

Supplementary Materials

The Association of Twelve Polymorphisms in Three Onco-lncRNA Gene with Hepatocellular Cancer Risk and Prognosis

Short title: lncRNA SNPs with HCC risk & prognosis

Ben-gang Wang, Tumor Etiology and Screening Department of Cancer Institute and General Surgery, the First Hospital of China Medical University, and Key Laboratory of Cancer Etiology and Prevention (China Medical University), Liaoning Provincial Education Department, Shenyang 110001, China. Hepatobiliary Surgery Department of General Surgery Institute, the First Hospital of China Medical University, Shenyang 110001, China.

Qian Xu, Tumor Etiology and Screening Department of Cancer Institute and General Surgery, the First Hospital of China Medical University, and Key Laboratory of Cancer Etiology and Prevention (China Medical University), Liaoning Provincial Education Department, Shenyang 110001, China

Zhi Lv, Tumor Etiology and Screening Department of Cancer Institute and General Surgery, the First Hospital of China Medical University, and Key Laboratory of Cancer Etiology and Prevention (China Medical University), Liaoning Provincial Education Department, Shenyang 110001, China

Xin-xin Fang, Tumor Etiology and Screening Department of Cancer Institute and General Surgery, the First Hospital of China Medical University, and Key Laboratory of Cancer Etiology and Prevention (China Medical University), Liaoning Provincial Education Department, Shenyang 110001, China

Han-xi Ding, Tumor Etiology and Screening Department of Cancer Institute and General Surgery, the First Hospital of China Medical University, and Key Laboratory of Cancer Etiology and Prevention (China Medical University), Liaoning Provincial Education Department, Shenyang 110001, China

Jing Wen, Tumor Etiology and Screening Department of Cancer Institute and General Surgery, the First Hospital of China Medical University, and Key Laboratory of Cancer

Etiology and Prevention (China Medical University), Liaoning Provincial Education Department, Shenyang 110001, China

Yuan Yuan*, Tumor Etiology and Screening Department of Cancer Institute and General Surgery, the First Hospital of China Medical University, and Key Laboratory of Cancer Etiology and Prevention (China Medical University), Liaoning Provincial Education Department, Shenyang 110001, China

***Corresponding author:** Dr. Yuan Yuan, Tumor Etiology and Screening Department of Cancer Institute and General Surgery, North Nanjing Street 155#, Heping District, Shenyang 110001, China. Telephone: +86-024-83282153; fax: +86-024-83282383. Email: yuanyuan@cmu.edu.cn.

Table Contents:

Supplementary Table S1. The primer information for the three lncRNA polymorphisms genotyping and mRNA expression

Supplementary Table S2. The baseline of the subjects participated in this study

[Supplementary Table S3. The association of lncRNA gene SNPs and risk of hepatocellular cancer](#)

Supplementary Table S4. The association of lncRNA polymorphisms and hepatocellular risk stratified by host characteristics

Supplementary Table S5. Epistatic effect of pair-wise interacting factors on the risks of hepatocellular cancer

[Supplementary Table S6. Univariate and multivariate cox proportional hazard analysis for the association of lncRNA polymorphisms and hepatocellular cancer](#)

[Supplementary Table S7. Univariate proportional hazard analysis stratified by host characteristics for the association of lncRNA polymorphisms and hepatocellular cancer](#)

Supplementary Table S8. The bioinformatical result from the GTExPortal website for the MALAT1 rs4102217 SNP

Supplementary Figure S1. Results from the Haploreg website for the promising SNPs in this study

Supplementary Table S1. The primer information for the three lncRNA polymorphisms genotyping and mRNA expression

For KASP					
ID	Primer_AlleleFAM	Primer_AlleleHEX	Primer_Common	Allele FAM	Allele HEX
rs3807598	GTGATGAGTCGTTCTGAG	GTGATGAGTCGTTCTGA	GTCCACACTGTTAGTGA	C	G
	TCTATG	GTCTATC	GCAATTTTCATAT		
rs17501292	CCCCACCAAGTGTGCCCT	CCCCCACCAAGTGTGCC	GGCAAATCAATATTTAC	G	T
	G	CTT	CCAGAACTGCTA		
rs2067087	GCCTAGAACCCTACTCTG	GCCTAGAACCCTACTCT	AGTGGCATTGTAAAACCT	C	G
	TCTG	GTCTC	CACAGTGACAAA		
rs17427960	CTAAATAAGCATGTCTTG	CTAAATAAGCATGTCTT	GTTCCCCGATGTGTCCC	A	C
	AGAGGGT	GAGAGGGG	TATCATTA		
rs78248039	CCAGAAACAGAAAACGA	CCAGAAACAGAAAACG	GCCGCTGACTCCAGAG	A	T
	CCTTGCT	ACCTTGCA	AAATGAAAA		
rs3843549	ATGTCTAACCTGCTCATT	GTCTAACCTGCTCATTAT	GAGAAAAAGAGGAAGA	A	G
	ATCTTGCAA	CTTGCA	TGCACAAAGTCAT		
rs138947056	AACTCTAAGGAGATTGG	CTCTAAGGAGATTGGGA	CAAATTTATTCTTCTCTT	A	G
	GAAATAATATAATTT	AATAATATAATTC	CCTGGGTACATA		
rs6983267	CATAAAAATTCTTTGTAC	CACATAAAAATTCTTTGT	CGTCCTTTGAGCTCAGC	G	T

	TTTTCTCAGTGC	ACTTTTCTCAGTGA	AGATGAAA		
	GAGAGACTGACAGAAGT	GAGAGACTGACAGAAGT	CACGTCCTGCTGCCTCC		
rs4102217	GCTGC	GCTGG	CTT	C	G
	AAACAAGCCATGGATAC	AAAAACAAGCCATGGAT	CTCCCTCACCCCCGGGT		
rs591291	AGGTTCC	ACAGGTTCT	CTT	C	T
	ATCTTAGCTGTCCTTATA	GCTATCTTAGCTGTCCTT	GGTTTTATCTAAATACC		
rs11227209	GGC	ATAGGG	ACCACCTGGAAT	C	G
	TCTTGTGTTCTCTTGAGGG	CTTGTGTTCTCTTGAGGG	CACACTTTAATCTTCCTT		
rs619586	ACAGT	ACAGC	CAAAAGGTGGTA	A	G

For mRNA
expression

	F:	R:
HOTTIP	CGACTGGGTCCCTCCTCA	GGCTCCTGCCGTCTTTTC
	C	T
	F:	R:
MALAT1	GACCACCACAGGTTTACA	AACTACCAGCCATTCTC
	G	C
	F:	R:
GAPDH	TGCACCACCAACTGCTTA	GGATGCAGGGATGATGT
	G	TC

Supplementary Table S2. The baseline of the subjects participated in this study

Variables	Controls (%)	HCC (%)	<i>P</i>
	n=817	n=521	
Age			0.587
Mean±SD	56.9±10.0	56.6±10.7	
Median	56	57	
Range	26-90	21-90	
Gender			0.056
Male	641(78.5)	431(82.7)	
Female	176(21.5)	90(17.3)	
Smoking			0.002
Ever	354(60.9)	239(71.1)	
Never	227(39.1)	97(28.9)	
Drinking			0.258
Ever	460(79.3)	276(82.4)	
Never	120(20.7)	59(17.6)	
HBsAg			
Negative	ND	40(40)	
Positive	ND	242(85.8)	
Anti-HCV			
Negative	ND	115(85.8)	
Positive	ND	19(14.2)	

ND: not known. HCC, Hepatocellular cancer patients.

