

Genetic variants in histone modification regions are associated with the prognosis of lung adenocarcinoma

Hyo-Gyoung Kang^{1,2,*}, Yong Hoon Lee^{3,*}, Shin Yup Lee^{3,4}, Jin Eun Choi^{1,2}, Sook Kyung Do^{1,2}, Mi Jeong Hong^{1,2}, Jang Hyuck Lee^{1,5}, Ji Yun Jeong⁶, Young Woo Do^{4,7}, Eung Bae Lee^{4,7}, Kyung Min Shin⁸, Won Kee Lee^{9,10}, Sun Ha Choi^{3,4}, Hye won Seo³, Seung Soo Yoo^{3,4}, Jaehye Lee³, Seung Ick Cha³, Chang Ho Kim³, Sukki Cho¹¹, Sanghoon Jheon¹¹, Jae Yong Park^{1,2,3,4,5}

*These authors contributed equally to this work.

Corresponding authors

Jae Yong Park, MD, PhD, Lung Cancer Center, Kyungpook National University Chilgok Hospital, 807, Hoguk-ro, Buk-gu, Daegu 41404, Korea; Tel: +82-53-200-2631; Fax: +82-53-200-2027, E-mail: jaeyong@knu.ac.kr

Shin Yup Lee, MD, PhD, Lung Cancer Center, Kyungpook National University Chilgok Hospital, 807, Hoguk-ro, Buk-gu, Daegu 41404, Korea; Tel: +82-53-200-2632; Fax: +82-53-200-2027, E-mail: shinyup@knu.ac.kr

Supplementary Information

Supplementary Figure S1, Supplementary Table S1, S2 and S3

A.

rs17583	Score
GGCCATCGC	14.3
GGCCATTGC	11.7



YY1 motif

B.

rs4751162	Score
CAAGTGTAG	-4.4
CAGGTGTAG	7.6



TFAP4 motif

Supplementary Figure S1. Matched motifs of YY1 and TFAP4, and the predicted binding scores of rs17583 and rs4751162. The rs17583 and rs4751162 are located in the binding motifs of YY1 and TFAP4, respectively. Predicted binding scores using the HaploReg database*

*Lucas D Ward, Manolis Kellis. HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. *Nucleic Acids Res.* 2012;40:D930-4.

Supplementary Table S1. List of genotyped SNPs and analysis for overall survival and disease-free survival in the discovery study.

Polymorphism/Gene ^a			Genotype		Overall survival, <i>P</i> -value ^b			Disease Free survival, <i>P</i> -value ^b		
ID No.	Alleles	Location	MAF	HWE- <i>p</i>	Dominant	Recessive	Codominant	Dominant	Recessive	Codominant
rs17583	C>T	O	0.34	0.53	0.001	0.96	0.02	0.15	0.24	0.09
rs4751162	A>G	C	0.16	0.47	0.23	0.56	0.21	0.04	0.92	0.06
rs1529959	G>A	O	0.49	0.58	0.06	0.71	0.34	0.03	0.61	0.33
rs2601006	C>T	O	0.26	0.24	0.75	0.10	0.30	0.65	0.02	0.15
rs757228	G>A	O	0.36	0.45	0.11	0.94	0.21	0.03	0.67	0.07
rs11188272	G>C	C	0.39	0.18	0.23	0.03	0.83	0.71	0.002	0.19
rs4669	T>C	O	0.39	0.05	0.03	0.69	0.19	0.07	0.39	0.45
rs6049283	A>C	O	0.21	0.07	0.04	0.19	0.19	0.46	0.11	0.99
rs1205366	C>T	O	0.15	0.38	0.03	0.88	0.05	0.16	0.28	0.11
rs17528989	G>A	C	0.14	0.07	0.89	0.20	0.60	0.47	0.01	0.15
rs2425047	A>C	O	0.19	0.28	0.78	0.02	0.56	0.87	0.16	0.75
rs1136267	C>A	O	0.21	0.11	0.07	1.00	0.11	0.02	1.00	0.04
rs1803956	T>C	O	0.41	0.14	0.62	0.02	0.11	0.64	0.03	0.16
rs34087264	C>T	O	0.39	0.76	0.47	0.11	0.69	0.93	0.02	0.22
rs3896021	G>T	C	0.52	0.13	0.10	0.89	0.30	0.01	0.17	0.01
rs13817	G>A	C	0.35	0.48	0.05	0.11	0.02	0.89	0.68	0.77
rs2234216	T>C	O	0.36	0.30	0.92	0.003	0.13	0.53	0.23	0.90
rs6547618	G>A	C	0.37	0.67	0.33	0.03	0.06	0.99	0.15	0.43
rs6601178	G>A	C	0.47	0.61	0.01	0.05	0.01	0.02	0.25	0.03
rs2270625	C>G	O	0.26	0.21	0.01	0.20	0.01	0.31	0.79	0.37
rs17122154	A>G	O	0.44	0.39	0.47	0.59	0.88	0.04	0.43	0.07
rs2548551	T>G	C	0.13	0.41	0.22	0.25	0.16	0.67	0.0003	0.22
rs10139029	A>G	O	0.19	0.09	0.03	0.53	0.05	0.78	0.82	0.75
rs665306	T>C	O	0.34	0.75	0.08	0.08	0.03	0.71	0.84	0.85
rs1010222	G>A	O	0.13	0.71	0.34	0.11	0.20	0.84	0.01	0.44
rs2271446	C>T	O	0.27	0.46	0.04	0.26	0.05	0.07	0.50	0.10
rs3825625	C>T	O	0.15	0.85	0.03	0.63	0.04	0.11	0.51	0.10
rs7513326	G>A	C	0.43	0.10	0.12	0.01	0.01	0.55	0.04	0.14
rs772254	C>T	O	0.21	0.14	0.02	0.39	0.03	0.09	0.29	0.08
rs11668444	G>T	C	0.18	0.30	0.09	0.02	0.02	0.38	0.29	0.27
rs1279738	C>G	C	0.46	0.63	0.001	0.004	0.0002	0.02	0.04	0.01
rs2075588	A>C	O	0.29	0.19	0.09	0.27	0.06	0.31	0.03	0.11
rs3806192	G>C	O	0.19	0.05	0.46	0.99	0.57	0.01	0.98	0.03
rs843346	C>T	O	0.37	0.13	0.94	0.01	0.09	0.65	0.01	0.11
rs1242095	A>C	O	0.36	1.00	0.55	0.03	0.15	0.07	0.01	0.01
rs2292807	T>C	O	0.44	0.94	0.70	0.03	0.29	0.31	0.16	0.88
rs6679	T>C	C	0.43	0.56	0.40	0.64	0.75	0.04	0.38	0.06
rs11809443	T>C	C	0.22	0.28	0.50	0.05	0.15	0.87	0.25	0.56

