17	
N	NO	509	4.57	0.632
	Yes	582	4.80	
M	NO	907	4.82	0.387
	Yes	184	3.91	

[a]P<0.05 was considered statistically significant. Nonparametric test was used to evaluate the differences between two groups with IBM SPSS Statistics V20.0 software. ER, estrogen receptor; HIST1, histone cluster 1; PR, progesterone receptor; M, metastasis; T, tumor.

Table SVII. Associations between *HIST1H2BI* expression and clinicopathological features in breast cancer, based on The Cancer Genome Atlas data

Clinicopathological features	Covariates	n	Median	P-value
Age (years)	<60	584	0.84	0.902
	≥60	508	0.86	
ER Status	Positive	591	0.95	0.047[a]
	Negative	178	0.82	
PR Status	Positive	514	0.89	0.777
	Negative	252	0.88	
HER2 Status	Positive	109	0.83	0.986
	Negative	646	0.89	
Stage	I-II	802	0.84	0.648
	III-IV	267	0.97	
T	T1-T2	639	0.85	0.738
	T3-T4	109	0.88	
N	NO	512	0.88	0.628
	Yes	580	0.84	
M	NO	907	0.85	0.384
	Yes	185	0.87	

[a]P<0.05 was considered statistically significant. Nonparametric test was used to evaluate the differences between two groups with IBM SPSS Statistics V20.0 software. ER, estrogen receptor; HIST1, histone cluster 1*;* PR, progesterone receptor; M, metastasis; T, tumor.

Table SVIII. Associations between *HIST1H2BO* expression and clinicopathological features in breast cancer, based on The Cancer Genome Atlas data

Clinicopathological features	Covariates	n	Median	P-value
Age (years)	<60	585	15.95	0.000[a]
	≥60	509	11.02	
ER Status	Positive	592	12.91	0.001[a]
	Negative	179	17.52	
PR Status	Positive	253	18.09	0.003[a]
	Negative	768	13.94	
HER2 Status	Positive	109	17.94	0.195
	Negative	648	13.44	
Stage	I-II	802	13.85	0.835
	III-IV	269	13.14	
T	T1-T2	914	13.85	0.428
	T3-T4	176	12.11	
N	NO	511	12.27	0.193
	Yes	582	14.38	
M	NO	909	14.31	0.001[a]
	Yes	184	8.88	

[a]P<0.05 was considered statistically significant. Nonparametric test was used to evaluate the differences between two groups with IBM SPSS Statistics V20.0 software. ER, estrogen receptor; PR, progesterone receptor; HIST1, histone cluster 1; PR, progesterone receptor; M, metastasis; T, tumor.

Table SIX. Associations between *HIST1H3F* expression and clinicopathological features in breast cancer, based on The Cancer Genome Atlas data

Clinicopathological features	Covariates	n	Median	P-value
Age (years)	<60	584	2.73	0.373
	≥60	504	2.58	
ER Status	Positive	587	2.74	0.220
	Negative	177	2.15	
PR Status	Positive	511	2.75	0.181
	Negative	250	2.24	
HER2 Status	Positive	108	2.23	0.684
	Negative	642	2.51	
Stage	I-II	799	2.73	0.985
	III-IV	266	2.85	
T	T1-T2	909	2.67	0.564
	T3-T4	175	2.96	
N	NO	509	2.59	0.451
	Yes	578	2.73	
M	NO	902	2.56	0.292
	Yes	185	3.09	

ER, estrogen receptor; PR, progesterone receptor; M, metastasis; T, tumor; HIST1, histone cluster 1.