Supplementary Table S3. The association of lncRNA gene SNPs and risk of hepatocellular cancer

Gene	Chr. Pos.	SNP ^a	Loc.	Genotype	Controls(%)	Cases(%)	<i>P</i> ^b	OR(95%CI)	<i>P</i> _{HWE}
HOTTIP	7p15.2	rs3807598	Exon	CC	222(28.2)	131(25.4)		1(Ref.)	0.849
				CG	390(49.5)	263(51.1)	0.323	1.14(0.88-1.49)	
				GG	176(22.3)	121(23.5)	0.338	1.17(0.85-1.61)	
		rs17501292	Exon	TT	732(91.2)	453(87.1)		1(Ref.)	0.190
				TG	71(8.8)	66(12.7)	0.021	1.52(1.06-2.17)	
				GG	0(0)	1(0.2)	NA	NA	
				TG+GG vs.			0.017	1.54(1.08-2.20)	
				TT					
				G vs. T			0.012	1.55(1.10-2.18)	
		rs2067087	Exon	GG	174(21.7)	88(16.9)		1(Ref.)	0.674
				GC	405(50.6)	263(50.7)	0.236	1.16(0.90-1.49)	
				CC	222(27.7)	168(32.4)	0.015	1.49(1.08-2.08)	
				CC vs.			0.035	1.35(1.02-1.82)	
				GG+GC					
		rs17427960	Intron	C vs. G			0.017	1.20(1.03-1.41)	0.613
				CC	172(21.7)	85(16.7)		1(Ref.)	
				CA	387(48.8)	259(50.9)	0.707	1.05(0.81-1.35)	

CCAT2	8q24.21			AA	234(29.5)	165(32.4)	0.032	1.78(1.03-2.00)			
				AA	vs.			0.028	1.39(1.03-1.85)		
				CC+CA							
				A vs. C			0.049	1.18(1.00-1.37)			
		rs78248039	Exon	AA	756(100)	467(100)	NA	NA	NA		
		rs3843549	Promoter	AA	807(99.9)	516(100)		1(Ref.)	0.986		
				AG	1(0.1)	0(0)	NA				
		rs138947056	Promoter	AA	792(99.2)	510(99.4)		1(Ref.)	0.915		
				AG	6(0.8)	2(0.40)	0.466	0.55(0.11-2.74)			
				GG	0(0)	1(0.20)	NA				
MALAT1	22q13.2			rs6983267	Exon	TT	301(37.3)	163(31.3)		NA	0.029
						TG	359(44.5)	262(50.4)	NA	NA	
						GG	147(18.2)	95(18.3)	NA	NA	
				rs4102217	Promoter	GG	608(75.1)	362(69.6)		1(Ref.)	0.055
				GC	180(22.2)	148(28.5)	0.011	1.39(1.08-1.79)			
				CC	22(2.7)	10(1.9)	0.481	0.76(0.36-1.63)			
				GC+CC	vs.			0.028	1.32(1.03-1.69)		
				GG							
				C vs. G			0.097	1.20(0.97-1.50)			
			rs591291	Promoter	CC	289(36.0)	171(33.0)		1(Ref.)	0.438	

		TC	376(46.9)	265(51.3)	0.165	1.19(0.93-1.52)	
		TT	137(17.1)	81(15.7)	0.974	0.99(0.71-1.39)	
rs11227209	Exon	CC	724(85.0)	459(88.3)		1(Ref.)	NA
		CG	79(9.3)	59(11.3)	0.338	1.19(0.83-1.70)	
		GG	49(5.7)	2(0.4)	0.783	0.79(0.14-4.33)	
rs619586	Exon	AA	684(84.9)	434(83.8)		1(Ref.)	0.083
		AG	113(14.0)	83(16.0)	0.326	1.17(0.86-1.59)	
		GG	9(1.1)	1(0.2)	0.100	0.18(0.02-1.40)	

NA, not available. Chr. Pos. = chromosomal position. Loc. = localisation. PHWE = P value for Hardy-Weinberg Equilibrium. a, the sort order was according to the SNP location in its genes from 5' starting to 3' ends. b, P value was calculated by adjusted

Supplementary Table S4. The association of lncRNA polymorphisms and hepatocellular risk stratified by host characteristics

Variables	Genotype	HCC CON	vs OR(95%CI)	<i>P</i>
HOTTIP				
rs3087598				
Gender				
Male	CC	105/175	1(Ref)	
	CG	219/308	1.19(0.88-1.60)	0.264
	GG	102/141	1.22(0.86-1.74)	0.265
Female	CC	26/47	1(Ref)	
	CG	44/83	0.80(0.43-1.50)	0.486
	GG	19/35	0.87(0.41-1.85)	0.715
Age				
≤60	CC	89/153	1(Ref)	
	CG	167/259	1.09(0.79-1.52)	0.606
	GG	73/114	1.10(0.74-1.63)	0.654
>60	CC	42/108	1(Ref)	
	CG	96/131	1.18(0.73-1.89)	0.500
	GG	42/69	1.31(0.76-2.26)	0.331
Smoking				
Never smoker	CC	23/66	1(Ref)	
	CG	48/104	1.32(0.73-2.37)	0.360
	GG	23/50	1.30(0.65-2.59)	0.453
Ever smoker	CC	62/90	1(Ref)	
	CG	123/176	0.92(0.61-1.40)	0.708
	GG	52/72	0.99(0.60-1.63)	0.964

Alcohol drinking

Nondrinker	CC	16/31	1(Ref)	
	CG	32/56	1.00(0.47-2.14)	0.997
	GG	9/30	0.51(0.19-1.37)	0.180
Drinker	CC	69/125	1(Ref)	
	CG	139/222	1.11(0.77-1.60)	0.583
	GG	65/93	1.24(0.80-1.92)	0.346

HOTTIP

rs17501292

Gender

Male	TT	377/574	1(Ref)	
	TG	52/56	1.44(0.96-2.15)	0.075
	GG	1/0	NA	NA
Female	TT	76/158	1(Ref)	
	TG	14/15	1.83(0.80-4.18)	0.150
	GG	0/0	NA	NA

Age

≤60	TT	295/491	1(Ref)	
	TG	38/42	1.53(0.96-2.44)	0.076
	GG	0/0	NA	NA
>60	TT	158/241	1(Ref)	
	TG	28/29	1.42(0.81-2.51)	0.223
	GG	1/0	NA	NA

Smoking

Never smoker	TT	81/201	1(Ref)	
	TG	16/21	2.02(1.00-4.11)	0.053
	GG	0/0	NA	NA
Ever smoker	TT	212/316	1(Ref)	

	TG	26/32	1.27(0.72-2.24)	0.406
	GG	1/0	NA	NA
Alcohol drinking				
Nondrinker	TT	48/108	1(Ref)	
	TG	11/9	3.45(1.26-9.46)	0.016
	GG	0/0	NA	NA
Drinker	TT	244/408	1(Ref)	
	TG	31/44	1.20(0.73-1.97)	0.471
	GG	1/0	NA	NA
HOTTIP				
rs2067087				
Gender				
Male	GG	70/134	1(Ref)	
	GC	221/315	1.11(0.84-1.47)	0.441
	CC	138/179	1.52(1.05-2.17)	0.027
Female	GG	18/40	1(Ref)	
	GC	42/90	1.38(0.74-2.63)	0.309
	CC	30/43	1.30(0.61-2.78)	0.495
Age				
≤60	GG	64/118	1(Ref)	
	GC	171/276	1.12(0.81-1.56)	0.471
	CC	98/139	1.28(0.86-1.92)	0.216
>60	GG	24/56	1(Ref)	
	GC	92/129	1.16(0.76-1.79)	0.474
	CC	70/83	2.08(1.15-3.70)	0.015
Smoking				
Never smoker	GG	13/49	1(Ref)	
	GC	50/109	1.19(0.75-1.92)	0.459

	CC	32/65	1.69(0.93-3.13)	0.088
Ever smoker	GG	46/74	1(Ref)	
	GC	122/181	1.10(0.64-1.89)	0.729
	CC	71/92	1.17(0.71-1.96)	0.512
Alcohol drinking				
Nondrinker	GG	10/23	1(Ref)	
	GC	31/59	0.89(0.43-1.85)	0.763
	CC	17/35	1.09(0.41-2.85)	0.872
Drinker	GG	49/100	1(Ref)	
	GC	141/229	1.10(0.77-1.56)	0.611
	CC	85/123	1.39(0.88-2.17)	0.150
HOTTIP				
rs17427960				
Gender				
Male	CC	66/133	1(Ref)	
	CA	217/300	1.02(0.78-1.35)	0.863
	AA	138/188	1.52(1.04-2.17)	0.029
Female	CC	19/39	1(Ref)	
	CA	42/87	1.14(0.60-2.17)	0.687
	AA	27/46	1.03(0.49-2.17)	0.945
Age				
≤60	CC	60/119	1(Ref)	
	CA	170/257	0.94(0.68-1.32)	0.747
	AA	98/153	1.25(0.84-1.89)	0.268
>60	CC	25/53	1(Ref)	
	CA	89/130	1.20(0.79-1.85)	0.385
	AA	67/81	1.85(1.03-3.33)	0.040
Smoking				

Never smoker	CC	15/49	1(Ref)	
	CA	47/103	1.11(0.64-1.92)	0.716
	AA	33/68	1.56(0.76-3.23)	0.220
Ever smoker	CC	41/69	1(Ref)	
	CA	119/173	1.03(0.69-1.54)	0.888
	AA	71/100	1.09(0.65-1.82)	0.735
Alcohol drinking				
Nondrinker	CC	10/20	1(Ref)	
	CA	31/55	0.82(0.40-1.69)	0.596
	AA	18/37	0.93(0.35-2.50)	0.893
Drinker	CC	46/98	1(Ref)	
	CA	135/2194	1.02(0.72-1.45)	0.905
	AA	85/132	1.35(0.86-2.13)	0.194
CCAT2				
rs138947056				
Gender				
Male	AA	423/622	1(Ref)	
	AG	1/4	0.42(0.05-3.81)	0.441
	GG	0/0	NA	NA
Female	AA	87/170	1(Ref)	
	AG	1/2	1.46(1.09-19.58)	0.775
	GG	1/0	NA	NA
Age				
≤60	AA	327/527	1(Ref)	
	AG	0/4	NA	NA
	GG	1/0	NA	NA
>60	AA	183/265	1(Ref)	0.651
	AG	2/2	1.30(0.17-9.79)	0.797