rs2271541	T>G	O	0.41	0.68	0.03	0.11	0.51	0.06	0.17	0.57
rs3813521	C>T	C	0.29	0.60	0.01	0.08	0.01	0.18	0.21	0.11
rs7897156	C>T	O	0.33	0.28	0.03	0.03	0.01	0.07	0.02	0.02
rs4713599	A>C	O	0.10	0.63	0.79	0.26	0.63	0.79	0.42	0.92
rs2295778	C>G	C	0.29	0.59	0.22	0.90	0.38	0.22	0.42	0.59
rs7631002	T>C	O	0.11	0.53	0.91	0.27	0.70	0.83	0.18	0.47
rs1053639	A>T	O	0.17	0.34	0.31	0.56	0.28	0.35	0.52	0.31
rs3806408	C>A	C	0.30	0.15	0.46	0.05	0.14	0.73	0.13	0.32
rs3767199	G>T	O	0.09	0.73	0.19	0.24	0.13	0.92	0.33	0.94
rs10859966	C>T	O	0.42	0.31	0.75	0.68	0.98	0.47	0.84	0.72
rs1351383	A>C	C	0.39	0.27	0.33	0.15	0.87	0.43	0.16	0.19
rs3986354	C>T	O	0.46	0.16	0.68	0.34	0.77	0.12	0.66	0.47
rs2958153	G>A	O	0.29	0.77	0.86	0.87	0.94	0.98	0.88	0.96
rs479572	C>G	O	0.09	0.73	0.24	0.99	0.24	0.32	0.99	0.29
rs2284190	T>C	C	0.18	0.49	0.86	0.99	0.56	0.53	0.30	0.88
rs1064585	T>G	O	0.16	0.38	0.86	0.66	0.76	0.93	0.29	0.61
rs2819360	C>T	O	0.44	0.66	0.89	0.46	0.61	0.58	0.44	0.42
rs3755140	C>T	O	0.20	0.41	0.16	0.38	0.24	0.13	0.42	0.11
rs6671141	T>G	O	0.36	0.37	0.66	0.96	0.73	0.72	0.68	0.97
rs4324103	G>A	C	0.43	0.16	0.95	0.68	0.79	0.23	0.20	0.13
rs3812445	A>G	C	0.10	0.06	0.98	0.59	0.87	0.14	0.71	0.18
rs11823704	C>A	O	0.14	0.06	0.42	0.53	0.38	0.15	0.96	0.26
rs2070626	T>C	O	0.47	0.91	0.37	0.54	0.36	0.14	0.67	0.24
rs7942159	A>G	C	0.35	0.90	0.15	0.23	0.10	0.25	0.66	0.28
rs5750508	C>T	C	0.44	0.46	0.37	0.26	0.94	0.19	0.94	0.38
rs13624	T>C	O	0.14	0.41	0.09	0.99	0.36	0.58	0.28	0.94
rs3821321	G>A	O	0.42	0.41	0.64	0.90	0.69	0.21	0.34	0.16
rs4645287	A>C	O	0.57	0.40	0.27	0.81	0.64	0.70	0.97	0.81
rs1461957	G>T	O	0.17	0.35	0.83	0.82	0.80	0.99	0.64	0.88
rs3829051	T>C	O	0.31	0.34	0.39	0.24	0.94	0.20	0.12	0.88
rs734380	T>G	O	0.40	0.10	0.81	0.72	0.98	0.87	0.50	0.84
rs2282694	G>A	O	0.34	0.06	0.53	0.29	0.34	0.82	0.55	0.66
rs2748240	G>A	O	0.42	0.06	0.32	0.32	0.92	0.33	0.55	0.75
rs613924	T>C	C	0.42	0.97	0.15	0.99	0.33	0.50	0.79	0.76
rs2908543	T>A	O	0.33	0.97	0.05	0.41	0.06	0.40	0.34	0.28
rs2288834	G>A	O	0.40	0.56	0.55	0.34	0.35	0.76	0.99	0.84
rs3760109	G>T	O	0.20	0.48	0.34	0.38	0.63	0.27	0.55	0.51
rs11102516	G>A	C	0.42	0.38	0.83	0.30	0.64	0.82	0.41	0.54
rs7314442	G>A	C	0.22	0.38	0.36	0.86	0.41	0.99	0.41	0.78
rs9700928	C>A	O	0.43	0.27	0.73	0.52	0.57	0.66	0.76	0.65
rs3827723	A>G	O	0.36	0.23	0.43	0.41	0.88	0.29	0.33	0.82
rs2857681	C>G	C	0.33	0.11	0.64	0.17	0.38	0.46	0.61	0.68