	GG	0/0	NA	NA
Smoking				
Never smoker	AA	95/222	1(Ref)	
	AG	0/1	NA	NA
	GG	0/0	NA	0.000
Ever smoker	AA	233/341	1(Ref)	
	AG	2/2	2.38(0.31-18.27)	0.406
	GG	0/0	NA	0.000
Alcohol drinking				
Nondrinker	AA	58/116	1(Ref)	
	AG	0/0	NA	NA
	GG	0/0	NA	NA
Drinker	AA	269/447	1(Ref)	
	AG	2/3	1.43(0.23-8.99)	0.701
	GG	0/0	NA	NA
CCAT2				
rs6983267				
Gender				
Male	TT	138/237	1(Ref)	
	TG	220/275	1.39(1.05-1.83)	0.020
	GG	73/121	1.04(0.73-1.49)	0.840
Female	TT	25/64	1(Ref)	
	TG	42/84	1.26(0.67-2.35)	0.475
	GG	22/26	2.37(1.09-5.15)	0.029
Age				
≤60	TT	98/202	1(Ref)	
	TG	177/233	1.62(1.18-2.22)	0.003
	GG	58/104	1.14(0.76-1.71)	0.520

>60	TT	65/99	1(Ref)	
	TG	85/126	1.04(0.68-1.59)	0.849
	GG	37/43	1.26(0.73-2.19)	0.409
Smoking				
Never smoker	TT	32/85	1(Ref)	
	TG	44/96	1.24(0.72-2.13)	0.448
	GG	21/46	1.20(0.62-2.31)	0.597
Ever smoker	TT	71/129	1(Ref)	
	TG	125/158	1.46(0.99-2.16)	0.056
	GG	42/63	1.22(0.74-2.01)	0.434
Alcohol drinking				
Nondrinker	TT	17/50	1(Ref)	
	TG	28/53	1.47(0.71-3.07)	0.303
	GG	14/17	2.61(1.04-6.53)	0.041
Drinker	TT	85/163	1(Ref)	
	TG	141/201	1.36(0.96-1.93)	0.083
	GG	49/92	1.00(0.64-1.54)	0.983
MALAT1				
rs4102217				
Gender				
Male	GG	298/477	1(Ref)	
	GC	123/139	1.45(1.09-1.93)	0.010
	CC	9/19	0.79(0.35-1.79)	0.577
Female	GG	64/131	1(Ref)	
	GC	25/41	1.29(0.70-2.38)	0.414
	CC	1/3	0.717(0.07-7.72)	0.784
Age				
≤60	GG	241/404	1(Ref)	

	GC	88/122	1.21(0.88-1.67)	0.237
	CC	4/13	0.49(0.16-1.54)	0.222
>60	GG	121/204	1(Ref)	
	GC	60/58	1.76(1.14-2.71)	0.010
	CC	6/9	1.21(0.42-3.51)	0.727
Smoking				
Never smoker	GG	67/169	1(Ref)	
	GC	28/50	1.42(0.82-2.44)	0.212
	CC	2/7	0.80(0.16-3.99)	0.781
Ever smoker	GG	159/257	1(Ref)	
	GC	74/84	1.43(0.97-2.10)	0.068
	CC	6/10	0.81(0.28-2.34)	0.692
Alcohol drinking				
Nondrinker	GG	41/82	1(Ref)	
	GC	17/35	1.05(0.52-2.12)	0.901
	CC	1/3	0.74(0.07-7.49)	0.797
Drinker	GG	185/344	1(Ref)	
	GC	84/98	1.61(1.14-2.29)	0.007
	CC	7/14	0.85(0.33-2.16)	0.726
MALAT1				
rs591291				
Gender				
Male	CC	143/223	1(Ref)	
	TC	215/303	1.13(0.86-1.49)	0.387
	TT	72/102	1.10(0.76-1.60)	0.601
Female	CC	28/66	1(Ref)	
	TC	50/73	1.53(0.83-2.81)	0.168
	TT	9/35	0.62(0.26-1.49)	0.288

Age

≤60	CC	115/193	1(Ref)	
	TC	162/247	1.08(0.80-1.47)	0.606
	TT	53/95	0.93(0.61-1.41)	0.724
>60	CC	56/96	1(Ref)	
	TC	103/129	1.35(0.88-2.07)	0.167
	TT	28/42	1.14(0.64-2.05)	0.660

Smoking

Never smoker	CC	33/69	1(Ref)	
	TC	48/119	0.86(0.50-1.48)	0.595
	TT	16/37	0.88(0.43-1.83)	0.738
Ever smoker	CC	81/127	1(Ref)	
	TC	118/158	1.18(0.81-1.72)	0.388
	TT	39/63	0.98(0.57-1.65)	0.946

Alcohol drinking

Nondrinker	CC	22/49	1(Ref)	
	TC	24/51	1.07(0.52-2.18)	0.857
	TT	13/18	1.61(0.67-3.95)	0.294
Drinker	CC	92/148	1(Ref)	
	TC	141/224	0.97(0.69-1.36)	0.858
	TT	42/82	0.80(0.50-1.28)	0.347

MALAT1 rs11227209

Gender

Male	CC	382/566	1(Ref)	
	CG	46/64	1.11(0.74-1.66)	0.617
	GG	2/3	1.03(0.17-6.20)	0.975
Female	CC	77/158	1(Ref)	
	CG	13/15	1.71(0.74-3.94)	0.210

	GG	0/1	NA	NA
Age				
≤60	CC	299/495	1(Ref)	
	CG	34/41	1.38(0.85-2.23)	0.193
	GG	1/3	0.55(0.06-5.43)	0.611
>60	CC	160/229	1(Ref)	
	CG	25/38	0.90(0.51-1.56)	0.697
	GG	1/1	1.60(0.10-25.80)	0.740
Smoking				
Never smoker	CC	79/199	1(Ref)	
	CG	17/24	1.93(0.98-3.83)	0.059
	GG	0/2	NA	0.995
Ever smoker	CC	220/322	1(Ref)	
	CG	18/28	1.00(0.53-1.89)	0.990
	GG	1/1	1.69(0.09-30.62)	0.723
Alcohol drinking				
Nondrinker	CC	51/113	1(Ref)	
	CG	8/8	3.28(1.05-10.24)	0.041
	GG	0/1	NA	NA
Drinker	CC	247/407	1(Ref)	
	CG	27/46	0.94(0.56-1.56)	0.796
	GG	1/2	0.81(0.07-9.34)	0.864
MALAT1 rs619586				
Gender				
Male	AA	362/534	1(Ref)	
	AG	66/91	1.11(0.78-1.57)	0.560
	GG	1/7	0.22(0.03-1.83)	0.162

Female	AA	72/150	1(Ref)	
	AG	17/22	1.70(0.82-3.52)	0.151
	GG	0/2	NA	NA
Age				
≤60	AA	280/466	1(Ref)	
	AG	52/65	1.36(0.91-2.02)	0.132
	GG	1/6	0.28(0.03-2.39)	0.245
>60	AA	154/218	1(Ref)	
	AG	31/48	0.92(0.56-1.52)	0.744
	GG	0/3	NA	NA
Smoking				
Never smoker	AA	77/187	1(Ref)	
	AG	20/36	1.14(0.65-1.99)	0.658
	GG	0/3	NA	NA
Ever smoker	AA	210/307	1(Ref)	
	AG	28/41	1.04(0.61-1.77)	0.889
	GG	1/3	NA	NA
Alcohol drinking				
Nondrinker	AA	49/105	1(Ref)	
	AG	10/13	1.64(0.66-4.05)	0.286
	GG	0/1	NA	NA
Drinker	AA	237/389	1(Ref)	
	AG	38/63	0.97(0.62-1.50)	0.874
	GG	1/5	0.31(0.04-2.73)	0.291

NA, not available.

Supplementary Table S5. Epistatic effect of pair-wise interacting factors on the risks of hepatocellular cancer

Interacted SNPs	pair-wise Comparison	Subset	HCC vs. CON	
			<i>P</i>	OR(95%CI)
HOTTIP rs3807598 interacted with	MALAT1 rs4102217	HOTTIP rs3807598 CG+GG vs. CC	0.750	0.93(0.58-1.48)
		MALAT1 rs4102217 CG+CC vs. GG	0.110	1.28(0.95-1.74)
MALAT1 rs4102217 interacted with	MALAT1 rs591291	HOTTIP rs3807598 CG+GG	0.212	1.21(0.90-1.62)
		HOTTIP rs3807598 CC	0.037	1.65(1.03-2.65)
HOTTIP rs3807598 interacted with	MALAT1 rs11227209	MALAT1 rs591291 TC+TT	0.570	1.05(0.77-1.44)
		MALAT1 rs591291 CC	0.235	1.30(0.84-2.02)
MALAT1 rs591291 interacted with	MALAT1 rs619586	HOTTIP rs3807598 CG+GG	0.625	1.07(0.81-1.41)
		HOTTIP rs3807598 CC	0.210	1.34(0.85-2.13)
HOTTIP rs3807598 interacted with	MALAT1 rs619586	MALAT1 rs11227209 CG+GG	0.623	1.23(0.54-2.82)
		MALAT1 rs11227209 CC	0.318	1.15(0.88-1.50)
MALAT1 rs11227209 interacted with	MALAT1 rs619586	HOTTIP rs3807598 CG+GG	0.364	1.21(0.81-1.80)
		HOTTIP rs3807598 CC	0.713	1.16(0.54-2.49)
HOTTIP rs3807598 interacted with	MALAT1 rs619586	MALAT1 rs619586 AG+GG	0.150	1.66(0.83-3.32)
		MALAT1 rs619586 AA	0.649	1.07(0.81-1.40)
MALAT1 rs619586 interacted with	MALAT1 rs619586	HOTTIP rs3807598 CG+GG	0.289	1.21(0.85-1.72)
		HOTTIP rs3807598 CC	0.511	0.81(0.42-1.54)

HOTTIP rs17501292	HOTTIP rs17501292 TG+GG vs. TT	MALAT1 rs4102217 CG+CC	0.047	2.03(1.01-4.06)
interacted with		MALAT1 rs4102217 GG	0.122	1.39(0.92-2.11)
MALAT1 rs4102217	MALAT1 rs4102217 CG+CC vs. GG	HOTTIP rs17501292 TG+GG	0.116	1.85(0.86-3.99)
		HOTTIP rs17501292 TT	0.078	1.27(0.97-1.65)
HOTTIP rs17501292	HOTTIP rs17501292 TG+GG vs. TT	MALAT1 rs591291 TC+TT	0.076	1.51(0.96-2.38)
interacted with		MALAT1 rs591291 CC	0.115	1.58(0.89-2.80)
MALAT1 rs591291	MALAT1 rs591291 TC+TT vs. CC	HOTTIP rs17501292 TG+GG	0.781	1.10(0.56-2.19)
		HOTTIP rs17501292 TT	0.239	1.16(0.91-1.49)
HOTTIP rs17501292	HOTTIP rs17501292 TG+GG vs. TT	MALAT1 rs11227209 CG+GG	0.753	0.84(0.29-2.48)
interacted with		MALAT1 rs11227209 CC	0.009	1.65(1.13-2.41)
MALAT1 rs11227209	MALAT1 rs11227209 CG+GG vs. CC	HOTTIP rs17501292 TG+GG	0.369	0.61(0.21-1.80)
		HOTTIP rs17501292 TT	0.243	1.25(0.86-1.81)
HOTTIP rs17501292	HOTTIP rs17501292 TG+GG vs. TT	MALAT1 rs619586 AG+GG	0.258	0.56(0.21-1.52)
interacted with		MALAT1 rs619586 AA	0.002	1.85(1.26-2.73)
MALAT1 rs619586	MALAT1 rs619586 AG+GG vs. AA	HOTTIP rs17501292 TG+GG	0.050	0.36(0.13-1.00)
		HOTTIP rs17501292 TT	0.223	1.22(0.87-1.68)
HOTTIP rs2067087	HOTTIP rs2067087 CC vs. GG+GC	MALAT1 rs4102217 CG+CC	0.163	0.68(0.41-1.17)
interacted with		MALAT1 rs4102217 GG	0.112	0.76(0.54-1.07)
MALAT1 rs4102217	MALAT1 rs4102217 CG+CC vs. GG	HOTTIP rs2067087 CC	0.547	1.19(0.68-2.10)
		HOTTIP rs2067087 GG+GC	0.030	1.36(1.03-1.79)

HOTTIP rs2067087	HOTTIP rs2067087 CC vs. GG+GC	MALAT1 rs591291 TC+TT	0.123	0.76(0.53-1.08)
interacted with		MALAT1 rs591291 CC	0.180	0.71(0.43-1.17)
MALAT1 rs591291	MALAT1 rs591291 TC+TT vs. CC	HOTTIP rs2067087 CC	0.523	1.20(0.69-2.09)
		HOTTIP rs2067087 GG+GC	0.389	1.12(0.86-1.46)
HOTTIP rs2067087	HOTTIP rs2067087 CC vs. GG+GC	MALAT1 rs11227209 CG+GG	0.163	0.50(0.19-1.32)
interacted with		MALAT1 rs11227209 CC	0.082	0.77(0.57-1.03)
MALAT1 rs11227209	MALAT1 rs11227209 CG+GG vs. CC	HOTTIP rs2067087 CC	0.691	0.83(0.33-2.10)
		HOTTIP rs2067087 GG+GC	0.357	1.20(0.82-1.76)
HOTTIP rs2067087	HOTTIP rs2067087 CC vs. GG+GC	MALAT1 rs619586 AG+GG	0.038	0.43(0.19-0.95)
interacted with		MALAT1 rs619586 AA	0.192	0.82(0.60-1.11)
MALAT1 rs619586	MALAT1 rs619586 AG+GG vs. AA	HOTTIP rs2067087 CC	0.300	0.66(0.30-1.44)
		HOTTIP rs2067087 GG+GC	0.283	1.20(0.86-1.68)
HOTTIP rs17427960	HOTTIP rs17427960 AA vs. CC+CA	MALAT1 rs4102217 CG+CC	0.458	0.82(0.48-1.39)
interacted with		MALAT1 rs4102217 GG	0.039	0.69(0.49-0.98)
MALAT1 rs4102217	MALAT1 rs4102217 CG+CC vs. GG	HOTTIP rs17427960 AA	0.161	1.50(0.85-2.64)
		HOTTIP rs17427960 CC+CA	0.043	1.34(1.01-1.77)
HOTTIP rs17427960	HOTTIP rs17427960 AA vs. CC+CA	MALAT1 rs591291 TC+TT	0.043	0.69(0.48-0.99)
interacted with		MALAT1 rs591291 CC	0.479	0.84(0.51-1.37)
MALAT1 rs591291	MALAT1 rs591291 TC+TT vs. CC	HOTTIP rs17427960 AA	0.932	0.98(0.56-1.70)
		HOTTIP rs17427960 CC+CA	0.165	1.21(0.93-1.57)

HOTTIP rs17427960	HOTTIP rs17427960 AA vs. CC+CA	MALAT1 rs11227209 CG+GG	0.120	0.47(0.18-1.22)
interacted with		MALAT1 rs11227209 CC	0.085	0.77(0.56-1.04)
MALAT1 rs11227209	MALAT1 rs11227209 CG+GG vs. CC	HOTTIP rs17427960 AA	0.637	0.80(0.32-2.02)
		HOTTIP rs17427960 CC+CA	0.258	1.25(0.85-1.84)
HOTTIP rs17427960	HOTTIP rs17427960 AA vs. CC+CA	MALAT1 rs619586 AG+GG	0.015	0.37(0.17-0.83)
interacted with		MALAT1 rs619586 AA	0.241	0.83(0.61-1.13)
MALAT1 rs619586	MALAT1 rs619586 AG+GG vs. AA	HOTTIP rs17427960 AA	0.200	0.60(0.28-1.31)
		HOTTIP rs17427960 CC+CA	0.204	1.25(0.89-1.75)

Note: All tests were adjusted by age, sex. Statistically significant associations were highlighted in bold (*P* values <0.05).

Note: HCC, hepatocellular cancer; CON, controls.