rs2913861	T>C	C	0.20	0.07	0.47	0.43	0.38	0.92	0.43	0.68
rs2297480	G>T	O	0.22	0.06	0.62	0.87	0.75	0.81	0.69	0.98
rs3738037	C>A	O	0.08	0.06	0.89	0.74	0.99	0.91	0.83	0.87
rs12434539	A>G	O	0.34	0.05	0.66	0.63	0.58	0.58	0.57	0.50
rs10877028	G>T	C	0.18	0.97	0.13	0.33	0.30	0.17	0.44	0.32
rs866484	C>G	O	0.28	0.81	0.25	0.44	0.23	0.35	0.43	0.29
rs2913856	A>G	O	0.43	0.47	0.35	0.91	0.60	0.99	0.73	0.85
rs7071351	C>A	O	0.47	0.45	0.45	0.58	0.42	0.99	0.31	0.54
rs7648309	G>A	O	0.37	0.37	0.76	0.83	0.90	0.27	0.50	0.26
rs284573	C>G	O	0.14	0.28	0.82	0.90	0.88	0.41	0.47	0.62
rs7089806	C>G	O	0.15	0.17	0.81	0.75	0.76	0.59	0.88	0.71
rs2072236	C>T	O	0.12	0.10	0.23		0.23	0.64		0.64
rs7948073	T>G	O	0.24	0.08	0.15	0.42	0.16	0.59	0.25	0.38
rs7926547	C>G	O	0.39	0.06	0.20	0.30	0.17	0.67	0.63	0.59
rs17629719	T>G	O	0.19	0.98	0.77	0.07	0.44	0.48	0.53	0.42
rs7117343	C>G	O	0.28	0.83	0.58	0.32	0.38	0.84	0.28	0.52
rs12452627	G>A	O	0.15	0.82	0.88	0.28	0.66	0.56	0.72	0.67
rs2712429	C>A	O	0.14	0.52	0.84	0.51	0.97	0.60	0.44	0.48
rs549794	A>G	O	0.32	0.19	0.59	0.33	0.40	0.17	1.00	0.31
rs2403279	C>A	O	0.36	0.17	0.18	0.83	0.27	0.21	0.70	0.27
rs28407517	C>T	O	0.34	0.16	0.92	0.62	0.76	0.25	0.95	0.40
rs1043968	C>G	C	0.18	0.12	0.35	0.46	0.69	0.88	0.84	0.96
rs10876254	A>G	O	0.49	0.07	0.88	0.22	0.41	0.73	0.90	0.90
rs7073334	C>T	O	0.16	0.07	0.79	0.81	0.76	0.61	0.80	0.76
rs158366	C>G	O	0.36	0.98	0.67	0.18	0.70	0.89	0.38	0.73
rs6502051	A>C	C	0.09	0.69	0.95	0.99	0.71	0.93	0.98	0.76
rs1122731	G>A	O	0.20	0.59	0.74	0.99	0.98	0.45	0.99	0.26
rs10149569	A>C	O	0.11	0.49	0.82	0.99	0.78	0.45	0.99	0.39
rs10840108	T>C	O	0.35	0.45	0.36	0.13	0.15	0.40	0.32	0.28
rs2272532	A>G	O	0.22	0.43	0.68	0.81	0.67	0.96	0.60	0.87
rs13167616	G>C	O	0.13	0.29	0.97	0.71	0.87	0.40	0.41	0.69
rs34291864	G>T	O	0.18	0.25	0.58	0.87	0.59	0.28	0.35	0.22
rs10781517	C>T	O	0.14	0.24	0.33	0.31	0.67	0.41	0.50	0.65
rs2240275	G>A	C	0.41	0.23	0.65	0.45	0.96	0.71	0.32	0.44
rs2227562	G>A	O	0.34	0.17	0.68	0.47	0.52	0.12	0.16	0.07
rs2071391	A>G	O	0.47	0.16	0.44	0.40	0.34	0.58	0.63	0.53
rs2247322	T>A	O	0.35	0.15	0.94	0.68	0.80	0.50	0.53	0.43
rs3750997	A>C	O	0.47	0.14	0.70	0.94	0.77	0.31	0.17	0.14
rs12609068	A>T	C	0.28	0.11	0.84	0.46	0.63	0.93	0.26	0.58
rs580808	C>T	O	0.17	0.08	0.18	0.98	0.10	0.53	0.18	0.30
rs1976700	G>C	O	0.45	0.07	0.11	0.68	0.43	0.07	0.44	0.11
rs3809112	C>T	C	0.30	0.06	0.13	0.72	0.22	0.30	0.33	0.23