Supplementary Table S6. Univariate and multivariate cox proportional hazard analysis for the association of lncRNA polymorphisms and hepatocellular cancer

Variables		All HCC n (%)	Death n	MST ^a (M)	Univariate Hazard ratio (95% CI)	<i>P</i> -value	Multivariate ^b Hazard ratio (95% CI)	<i>P</i> -value
HOTTIP	rs3807598	n=346	n=135					
	CC	86(24.86)	35(25.93)	61.0	1(Ref)		1(Ref)	
	CG	174(50.29)	66(48.89)	48.0	0.96(0.64-1.45)	0.843	0.96(0.63-1.44)	0.828
	GG	86(24.85)	34(25.18)	56.0	0.85(0.53-1.37)	0.511	0.84(0.52-1.36)	0.476
	rs17501292	n=350	n=137					
	TT	309(88.29)	120(87.59)	51.0	1(Ref)		1(Ref)	
	TG	41(11.71)	17(12.41)	48.0	0.93(0.56-1.54)	0.764	1.08(0.65-1.80)	0.758
	GG	NA	NA		NA	NA	NA	NA
	rs2067087	n=349	n=136					
	GG	57(16.33)	22(16.18)	61.0	1(Ref)		1(Ref)	
	GC	176(50.43)	70(51.47)	48.0	1.16(0.72-1.87)	0.549	1.25(0.86-1.84)	0.244
	CC	116(33.24)	44(32.35)	56.0	0.94(0.56-1.56)	0.800	1.13(0.67-1.90)	0.654
	rs17427960	n=342	n=133					
	CC	54(15.79)	21(15.79)	51.0	1(Ref)		1(Ref)	

CCAT2	rs78248039	CA	178(52.05)	67(50.38)	51.0	1.09(0.67-1.78)	0.727	1.12(0.77-1.64)	0.559
		AA	110(32.16)	45(33.83)	55.0	0.99(0.59-1.66)	0.954	1.04(0.61-1.76)	0.892
			n=314	n=121					
	rs3843549	AA	314(100)	121(100)	NA	NA	NA	NA	NA
			n=347	n=137					
	rs138947056	AA	347(100)	137(100)	NA	NA	NA	NA	NA
			n=345	n=136					
	rs6983267	AA	343(99.42)	136(100)	51.0	1(Ref)		1(Ref)	
		AG	2(0.58)	0	NA	NA	NA	NA	NA
			n=350	n=137					
MALAT1	rs4102217	TT	112(32.00)	42(30.66)	56.0	1(Ref)		1(Ref)	
		TG	182(52.00)	78(56.93)	47.0	1.13(0.77,1.64)	0.533	1.15(0.79-1.67)	0.478
		GG	56(16.00)	17(12.41)	69.0	0.91(0.52,1.60)	0.734	0.93(0.53-1.64)	0.807
			n=350	n=137					
	rs591291	GG	246(70.29)	93	51.0	1(Ref)		1(Ref)	
		GC	99(28.29)	41	56.0	1.03(0.71,1.49)	0.872	1.02(0.71-1.48)	0.907
		CC	5(1.42)	3	36.0	1.98(0.62,6.30)	0.246	2.04(0.64-6.47)	0.229
			n=350	n=136					
		CC	120(34.29)	52(38.24)	47.0	1(Ref)		1(Ref)	
		TC	183(52.29)	65(47.79)	56.0	0.80(0.55,1.15)	0.223	0.79(0.55-1.14)	0.208

rs11227209	TT	47(13.42)	19(13.97)	90.0	0.91(0.54,1.55)	0.737	0.94(0.56-1.60)	0.829
		n=350	n=137					
rs619586	CC	313(89.43)	120(87.59)	51.0	1(Ref)		1(Ref)	
	CG	36(10.29)	16(11.68)	55.0	1.11(0.66,1.87)	0.698	1.10(0.65-1.85)	0.734
	GG	1(0.28)	1(0.73)	33.0	2.85(0.40,20.49)	0.298	2.82(0.39-20.38)	0.304
		n=350	n=136					
	AA	295(84.29)	113(83.09)	52.0	1(Ref)		1(Ref)	
	AG	55(15.71)	23(16.91)	47.0	1.10(0.70,1.72)	0.688	1.09(0.70-1.71)	0.698
	GG	NA	NA	NA	NA	NA	NA	NA

HR, hazard rate; CI, confidence interval; a, MST, median survival time (months). b, Multivariate survival analysis was adjusted by age and gender. NA, not available.

Supplementary Table S7. Univariate proportional hazard analysis stratified by host characteristics for the association of lncRNA polymorphisms and hepatocellular cancer

Gene	SNP	Stratified	Stratified	Genotype	HCC	[n	Death	MST ^a (M	P-value	Hazard	ratio
		d	factors	e	(%)]		(n))	e	(95% CI)	

HOTTIP	rs3807598			n=282					
		Gender	Male	CC	68(24.11)	29	51.0		1(Ref)
				CG	143(50.71)	57	48.0	0.874	0.96(0.62-1.51)
				GG	71(25.18)	27	69.0	0.503	0.84(0.49-1.41)
				n=64					
			Female	CC	18(28.12)	6	46.4 ^b		1(Ref)
				CG	31(48.44)	9	51.0	0.829	0.89(0.32-2.51)
				GG	15(23.44)	7	55.0	0.937	1.05(0.34-3.3)
				n=214					
		Age	≤60	CC	59(27.57)	25	51.0		1(Ref)
				CG	105(49.07)	41	48.0	0.764	0.93(0.56-1.53)
				GG	50(23.36)	20	56.0	0.484	0.81(0.45-1.47)
				n=132					
			>60	CC	27(20.46)	10	62.0		1(Ref)
				CG	69(52.27)	25	56.0	0.980	0.99(0.47-2.07)
				GG	36(27.27)	14	55.0	0.817	0.91(0.40-2.05)
				n=33					
		Smoking	Ever smoker	CC	7(21.21)	3	81.0 ^b		1(Ref)
				CG	15(45.46)	5	98.3 ^b	0.745	0.79(0.19-3.32)

Alcohol drinking	Never smoker	GG	11(33.33) n=170	3	72.6 ^b	0.570	0.63(0.13-3.12)
		CC	40(23.53)	17	35.0		1(Ref)
		CG	91(53.53)	27	89.9 ^b	0.260	0.71(0.38-1.30)
		GG	39(22.94) n=20	15	69.0	0.548	0.81(0.40-1.63)
	Drinker	CC	3(15.00)	2	43.0		1(Ref)
		CG	13(65.00)	2	105.4 ^b	0.263	0.32(0.04-2.34)
		GG	4(20.00) n=182	1	43.0	0.519	0.45(0.04-5.02)
		CC	44(24.18)	18	35.0		1(Ref)
	Nondrinker	CG	93(51.10)	30	89.4 ^b	0.428	0.79(0.44-1.42)
		GG	45(24.72) n=136	17	69.0	0.618	0.84(0.43-1.65)
		CC	30(22.06)	12	90.0		1(Ref)
	Positive	CG	73(53.68)	23	90.1 ^b	0.391	0.74(0.37-1.48)
		GG	33(24.26)	11	64.1 ^b	0.680	0.84(0.37-1.91)

rs1750129 2	Gender	Negative	CC	n=31 10(32.26)	7	21.0		1(Ref)
			CG	13(41.94)	4	41.8 ^b	0.374	0.60(0.16-1.97)
			GG	8(25.80)	1	70.3 ^b	0.049	0.12(0.02-0.99)
		Male		n=285				
			TT	252(88.42)	100	51.0		1(Ref)
			TG	33(11.58)	14	48.0	0.693	0.89(0.51-1.56)
			GG	0	0	NA	NA	NA
			Female		n=65			
				TT	57(87.69)	20	51.0	
	TG	8(12.31)		3	44.0 ^b	0.885	1.09(0.32-3.69)	
	Age	≤60	GG	0	0	NA	NA	NA
				n=217				
			TT	193(88.94)	77	51.0		1(Ref)
		>60	TG	24(11.06)	10	48.0	0.815	0.92(0.48-1.79)
			GG	0	0	NA	NA	NA
			n=133					
	TT	116(87.22)	43			1(Ref)		
	TG	17(12.78)	7	56.0	0.909	0.95(0.43-2.13)		

Smoking	Ever smoker	GG	0 n=36	0	NA	NA	NA
		TT	28(77.78)	10	92.8 ^b		1(Ref)
		TG	8(22.22)	2	107.9 ^b	0.316	0.46(0.10-2.11)
		GG	0 n=171	0	NA	NA	NA
		TT	155(90.64)	51	90.0		1(Ref)
		TG	16(9.36)	8	33.0	0.236	1.57(0.74-3.32)
	Never smoker	GG	0 n=22	0	NA	NA	NA
		TT	17(77.27)	5	45.0		1(Ref)
		TG	5(22.73)	1	64.0 ^b	0.364	0.37(0.04-3.21)
		GG	0 n=184	0	NA	NA	NA
Alcohol drinking	Drinker	TT	165(89.67)	56	90.0		1(Ref)
		TG	19(10.33)	9	48.0	0.537	1.25(0.62-2.53)
	Nondrinker	TT					
		TG					

rs2067087	HBV	Positive	GG	0	0	NA	NA	NA
				n=139				
			TT	124(89.21)	41	90.0		1(Ref)
		Negative	TG	15(10.79)	5	90.7 ^b	0.545	0.75(0.30-1.90)
			GG	0	0	NA	NA	NA
				n=31				
			TT	27(87.10)	9	49.6 ^b		1(Ref)
			TG	4(12.90)	3	9.0	0.217	2.29(0.62-8.51)
			GG	0	0	NA	NA	NA
	Gender	Male		n=284				
			GG	95(33.45)	34	64.0 ^b		1(Ref)
			GC	144(50.70)	60	48.0	0.157	1.36(0.89-2.07)
		Female	CC	45(15.85)	19	61.0	0.618	1.15(0.66-2.03)
				n=65				
			GG	21(32.31)	10	55.0		1(Ref)
			GC	32(49.23)	10	51.0	0.780	0.88(0.36-2.15)
			CC	12(18.46)	3	36.9 ^b	0.607	0.71(0.19-2.67)
				n=217				
	Age	≤60	GG	64(29.49)	22	65.1 ^b		1(Ref)
			GC	112(51.62)	48	47.0	0.128	1.48(0.89-2.56)

Smoking	>60	CC	41(18.89)	16	61.0	0.645	1.16(0.61-2.22)
		n=132					
		GG	52(39.40)	22	45.0		1(Ref)
		GC	64(48.48)	22	87.0 ^b	0.950	0.98(0.54-1.78)
	Ever smoker	CC	16(12.12)	6	62.0	0.971	1.02(0.41-2.52)
		n=34					
		GG	15(44.12)	4	73.4 ^b		1(Ref)
		GC	18(52.94)	6	95.1 ^b	0.604	1.40(0.39-5.00)
		CC	1(2.94)	0	19.0	0.195	4.48(0.47-43.10)
		n=171					
	Never smoker	GG	51(29.82)	17	61.4 ^b		1(Ref)
		GC	91(53.22)	32	56.0	0.503	1.22(0.68-2.21)
		CC	29(16.96)	10	69.0	0.948	0.97(0.45-2.13)
		n=47					
Alcohol drinking	Drinker	GG	9(19.15)	2	63.4 ^b		1(Ref)
		GC	11(23.40)	2	88.9 ^b	0.903	1.13(0.16-8.19)
		CC	27(57.45)	11	19.0	0.131	8.49(0.53-135.82)

rs1742796		Nondrinker	GG	56(36.13)	19	63.2 ^b		1(Ref)
			GC	98(63.23)	36	56.0	0.517	1.20(0.69-2.10)
			CC	1(0.64)	0	69.0	0.959	0.98(0.46-2.11)
	HBV	Positive	n=138					
			GG	43(31.16)	12	69.1 ^b		1(Ref)
			GC	76(55.07)	26	86.3 ^b	0.342	1.39(0.70-2.78)
		CC	19(13.77)	8	69.0	0.419	1.45(0.59-3.56)	
		Negative	n=31					
			GG	11(35.48)	3	60.0 ^b		1(Ref)
			GC	13(41.94)	5	27.0	0.528	1.59(0.38-6.69)
		CC	7(22.58)	4	21.0	0.227	2.55(0.56-11.68)	
		279						
	Gender	Male	CC	92(32.97)	35	62.8 ^b		1(Ref)
CA			146(52.33)	59	48.0	0.267	1.27(0.83-1.93)	
AA			41(14.70)	17	51.0	0.848	1.06(0.59-1.89)	
n=63								
	Female	CC	18(28.57)	10	38.0		1(Ref)	

Age	≤60	CA	32(50.79)	8	51.0	0.371	0.64(0.25-1.69)
		AA	13(20.64)	4	46.3 ^b	0.646	0.76(0.24-2.46)
		n=214					
		CC	62(28.97)	26	47.0		1(Ref)
		CA	114(53.27)	45	48.0	0.657	1.12(0.69-1.81)
		AA	38(17.76)	15	51.0	0.879	0.95(0.50-1.80)
	>60	n=128					
		CC	48(37.50)	19	55.0		1(Ref)
		CA	64(50.00)	22	56.0	0.747	1.11(0.60-2.06)
		AA	16(12.50)	6	62.0	0.734	1.17(0.47-2.95)
		n=35					
		CC	14(40.00)	4	71.8 ^b		1(Ref)
Smoking	Ever smoker	CA	18(51.43)	6	95.5 ^b	0.703	1.28(0.36-4.54)
		AA	3(8.57)	2	48.0	0.423	2.00(0.37-10.95)
		n=165					
	Never smoker	CC	49(29.70)	18	60.4 ^b		1(Ref)
		CA	90(54.55)	29	83.5 ^b	0.841	1.06(0.59-1.92)
		AA	26(15.75)	9	90.0	0.947	0.97(0.44-2.17)

				n=22					
CCAT2	rs6983267	Alcohol drinking	Drinker	CC	9(40.91)	2	63.4 ^b		1(Ref)
				CA	12(54.55)	3	45.0	0.616	1.59(0.26-9.61)
				AA	1(4.54)	0	19.0	0.131	8.39(0.53-135.8)
				n=177					
			Nondrinker	CC	53(29.94)	20	61.3 ^b		1(Ref)
				CA	96(54.24)	32	88.4 ^b	0.981	1.01(0.58-1.76)
				AA	28(15.82)	10	90.0	0.822	0.92(0.43-1.96)
				n=133					
		HBV	Positive	CC	42(31.58)	13	67.1 ^b		1(Ref)
				CA	73(54.89)	24	85.8 ^b	0.568	1.22(0.62-2.40)
AA	18(13.53)			7	90.0	0.866	1.08(0.43-2.73)		
		n=30							
		Negative	CC	9(30.00)	2	64.2 ^b		1(Ref)	
			CA	13(43.33)	4	27.0	0.552	1.68(0.30-9.34)	
			AA	8(26.67)	5	21.0	0.088	4.28(0.81-22.69)	
		n=286							
		Gender	Male	TT	91(31.82)	35	61.0		1(Ref)

Age	Female	TG	152(53.15)	63	48.0	0.873	1.03(0.68-1.56)
		GG	43(15.03)	16	56.0	0.680	1.13(0.63-2.05)
		n=64					
		TT	21(32.81)	7	56.0		1(Ref)
		TG	30(46.88)	15	37.0	0.240	1.71(0.70-4.22)
		GG	13(20.31)	1	75.1 ^b	0.141	0.21(0.03-1.69)
	≤60	n=217					
		TT	64(29.49)	27	52.0		1(Ref)
		TG	124(57.14)	52	48.0	0.906	0.97(0.61-1.55)
		GG	29(13.35)	8	69.0	0.391	0.71(0.32-1.56)
		n=133					
		TT	48(36.09)	15	68.8 ^b		1(Ref)
	>60	TG	58(43.61)	26	45.0	0.238	1.47(0.78-2.77)
		GG	27(20.30)	9	56.0	0.748	1.15(0.50-2.62)
		n=36					
		TT	14(38.89)	3	104.7 ^b		1(Ref)
Smoking	Ever smoker	TG	17(47.22)	7	48.0	0.296	2.06(0.53-8.02)
		GG	5(13.89)	2	45.0 ^b	0.520	1.80(0.30-10.79)
		n=170					

Alcohol drinking	Never smoker	TT	50(29.42)	14	84.6 ^b		1(Ref)
		TG	94(55.29)	39	45.0	0.218	1.47(0.80-2.71)
		GG	26(15.29)	6	69.0	0.785	0.88(0.34-2.28)
		n=22					
	Drinker	TT	6(27.27)	0	NA		1(Ref)
		TG	12(54.55)	4	NA	NA	NA
		GG	4(18.18)	2	NA	NA	NA
		n=183					
	Nondrinker	TT	57(31.15)	17	90.6 ^b		1(Ref)
		TG	99(54.10)	42	47.0	0.197	1.45(0.83-2.55)
GG		27(14.75)	6	69.0	0.709	0.84(0.33-2.13)	
n=139							
HBV	Positive	TT	50(35.97)	15	90.0		1(Ref)
		TG	72(51.80)	28	87.2 ^b	0.484	0.72(0.28-1.82)
		GG	17(12.23)	3	NA	NA	
	n=31						
	Negative	TT	7(22.58)	2	27.0		1(Ref)