rs839763	T>C	O	0.14	0.05	0.85	0.64	0.99	0.47	0.44	0.80
rs625750	C>T	O	0.37	0.84	0.39	0.88	0.58	0.16	0.50	0.51
rs3827550	C>G	C	0.33	0.69	0.79	0.86	0.78	0.94	0.34	0.63
rs2954657	C>T	O	0.28	0.67	0.27	0.69	0.29	0.41	0.32	0.81
rs3849682	G>A	O	0.25	0.53	0.99	0.44	0.77	0.40	0.34	0.29
rs4645943	C>T	O	0.28	0.51	0.53	0.38	0.38	0.75	0.88	0.75
rs929953	A>G	O	0.35	0.34	0.76	0.32	0.78	0.30	0.31	0.22
rs10747783	C>T	O	0.27	0.26	0.61	0.85	0.78	0.64	0.81	0.81
rs1889532	G>A	O	0.14	0.25	0.47	0.42	0.69	0.55	1.00	0.60
rs3757672	T>C	O	0.11	0.10	0.41	0.74	0.41	0.69	0.16	0.48
rs629426	A>G	O	0.20	0.07	0.31	0.96	0.42	0.97	0.44	0.77
rs4135159	A>C	O	0.42	0.06	0.12	0.27	0.10	0.78	0.28	0.44
rs7366009	A>G	O	0.21	0.05	0.33	0.60	0.34	0.64	0.49	0.51
rs1567583	G>T	C	0.08	0.93	0.13	0.99	0.57	0.44	0.99	0.95
rs31726	A>G	C	0.43	0.91	0.31	0.44	0.28	0.11	0.90	0.34
rs3741440	C>T	O	0.07	0.71	0.88	0.99	0.86	0.09	0.99	0.12
rs2070912	A>G	O	0.13	0.63	0.88	0.99	1.00	0.84	0.38	0.74
rs3803800	G>A	C	0.34	0.48	0.91	0.51	0.69	0.31	0.36	0.75
rs1723285	G>A	O	0.14	0.47	0.29	0.99	0.23	0.37	0.79	0.37
rs2291617	G>T	C	0.27	0.22	0.20	0.75	0.28	0.35	0.63	0.36
rs2735784	A>G	O	0.43	0.88	0.79	0.90	0.80	0.37	0.84	0.48
rs2273913	T>C	C	0.47	0.84	0.70	0.48	0.85	0.96	0.20	0.42
rs1002193	C>G	O	0.34	0.84	0.41	0.22	0.21	0.13	0.28	0.10
rs4148879	G>A	C	0.17	0.84	0.43	0.24	0.30	0.34	0.24	0.23
rs3813570	T>C	O	0.48	0.79	0.93	0.11	0.29	0.54	0.49	0.96
rs2295685	G>A	O	0.24	0.71	0.29	0.97	0.38	0.62	0.63	0.56
rs228272	T>C	C	0.41	0.64	0.67	0.98	0.76	0.58	0.63	0.53
rs1461496	G>A	O	0.45	0.53	0.69	0.12	0.26	0.96	0.13	0.37
rs2079786	T>G	O	0.14	0.49	0.88	0.99	0.89	0.74	0.98	0.46
rs2070876	T>C	C	0.48	0.48	0.51	0.52	0.97	0.31	0.67	0.38
rs4735054	G>T	O	0.42	0.44	0.37	0.81	0.48	0.27	0.45	0.25
rs10424568	G>A	O	0.28	0.27	0.17	0.73	0.37	0.21	0.60	0.24
rs2845597	G>A	O	0.30	0.24	0.61	0.32	0.95	0.14	0.09	0.07
rs3806515	C>T	O	0.13	0.08	0.31	0.41	0.25	0.25	0.95	0.34
rs13169435	C>T	C	0.15	0.78	0.47	0.88	0.54	0.29	0.62	0.28
rs3789039	T>C	O	0.26	0.71	0.47	0.39	0.88	0.13	0.26	0.55
rs3809173	G>T	O	0.30	0.69	0.24	0.18	0.13	0.45	0.50	0.37
rs12901682	C>A	O	0.10	0.57	0.56	0.75	0.55	0.74	0.74	0.81
rs937215	T>C	O	0.19	0.87	0.47	0.58	0.42	0.74	0.75	0.70
rs2930975	C>G	O	0.19	0.79	0.27	0.60	0.26	0.08	0.70	0.10
rs17305311	T>C	O	0.38	0.58	0.67	0.54	1.00	0.93	0.66	0.88
rs2284992	G>T	C	0.32	0.46	0.48	0.72	0.49	0.31	0.36	0.24

rs17182246	G>C	O	0.35	0.42	0.35	0.35	0.88	0.42	0.09	0.75
rs7935835	G>A	C	0.23	0.31	0.07	0.25	0.21	0.08	0.58	0.18
rs3820312	A>C	O	0.37	0.06	0.54	0.56	0.90	0.75	0.93	0.86
rs8003631	T>C	C	0.38	0.86	0.62	0.85	0.79	0.24	0.30	0.71
rs3810288	C>G	C	0.30	0.68	0.80	0.55	0.65	0.16	0.59	0.18
rs2424993	C>G	O	0.45	0.60	0.18	0.86	0.45	0.08	0.84	0.22
rs1127155	G>A	O	0.38	0.39	0.38	0.30	0.25	0.95	0.49	0.69
rs2286620	T>C	O	0.22	0.22	0.43	0.58	0.61	0.90	0.34	0.66
rs2966449	C>T	C	0.22	0.11	0.47	0.69	0.71	0.43	0.75	0.45
rs2012124	C>T	O	0.41	0.97	0.18	0.86	0.41	0.30	0.28	0.90
rs10902227	C>T	C	0.36	0.73	0.52	0.93	0.62	0.05	0.51	0.09
rs9427715	T>G	O	0.51	0.69	0.47	0.70	0.83	0.78	0.21	0.33
rs534812	A>G	O	0.36	0.55	0.17	0.62	0.21	0.09	0.88	0.20
rs1467110	G>C	O	0.42	0.30	0.18	0.12	0.07	0.90	0.52	0.66
rs2303040	T>C	O	0.43	0.81	0.68	0.36	0.43	0.26	0.48	0.24
rs800351	T>C	O	0.45	0.70	0.71	0.89	0.88	0.92	0.61	0.72
rs7132224	A>G	O	0.52	0.42	0.37	0.37	0.27	0.83	0.14	0.29
rs3740883	C>T	O	0.17	0.10	0.93	0.21	0.62	0.56	0.33	0.40
rs9981301	G>C	C	0.50	0.94	0.64	0.71	0.94	0.56	0.59	0.99
rs12485058	A>G	O	0.24	0.19	0.56	0.93	0.64	0.91	0.53	0.91

Abbreviations: MAF, minor allele frequency; HWE-*P*, *P* for Hardy-Weinberg equilibrium test.