MALAT1	rs4102217			TG	16(51.61)	6	42.5 ^b	0.815	1.17(0.32-4.34)
				GG	8(25.81)	4	NA	NA	
				n=284					
		Gender	Male	GG	200(70.42)	75	51.0		1(Ref)
				GC	81(28.52)	36	52.0	0.553	1.13(0.76-1.68)
				CC	3(1.06)	1	36.0	0.137	2.41(0.76-7.72)
				n=65					
			Female	GG	46(70.77)	18	39.0		1(Ref)
				GC	18(27.69)	5	56.0	0.322	0.61(0.22-1.64)
				CC	1(1.54)	0	NA	NA	NA
				n=217					
		Age	≤60	GG	158(72.81)	60	48.0		1(Ref)
				GC	57(26.27)	26	52.0	0.541	1.15(0.73-1.83)
				CC	2(0.92)	1	36.0	0.635	1.62(0.22-11.81)
				n=133					
			>60	GG	88(66.17)	33	56.0		1(Ref)
				GC	42(31.58)	15	62.0	0.616	0.86(0.46-1.58)
				CC	3(2.25)	2	22.0	0.343	2.01(0.48-8.45)
				n=36					
		Smokin	Ever	GG	26(72.22)	9	92.1 ^b		1(Ref)

g	smoker	GC	10(27.78)	3	103.3 ^b	0.792	1.19(0.32-4.42)
		CC	0	0	NA	NA	NA
		n=171					
	Never smoker	GG	115(67.25)	37	85.9 ^b		1(Ref)
		GC	53(30.99)	21	47.0	0.863	0.95(0.56-1.63)
		CC	3(1.76)	1	22.0	0.974	1.03(0.14-7.57)
		n=22					
Alcohol drinking	Drinker	GG	17(77.27)	5	45.0		1(Ref)
		GC	5(22.73)	1	103.0 ^b	0.364	0.37(0.04-3.21)
		CC	0	0	NA	NA	
	Nondrinker	n=184					
		GG	124(67.39)	41	87.5 ^b		1(Ref)
		GC	57(30.98)	23	47.0	0.645	1.13(0.68-1.88)
		CC	3(1.63)	1	22.0	0.966	1.04(0.14-7.62)
		n=139					
HBV	Positive	GG	96(69.06)	28	91.7 ^b		1(Ref)

rs591291	Gender	Negative	GC	40(28.78)	17	52.0	0.342	1.34(0.73-2.45)
			CC	3(2.16)	1	22.0	0.778	1.33(0.18-9.90)
			n=31					
			GG	22(70.97)	9	48.7 ^b		1(Ref)
			GC	9(29.03)	3	27.0	0.312	0.50(0.13-1.91)
			CC	0	0	NA	NA	NA
		Male	n=286					
			CC	98(34.27)	39	48.0		1(Ref)
			TC	146(51.05)	56	56.0	0.865	0.97(0.64-1.45)
			TT	42(14.68)	19	47.0	0.678	1.12(0.65-1.94)
			n=64					
			CC	22(34.38)	13	32.0		1(Ref)
		Female	TC	37(57.81)	9	56.0	0.022	0.37(0.16-0.87)
			TT	5(7.81)	0	NA	0.286	0.04(0.00-16.09)
			n=217					
	Age	≤60	CC	81(37.33)	35	47.0		1(Ref)
			TC	107(49.31)	39	56.0	0.454	0.84(0.53-1.33)
			TT	29(13.36)	12	90.0	0.881	0.95(0.49-1.83)
		>60	n=133					
			CC	39(29.32)	17	75.6 ^b		1(Ref)

Smoking	Ever smoker	TC	76(57.15)	26	56.0	0.235	0.69(0.37-1.27)
		TT	18(13.53)	7	43.0	0.596	0.79(0.33-1.90)
		n=36					
		CC	11(30.56)	4	87.4 ^b		1(Ref)
		TC	21(58.33)	7	96.7 ^b	0.945	1.04(0.31-3.57)
		TT	4(11.11)	1	55.0 ^b	0.713	0.66(0.07-5.95)
	Never smoker	n=171					
		CC	63(36.84)	25	69.0		1(Ref)
		TC	83(48.54)	24	73.1 ^b	0.202	0.69(0.40-1.22)
		TT	25(14.62)	10	47.0	0.822	0.92(0.44-1.92)
		n=22					
		CC	8(36.36)	2	58.5 ^b		1(Ref)
Alcohol drinking	Drinker	TC	9(40.91)	3	45.0	0.881	1.15(0.19-6.87)
		TT	5(22.73)	1	102.2 ^b	0.780	0.71(0.06-7.86)
		n=184					
	Nondrinker	CC	66(35.87)	27	69.0		1(Ref)

rs1122720 9	HBV	Positive	TC	94(51.09)	28	92.5 ^b	0.210	0.71(0.42-1.21)	
			TT	24(13.04)	10	47.0	0.972	0.99(0.48-2.04)	
			n=139						
			Positive	CC	54(38.85)	18	69.0		1(Ref)
				TC	69(49.64)	21	92.1 ^b	0.816	0.93(0.49-1.74)
				TT	16(11.51)	7	90.0	0.965	0.98(0.41-2.35)
		n=31							
			Negative	CC	8(25.81)	5	6.0		1(Ref)
				TC	16(51.61)	4	27.0	0.042	0.25(0.07-0.95)
				TT	7(22.58)	3	21.0	0.215	0.40(0.09-1.71)
		n=285							
	Gender	Male	CC	256(89.83)	99	52.0		1(Ref)	
			CG	28(9.82)	14	47.0	0.427	1.26(0.72-2.20)	
			GG	1(0.35)	0	33.0	0.277	2.99(0.42-21.57)	
			n=65						
			Female	CC	57(87.69)	21	51.0		1(Ref)
				CG	8(12.31)	2	55.0	0.522	0.62(0.15-2.67)
				GG	0	0	NA	NA	
				n=218					

Age	≤60	CC	200(91.74)	79	51.0		1(Ref)
		CG	18(8.26)	8	47.0	0.700	1.15(0.56-2.39)
		GG	0	0	NA	NA	
	n=132						
	>60	CC	113(85.61)	41	62.0		1(Ref)
		CG	18(13.64)	8	55.0	0.770	1.12(0.52-2.40)
		GG	1(0.75)	0	33.0	0.376	2.46(0.27-18.03)
	n=35						
Smoking	Ever smoker	CC	29(82.86)	9	101.2 ^b		1(Ref)
		CG	6(17.14)	3	19.0	0.309	1.97(0.53-7.32)
		GG	0	0	NA	NA	
	n=171						
	Never smoker	CC	158(92.40)	54	90.0		1(Ref)
		CG	12(7.02)	4	56.0	0.614	0.77(0.28-2.13)
		GG	1(0.59)	0	33.0	0.490	2.01(0.28-14.61)
	n=22						
Alcohol drinking	Drinker	CC	19(86.36)	5	84.3 ^b		1(Ref)

rs619586	HBV	Nondrinker	CG	3(13.64)	1	51.0 ^b	0.831	1.26(0.15-10.87)		
			GG	0	0	NA	NA			
			n=183							
			CC	167(91.26)	58	90.0		1(Ref)		
			CG	15(8.20)	6	56.0	0.926	1.04(0.45-2.42)		
			GG	1(0.54)	0	33.0	0.464	2.10(0.29-15.20)		
			n=138							
			CC	127(92.03)	42	90.0		1(Ref)		
			CG	10(7.25)	3	69.9 ^b	0.497	0.67(0.21-2.15)		
		Positive	GG	1(0.72)	0	33.0	0.412	2.30(0.31-16.85)		
			n=31							
			Negative	CC	26(83.87)	10	27.0		1(Ref)	
				CG	5(16.13)	2	44.9 ^b	0.919	0.92(0.20-4.23)	
				GG	0	0	NA	NA	NA	
			n=285							
			Gender	Male	AA	241(84.56)	92	61.0		1(Ref)
					AG	44(15.44)	21	45.0	0.372	1.24(0.77-1.99)
					GG	0	0	NA	NA	NA
		n=65								

Age	Female	AA	54(83.08)	21	51.0		1(Ref)
		AG	11(16.92)	2	42.0 ^b	0.431	0.56(0.13-2.40)
		GG	0	0	NA	NA	NA
	n=218						
	≤60	AA	186(85.32)	74	51.0		1(Ref)
		AG	32(14.68)	13	47.0	0.899	1.04(0.58-1.88)
		GG	0	0	NA	NA	NA
	n=132						
	>60	AA	109(82.58)	39	62.0		1(Ref)
		AG	23(17.42)	10	45.0	0.574	1.22(0.61-2.45)
		GG	0	0	NA	NA	NA
	n=36						
Smoking	Ever smoker	AA	27(75.00)	8	102.9 ^b		1(Ref)
		AG	9(25.00)	4	45.0	0.423	1.64(0.49-5.44)
		GG	0	0	NA	NA	NA
	n=171						
	Never smoker	AA	151(88.30)	52	90.0		1(Ref)
		AG	20(11.70)	7	56.0	0.847	0.93(0.42-2.04)

Alcohol drinking	Drinker	GG	0 n=22	0	NA	NA	NA
		AA	17(77.27)	4	89.4 ^b		1(Ref)
		AG	5(22.73)	2	45.0	0.588	1.60(0.29-8.75)
	Nondrinker	GG	0 n=184	0	NA	NA	NA
		AA	160(86.96)	56	90.0		1(Ref)
		AG	24(13.04)	9	56.0	0.946	1.03(0.51-2.07)
		GG	0 n=139	0	NA	NA	NA
		AA	122(87.77)	41	90.0		1(Ref)
		AG	17(12.23)	5	67.2 ^b	0.484	0.71(0.28-1.82)
		GG	0 n=31	0	NA	NA	NA
HBV	Positive	AA	122(87.77)	41	90.0		1(Ref)
		AG	17(12.23)	5	67.2 ^b	0.484	0.71(0.28-1.82)
		GG	0 n=31	0	NA	NA	NA
	Negative	AA	24(77.42)	9	27.0		1(Ref)
		AG	7(22.58)	3	42.5 ^b	0.815	1.17(0.32-4.34)
		GG	0	0	NA	NA	

HR, hazard rate; CI, confidence interval; a, MST, median survival time (months). NA, not available.