^a O: SNP located on the gene, C: SNP closest to the gene.

^b *P*-values were calculated using multivariate Cox proportional hazard models, adjusted for age, sex, smoking status, pathologic stage, and adjuvant therapy.

	Dominant	1.85(1.07-3.23)	0.03	0.60(0.28-1.29)	0.19	0.02	1.40(0.88-2.24)	0.16	0.88(0.56-1.39)	0.59	0.17
	Recessive	1.12(0.26-4.88)	0.88	0(0-.)	0.99		1.78(0.63-5.04)	0.28	0.42(0.06-3.11)	0.40	0.21
	Codominant	1.57(0.99-2.48)	0.05	0.57(0.29-1.14)	0.11	0.02	1.37(0.93-2.03)	0.11	0.86(0.57-1.30)	0.46	0.11
rs17528989											
	Dominant	1.04(0.58-1.89)	0.89	0.53(0.23-1.22)	0.13	0.20	1.20(0.74-1.93)	0.47	0.80(0.49-1.30)	0.37	0.24
	Recessive	2.19(0.67-7.21)	0.20	0.72(0.10-5.40)	0.75	0.35	3.61(1.43-9.13)	0.01	0.47(0.11-1.93)	0.29	0.02
	Codominant	1.14(0.70-1.88)	0.60	0.60(0.29-1.24)	0.17	0.15	1.35(0.90-2.02)	0.15	0.79(0.52-1.19)	0.26	0.07
rs2425047											
	Dominant	0.92(0.51-1.64)	0.78	0.67(0.31-1.44)	0.30	0.52	0.96(0.61-1.52)	0.87	1.08(0.67-1.74)	0.76	0.73
	Recessive	3.28(1.25-8.62)	0.02	0(0-.)	0.99		1.95(0.77-4.94)	0.16	1.25(0.31-5.15)	0.75	0.61
	Codominant	1.15(0.71-1.86)	0.56	0.65(0.31-1.37)	0.26	0.21	1.07(0.72-1.57)	0.75	1.08(0.71-1.66)	0.71	0.97
rs1136267											
	Dominant	1.64(0.97-2.78)	0.07	1.03(0.54-1.98)	0.92	0.28	1.66(1.08-2.56)	0.02	1.01(0.67-1.53)	0.96	0.10
	Recessive	1.00(0.22-4.53)	1.00	0.88(0.12-6.47)	0.90	0.92	1.00(0.24-4.19)	1.00	0.23(0.03-1.66)	0.15	0.24
	Codominant	1.43(0.92-2.22)	0.11	1.01(0.57-1.81)	0.96	0.35	1.48(1.02-2.15)	0.04	0.91(0.63-1.30)	0.60	0.06
rs1803956											
	Dominant	1.15(0.66-2.02)	0.62	1.04(0.52-2.08)	0.91	0.83	1.11(0.71-1.75)	0.64	0.91(0.59-1.40)	0.65	0.53
	Recessive	2.19(1.16-4.13)	0.02	1.20(0.54-2.67)	0.65	0.25	1.78(1.04-3.04)	0.03	1.46(0.89-2.42)	0.14	0.60
	Codominant	1.36(0.93-2.00)	0.11	1.08(0.68-1.71)	0.74	0.45	1.25(0.92-1.70)	0.16	1.08(0.80-1.46)	0.61	0.51
rs34087264											
	Dominant	1.24(0.70-2.19)	0.47	1.07(0.53-2.18)	0.85	0.75	1.02(0.66-1.59)	0.93	1.04(0.66-1.64)	0.88	0.95
	Recessive	0.51(0.22-1.16)	0.11	1.12(0.51-2.48)	0.78	0.18	0.43(0.21-0.88)	0.02	0.97(0.58-1.63)	0.90	0.07
	Codominant	0.93(0.64-1.34)	0.69	1.07(0.67-1.70)	0.78	0.64	0.83(0.62-1.12)	0.22	1.01(0.75-1.35)	0.98	0.36
rs3896021											
	Dominant	0.60(0.32-1.11)	0.10	1.28(0.55-2.98)	0.57	0.16	0.50(0.30-0.81)	0.01	0.82(0.51-1.31)	0.40	0.15
	Recessive	0.96(0.53-1.75)	0.89	0.89(0.36-2.18)	0.79	0.89	0.70(0.42-1.17)	0.17	0.76(0.41-1.39)	0.37	0.84
	Codominant	0.82(0.57-1.2)	0.30	1.06(0.63-1.79)	0.83	0.44	0.67(0.49-0.92)	0.01	0.83(0.60-1.16)	0.28	0.36
rs13817											
	Dominant	1.80(1.00-3.23)	0.05	1.16(0.59-2.27)	0.67	0.33	1.03(0.66-1.62)	0.89	1.24(0.80-1.92)	0.33	0.56
	Recessive	1.94(0.86-4.40)	0.11	0.34(0.08-1.42)	0.14	0.04	1.16(0.58-2.34)	0.68	1.13(0.59-2.15)	0.71	0.96
	Codominant	1.63(1.07-2.48)	0.02	0.89(0.55-1.45)	0.63	0.07	1.05(0.75-1.48)	0.77	1.16(0.85-1.59)	0.36	0.68
rs2234216											
	Dominant	1.03(0.60-1.78)	0.92	0.71(0.36-1.40)	0.33	0.40	0.87(0.57-1.34)	0.53	0.86(0.56-1.31)	0.48	0.97
	Recessive	2.84(1.45-5.60)	0.00	1.52(0.62-3.73)	0.36	0.28	1.44(0.79-2.61)	0.23	1.05(0.54-2.04)	0.89	0.49
	Codominant	1.37(0.91-2.07)	0.13	0.93(0.56-1.54)	0.77	0.24	1.02(0.74-1.41)	0.90	0.93(0.67-1.28)	0.65	0.69
rs6547618											
	Dominant	0.74(0.41-1.34)	0.33	1.35(0.69-2.62)	0.38	0.19	1.00(0.63-1.59)	0.99	1.20(0.78-1.86)	0.41	0.58
	Recessive	0.28(0.09-0.91)	0.03	0.92(0.27-3.17)	0.89	0.17	0.59(0.29-1.20)	0.15	0.75(0.34-1.65)	0.47	0.66
	Codominant	0.66(0.43-1.02)	0.06	1.18(0.71-1.96)	0.52	0.09	0.88(0.64-1.21)	0.43	1.05(0.76-1.45)	0.77	0.45

rs6601178										
Dominant	2.33(1.22-4.43)	0.01	0.64(0.32-1.27)	0.20	0.01	1.85(1.12-3.05)	0.02	0.92(0.59-1.46)	0.73	0.04
Recessive	1.80(1.00-3.27)	0.05	1.24(0.54-2.83)	0.62	0.47	1.35(0.81-2.23)	0.25	1.51(0.90-2.55)	0.12	0.76
Codominant	1.66(1.16-2.38)	0.01	0.86(0.51-1.43)	0.55	0.04	1.40(1.04-1.87)	0.03	1.11(0.80-1.53)	0.54	0.29
rs2270625										
Dominant	2.08(1.2-3.58)	0.01	1.02(0.52-1.97)	0.96	0.10	1.26(0.81-1.95)	0.31	0.80(0.52-1.23)	0.31	0.15
Recessive	1.78(0.74-4.30)	0.20	1.79(0.54-5.97)	0.34	0.99	1.11(0.52-2.34)	0.79	0.60(0.19-1.91)	0.39	0.38
Codominant	1.67(1.13-2.47)	0.01	1.11(0.65-1.91)	0.70	0.23	1.16(0.84-1.60)	0.37	0.80(0.55-1.16)	0.24	0.14
rs17122154										
Dominant	1.26(0.68-2.36)	0.47	1.25(0.60-2.62)	0.55	0.99	1.76(1.04-3.00)	0.04	1.12(0.71-1.77)	0.63	0.21
Recessive	0.83(0.42-1.64)	0.59	2.44(1.21-4.92)	0.01	0.03	1.23(0.74-2.03)	0.43	1.05(0.61-1.82)	0.86	0.68
Codominant	1.03(0.71-1.50)	0.88	1.55(0.96-2.48)	0.07	0.18	1.31(0.97-1.77)	0.07	1.07(0.79-1.44)	0.67	0.35
rs2548551										
Dominant	1.46(0.79-2.70)	0.22	0.75(0.32-1.77)	0.51	0.22	1.12(0.68-1.84)	0.67	0.79(0.45-1.39)	0.42	0.36
Recessive	2.11(0.59-7.55)	0.25	0(0-.)	0.99		8.04(2.60-24.88)	0.00	2.01(0.27-15.05)	0.50	0.24
Codominant	1.43(0.87-2.34)	0.16	0.75(0.32-1.75)	0.50	0.20	1.32(0.85-2.07)	0.22	0.84(0.49-1.43)	0.52	0.20
rs10139029										
Dominant	1.92(1.05-3.49)	0.03	1.05(0.52-2.10)	0.90	0.20	1.08(0.65-1.77)	0.78	1.05(0.67-1.64)	0.84	0.93
Recessive	1.46(0.45-4.80)	0.53	1.30(0.17-9.92)	0.80	0.92	1.11(0.45-2.78)	0.82	1.13(0.35-3.68)	0.84	0.98
Codominant	1.58(1.00-2.50)	0.05	1.06(0.57-1.99)	0.86	0.32	1.06(0.73-1.56)	0.75	1.05(0.71-1.55)	0.81	0.97
rs665306										
Dominant	1.71(0.95-3.09)	0.08	1.23(0.63-2.40)	0.54	0.47	0.92(0.58-1.45)	0.71	1.26(0.82-1.94)	0.29	0.33
Recessive	2.08(0.91-4.76)	0.08	0.36(0.09-1.51)	0.16	0.04	1.07(0.53-2.17)	0.84	1.11(0.59-2.12)	0.74	0.94
Codominant	1.62(1.05-2.49)	0.03	0.94(0.58-1.51)	0.79	0.10	0.97(0.69-1.36)	0.85	1.16(0.85-1.59)	0.34	0.45
rs1010222										
Dominant	1.37(0.72-2.6)	0.34	0.87(0.42-1.81)	0.72	0.36	1.06(0.62-1.79)	0.84	1.14(0.72-1.81)	0.57	0.84
Recessive	3.28(0.76-14.16)	0.11	0(0-.)	0.99		4.55(1.35-15.32)	0.01	1.45(0.58-3.64)	0.43	0.14
Codominant	1.45(0.83-2.53)	0.20	0.74(0.40-1.37)	0.34	0.11	1.21(0.75-1.95)	0.44	1.15(0.80-1.67)	0.45	0.87
rs2271446										
Dominant	1.79(1.02-3.14)	0.04	1.13(0.58-2.19)	0.72	0.30	1.52(0.97-2.40)	0.07	1.11(0.72-1.71)	0.63	0.33
Recessive	1.62(0.70-3.72)	0.26	0.55(0.13-2.28)	0.41	0.20	1.30(0.61-2.76)	0.50	0.77(0.36-1.68)	0.51	0.34
Codominant	1.48(1.01-2.17)	0.05	0.97(0.59-1.61)	0.91	0.19	1.32(0.95-1.84)	0.10	1.01(0.74-1.39)	0.95	0.25
rs3825625										
Dominant	1.90(1.05-3.44)	0.03	1.53(0.74-3.13)	0.25	0.65	1.49(0.92-2.43)	0.11	1.02(0.62-1.66)	0.95	0.28
Recessive	1.66(0.22-12.71)	0.63	0(0-.)	0.99		1.62(0.38-6.95)	0.51	1.45(0.19-11.05)	0.72	0.93
Codominant	1.75(1.04-2.97)	0.04	1.45(0.72-2.9)	0.30	0.67	1.44(0.93-2.22)	0.10	1.03(0.65-1.65)	0.90	0.30
rs7513326										
Dominant	1.64(0.88-3.05)	0.12	0.87(0.44-1.74)	0.69	0.18	1.16(0.72-1.87)	0.55	1.12(0.70-1.81)	0.63	0.92
Recessive	2.37(1.24-4.56)	0.01	0.75(0.26-2.13)	0.59	0.07	1.74(1.02-2.96)	0.04	1.62(0.94-2.79)	0.08	0.85