Supplementary Table S8. The bioinformatical result from the GTExPortal website for the MALAT1 rs4102217 SNP

Variant Id	SNP Id	Gencode Id	Gene Symbol	P-Value	Effect Size	Tissue
11_65263895_G_C_b37	rs4102217	ENSG00000168056.10	LTBP3	5.10E-12	0.25	Nerve - Tibial
11_65263895_G_C_b37	rs4102217	ENSG00000173727.7	AP000769.1	2.70E-08	0.35	Muscle - Skeletal
11_65263895_G_C_b37	rs4102217	ENSG00000168056.10	LTBP3	3.90E-08	0.26	Breast - Mammary Tissue
11_65263895_G_C_b37	rs4102217	ENSG00000168056.10	LTBP3	4.00E-08	0.15	Whole Blood
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	1.00E-07	0.52	Esophagus - Mucosa
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	1.80E-07	0.5	Stomach
						Adipose - Visceral
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	4.30E-07	0.49	(Omentum)
11_65263895_G_C_b37	rs4102217	ENSG00000245532.4	NEAT1	5.90E-07	0.26	Lung
11_65263895_G_C_b37	rs4102217	ENSG00000173727.7	AP000769.1	9.70E-07	0.31	Nerve - Tibial
11_65263895_G_C_b37	rs4102217	ENSG00000168056.10	LTBP3	0.0000011	0.18	Muscle - Skeletal
11_65263895_G_C_b37	rs4102217	ENSG00000168056.10	LTBP3	0.0000017	0.14	Adipose - Subcutaneous
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	0.0000017	0.44	Thyroid
11_65263895_G_C_b37	rs4102217	ENSG00000245532.4	NEAT1	0.0000018	0.39	Colon - Transverse
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	0.0000027	0.39	Skin - Sun Exposed (Lower

						leg)
						Cells - Transformed
11_65263895_G_C_b37	rs4102217	ENSG00000173727.7	AP000769.1	0.0000057	0.27	fibroblasts
11_65263895_G_C_b37	rs4102217	ENSG00000172543.3	CTSW	0.000006	-0.63	Vagina
11_65263895_G_C_b37	rs4102217	ENSG00000172922.4	RNASEH2C	0.0000098	-0.15	Artery - Tibial
11_65263895_G_C_b37	rs4102217	ENSG00000172922.4	RNASEH2C	0.000011	-0.16	Muscle - Skeletal
						Skin - Sun Exposed (Lower
11_65263895_G_C_b37	rs4102217	ENSG00000168056.10	LTBP3	0.000017	0.13	leg)
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	0.000018	0.49	Pancreas
11_65263895_G_C_b37	rs4102217	ENSG00000245532.4	NEAT1	0.000019	0.25	Nerve - Tibial
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	0.000021	0.33	Nerve - Tibial
11_65263895_G_C_b37	rs4102217	ENSG00000172543.3	CTSW	0.000022	-0.31	Thyroid
						Adipose - Visceral
11_65263895_G_C_b37	rs4102217	ENSG00000172543.3	CTSW	0.000026	-0.26	(Omentum)
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	0.000029	0.36	Esophagus - Muscularis
11_65263895_G_C_b37	rs4102217	ENSG00000260233.2	SSSCA1-AS1	0.000032	0.29	Thyroid
11_65263895_G_C_b37	rs4102217	ENSG00000260233.2	SSSCA1-AS1	0.000039	0.23	Muscle - Skeletal
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	0.000039	0.44	Artery - Aorta
11_65263895_G_C_b37	rs4102217	ENSG00000172922.4	RNASEH2C	0.000044	-0.17	Adipose - Subcutaneous
11_65263895_G_C_b37	rs4102217	ENSG00000245532.4	NEAT1	0.000047	0.25	Adipose - Subcutaneous

11_65263895_G_C_b37	rs4102217	ENSG00000251562.3	MALAT1	0.000057	-0.19	Muscle - Skeletal
11_65263895_G_C_b37	rs4102217	ENSG00000245532.4	NEAT1	0.000072	0.25	Esophagus - Muscularis
11_65263895_G_C_b37	rs4102217	ENSG00000172803.13	SNX32	0.000073	0.38	Skin - Not Sun Exposed (Suprapubic)
11_65263895_G_C_b37	rs4102217	ENSG00000174996.7	KLC2	0.000093	-0.17	Esophagus - Mucosa

FigS1A

Position Weight Matrix ID (Library from Kheradpour and Kellis, 2013)	Strand	Ref	Alt	Match on:
				Ref: ACCAGCCACCCCCACCAAGTGTGCCCTTTCCTTCTTGACTTTTATAGCAGTTCTGGGT Alt: ACCAGCCACCCCCACCAAGTGTGCCCTGTCTTCTTGACTTTTATAGCAGTTCTGGGT
GATA_disc3	+	12.9	1	YVHYTTCCTBY
PU.1_disc3	-	11.8	11.5	SHSHBSCHNBBCY
T3R	-	7.5	11.9	HNISWCCTB
VDR_4	-	-0.8	10.7	RRYSVMCYYHMTSMMCYKBBK
p300_disc10	-	13.8	1.8	MHTTCCTBYT

FigS1B

Position Weight Matrix ID (Library from Kheradpour and Kellis, 2013)	Strand	Ref	Alt	Match on:
				Ref: AGTGGCATTGTAAAACTCACAGTGACAAAGACAGAGTAGGGTTCTAGGCCCTGTTC Alt: AGTGGCATTGTAAAACTCACAGTGACAAACAGACAGAGTAGGGTTCTAGGCCCTGTTC
AP-1_known1	+	11.8	10	RVIGACTMMKW

FigS1C

Position Weight Matrix ID (Library from Kheradpour and Kellis, 2013)	Strand	Ref	Alt	Match on:
				Ref: TCATTAAAAAAAAAAAAAAAAAAAAAAAAACCCCTCTCAAGACATGCTTATTAGAGGAA Alt: TCATTAAAAAAAAAAAAAAAAAAAAAAAAACCCCTCTCAAGACATGCTTATTAGAGGAA
Foxp1	-	-8.2	3.8	ANAMWMRMMAAYAYAAATAA
HDAC2_disc6	+	7.5	19.1	DRRRRRRAARRRMW
NF-kappaB_disc3	+	14.4	11.5	AAAYCCCTTN
Pax-4_4	+	15.5	14.3	RRWAAWWRNNMHNVHHNVHMNNHYSAYHSB
Pax-4_5	+	15.4	14.4	RAANWWWDHVVHHVNBMMHNNHMYMYMC
Zfp105	+	12	13.8	HDYAAWHAAMAWDND
p300_disc5	+	9.3	13.6	ARARMRRAAVWGARA

FigS1D

Position Weight Matrix ID (Library from Kheradpour and Kellis, 2013)	Strand	Ref	Alt	Match on:
				Ref: CGCAGITGGAGAGACTGACAGAAGTGCTGGAGAGGAAGGGAGGCAGCAGGACGTGGAAA Alt: CGCAGITGGAGAGACTGACAGAAGTGCTGCAGAGGAAGGGAGGCAGCAGGACGTGGAAA
AP-1_disc6	-	12.4	8.1	AAARCCYGGMSHRSR
EWSR1-FLI1	+	7.3	-4.7	GGAAGGAAGGAAGGAAGG
NRSF_known3	-	-3.2	-3.7	GSYKCTGTCCGYGGTGCTGAA

Supplementary Figure S1. Results from the Haploreg website for the promising SNPs in this study