rs772254	Codominant	1.66(1.11-2.47)	0.01	0.86(0.51-1.44)	0.56	0.05	1.27(0.93-1.75)	0.14	1.25(0.89-1.75)	0.20	0.95
	Dominant	2.03(1.12-3.68)	0.02	0.75(0.36-1.55)	0.43	0.04	1.51(0.94-2.42)	0.09	0.68(0.43-1.09)	0.11	0.02
	Recessive	1.59(0.55-4.62)	0.39	0(0-.)	0.99		1.60(0.67-3.79)	0.29	1.35(0.42-4.40)	0.62	0.82
rs11668444	Codominant	1.61(1.05-2.48)	0.03	0.71(0.36-1.39)	0.31	0.04	1.38(0.97-1.98)	0.08	0.76(0.50-1.15)	0.19	0.03
	Dominant	1.74(0.93-3.25)	0.09	1.06(0.53-2.13)	0.87	0.30	1.25(0.76-2.04)	0.38	0.63(0.38-1.03)	0.06	0.05
	Recessive	3.46(1.21-9.94)	0.02	2.13(0.26-17.43)	0.48	0.69	1.75(0.62-4.88)	0.29	3.42(1.14-10.26)	0.03	0.38
rs1279738	Codominant	1.74(1.08-2.82)	0.02	1.11(0.59-2.11)	0.75	0.27	1.26(0.84-1.88)	0.27	0.76(0.49-1.19)	0.24	0.10
	Dominant	3.40(1.63-7.09)	0.00	1.01(0.51-2.01)	0.97	0.02	1.92(1.12-3.30)	0.02	0.79(0.51-1.21)	0.28	0.01
	Recessive	2.48(1.34-4.60)	0.00	1.83(0.82-4.08)	0.14	0.56	1.74(1.02-2.97)	0.04	1.48(0.85-2.58)	0.16	0.68
rs2075588	Codominant	2.09(1.42-3.08)	0.00	1.22(0.75-1.98)	0.43	0.09	1.56(1.13-2.15)	0.01	0.99(0.72-1.37)	0.95	0.05
	Dominant	1.63(0.93-2.85)	0.09	0.62(0.32-1.18)	0.14	0.03	1.26(0.81-1.95)	0.31	0.67(0.44-1.03)	0.07	0.04
	Recessive	1.69(0.66-4.33)	0.27	0.29(0.04-2.12)	0.22	0.12	2.42(1.07-5.47)	0.03	0.51(0.21-1.28)	0.15	0.01
rs3806192	Codominant	1.50(0.98-2.30)	0.06	0.61(0.35-1.07)	0.08	0.01	1.36(0.94-1.97)	0.11	0.69(0.49-0.98)	0.04	0.01
	Dominant	1.24(0.70-2.21)	0.46	0.99(0.50-1.95)	0.97	0.62	1.81(1.13-2.9)	0.01	0.76(0.48-1.19)	0.23	0.01
	Recessive	0(0-.)	0.99	1.90(0.40-8.97)	0.42		0(0-.)	0.98	1.10(0.33-3.71)	0.88	
rs843346	Codominant	1.17(0.68-2.03)	0.57	1.07(0.59-1.95)	0.82	0.83	1.59(1.03-2.44)	0.03	0.81(0.54-1.22)	0.31	0.03
	Dominant	0.98(0.55-1.75)	0.94	1.11(0.57-2.15)	0.76	0.78	0.90(0.57-1.42)	0.65	0.99(0.64-1.52)	0.95	0.77
	Recessive	0.08(0.01-0.58)	0.01	0.68(0.23-2.01)	0.49	0.06	0.32(0.13-0.79)	0.01	0.92(0.46-1.85)	0.82	0.07
rs1242095	Codominant	0.70(0.46-1.06)	0.09	0.97(0.61-1.56)	0.90	0.31	0.77(0.55-1.06)	0.11	0.98(0.71-1.35)	0.88	0.30
	Dominant	1.19(0.67-2.12)	0.55	0.95(0.48-1.86)	0.87	0.62	1.53(0.96-2.44)	0.07	0.89(0.58-1.36)	0.59	0.09
	Recessive	2.69(1.13-6.38)	0.03	0.92(0.40-2.10)	0.84	0.08	2.19(1.18-4.07)	0.01	0.79(0.46-1.39)	0.42	0.02
rs2292807	Codominant	1.40(0.89-2.21)	0.15	0.95(0.61-1.49)	0.83	0.24	1.53(1.09-2.13)	0.01	0.89(0.67-1.19)	0.42	0.02
	Dominant	1.13(0.60-2.14)	0.70	1.00(0.51-1.94)	0.99	0.79	1.29(0.79-2.12)	0.31	0.57(0.37-0.88)	0.01	0.02
	Recessive	0.43(0.20-0.92)	0.03	0.86(0.37-1.96)	0.71	0.23	0.66(0.37-1.18)	0.16	0.70(0.40-1.23)	0.22	0.89
rs6679	Codominant	0.82(0.56-1.19)	0.29	0.96(0.62-1.47)	0.83	0.59	0.98(0.73-1.31)	0.88	0.70(0.52-0.94)	0.02	0.11
	Dominant	1.29(0.71-2.36)	0.40	2.15(0.93-4.96)	0.07	0.33	1.66(1.01-2.73)	0.04	1.11(0.70-1.76)	0.66	0.24
	Recessive	0.83(0.38-1.80)	0.64	0.54(0.23-1.30)	0.17	0.47	1.31(0.72-2.38)	0.38	0.83(0.50-1.37)	0.47	0.25
rs11809443	Codominant	1.07(0.72-1.57)	0.75	1.07(0.70-1.63)	0.77	1.00	1.35(0.98-1.85)	0.06	0.98(0.74-1.29)	0.88	0.13
	Dominant	0.82(0.46-1.46)	0.50	1.05(0.53-2.09)	0.89	0.59	0.96(0.61-1.52)	0.87	1.05(0.67-1.64)	0.84	0.78

	Recessive	0.23(0.05-1.00)	0.05	2.98(0.68-13.04)	0.15	0.02	0.50(0.15-1.66)	0.25	1.84(0.57-5.91)	0.31	0.13
	Codominant	0.72(0.46-1.13)	0.15	1.18(0.64-2.18)	0.59	0.20	0.90(0.62-1.30)	0.56	1.10(0.73-1.65)	0.65	0.47
rs2271541											
	Dominant	0.55(0.32-0.95)	0.03	0.96(0.48-1.91)	0.91	0.21	0.64(0.41-1.02)	0.06	0.70(0.45-1.08)	0.10	0.78
	Recessive	1.77(0.88-3.54)	0.11	0.59(0.21-1.67)	0.32	0.09	1.50(0.85-2.66)	0.17	0.71(0.38-1.32)	0.28	0.08
	Codominant	0.87(0.57-1.32)	0.51	0.86(0.53-1.39)	0.53	0.97	0.91(0.64-1.28)	0.57	0.76(0.55-1.04)	0.08	0.45
rs3813521											
	Dominant	0.47(0.27-0.84)	0.01	0.61(0.31-1.19)	0.15	0.56	0.74(0.47-1.15)	0.18	1.06(0.70-1.62)	0.77	0.25
	Recessive	0.27(0.06-1.17)	0.08	0.26(0.04-1.90)	0.18	0.98	0.55(0.22-1.40)	0.21	1.14(0.57-2.31)	0.71	0.22
	Codominant	0.51(0.32-0.83)	0.01	0.61(0.34-1.07)	0.08	0.64	0.75(0.52-1.07)	0.11	1.06(0.78-1.46)	0.70	0.16
rs7897156											
	Dominant	1.97(1.08-3.57)	0.03	1.02(0.52-1.99)	0.96	0.15	1.54(0.97-2.45)	0.07	0.93(0.60-1.44)	0.73	0.12
	Recessive	2.37(1.11-5.07)	0.03	1.28(0.39-4.22)	0.69	0.39	2.16(1.12-4.14)	0.02	1.56(0.71-3.45)	0.27	0.53
	Codominant	1.76(1.17-2.64)	0.01	1.06(0.62-1.79)	0.83	0.13	1.51(1.08-2.12)	0.02	1.03(0.72-1.47)	0.89	0.13

^a Hazard ratios (HRs), 95% confidence intervals (CIs) and corresponding *P*-values were calculated using multivariate Cox proportional hazard models, adjusted for age, gender, smoking status, pathologic stage and adjuvant therapy.

^b P_H , *P* for heterogeneity test.

Supplementary Table S3. Primers used in this study

Assay	Gene	Primers
Promoter assay	rs17583 forward	5'-CCGCTCGAGAACCCCTCCCTCTTGCAAGC -3'
	rs17583 reverse	5'-CCCAAGCTTGGTCATCCTTCCGCATCTCC -3'
	<i>GLRX3</i> pro forward	5'-CCGCTCGAGGGACTGAATTGGAAGCACCC-3'
	<i>GLRX3</i> pro reverse	5'-CATGCCATGGCGCCAGACAGAAGCAATCCA-3'
	rs4751162 forward	5'-CGGGATCCGTGCAAGTCTCCCCATTACC-3'
	rs4751162 reverse	5'-ACGCGTCGACAGACCCAGGCTCCCTAAAAC-3'
qRT-PCR	<i>CAPN1</i> forward	5'-ATTTCCAGCTGTGGCAATTT-3'
	<i>CAPN1</i> reverse	5'-CTCCAGAACTCGTTGCCTTC-3'
	<i>LINC00959</i> forward	5'-TGCTCCCATCCCTGCCATGT-3'
	<i>LINC00959</i> reverse	5'-AAGACAGGAATCTCGGGTGGGC-3'
	<i>GLRX3</i> forward	5'-AGATGAACGAAGTTATGGCAGAG-3'
	<i>GLRX3</i> reverse	5'-ACAGAAAAGTGGGAACAGAGC-3'
	<i>β-actin</i> forward	5'-TTGTTACAGGAAGTCCCTTGCC-3'
	<i>β-actin</i> reverse	5'-ATGCTATCACCTCCCCTGTGT-3'
ChIP-qPCR	rs17583 forward	5'-GATTCTCCCTAGCACCCGCT-3'
	rs17583 reverse	5'-TGCCGGCATAGCCATTCTGG-3'
	rs4751162 forward	5'-TACTCGTCCCCAACACCCA-3'
	rs4751162 reverse	5'-GGCCGAGACTCATTGCAGGA-3'