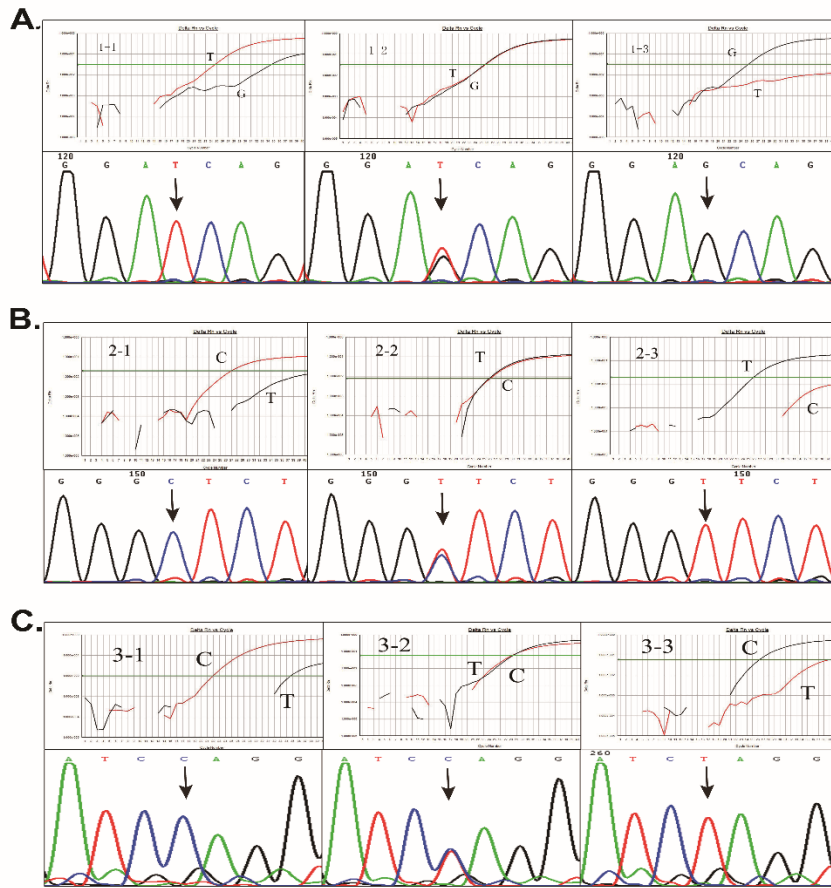


Supplementary materials

Supplementary Table 1 Primers and probes used for genotyping HNF1A SNPs

SNP	Region	Primer name	Sequence (5' to 3')
rs1169288 (A/C)	exon 1	Forward primer A	5'-GGC TGA GCA AAG AGG CAC T <u><i>AA</i></u> -3'
		Forward primer C	5'-GGC TGA GCA AAG AGG CAC T <u><i>AC</i></u> -3'
		Reverse primer	5'- CAG GAC TCC CCC TTG TCC AG-3'
		Probe	5'-FAM-CCA GGC ACT GGG TGA GCC GGG GCC- BHQ-1-3'
rs2464196 (G/A)	exon 7	Forward primer G	5'-GCA GAG CCA TGT GAC CCA G <u><i>TG</i></u> -3'
		Forward primer A	5'-GCA GAG CCA TGT GAC CCA G <u><i>TA</i></u> -3'
		Reverse primer	5'-GCT CAC CGT GGG GGC TCT-3'
		Probe	5'-FAM-CCC TTC ATG GCC ACC ATG GCT CAG CTG- BHQ-1-3'
rs1169310 (C/T)	3'UTR	Forward primer	5'-GGA CCG CTA CAC CAC TCT G-3'
		Reverse primer C	5'-GAA CAA GGC CAC GCT GAT <u><i>AC</i></u> -3'
		Reverse primer T	5'-AGA ACA AGG CCA CGC TGA T <u><i>AT</i></u> -3'
		Probe	5'-FAM-AGC TCA GCA GGT CAC AGC TAC ACA GGC C-BHQ-1-3'

The underlined *italic* bases near the 3'end of the primers are mismatched to increase the specificity of allele discrimination.



Supplementary Figure 1 HNF1A SNP genotyping and DNA sequencing results. **A.** Real-time ARMS-PCR amplification plots and sequencing results for HNF1A-rs1169288 (T/G). ARMS-PCR was performed using two reactions. T: Amplification curves of T allele; G: amplification curves of G allele. The different Δ cycle thresholds (Δ ct= Ct value of T allele minus Ct value of G allele) were used to determine the TT, TG or GG alleles, and the corresponding sequencing results are shown below with black arrows. 1-1: TT genotype, 1-2: TG genotype, 1-3: GG genotype. **B.** Real-time ARMS-PCR amplification plots and sequencing results for HNF1A-rs2464196 (C/T). ARMS-PCR was performed using two reactions. C: Amplification curves of C allele; T: amplification curves of T allele. The different Δ cycle thresholds (Δ ct= Ct value of C allele minus Ct value of T allele) were used to determine the CC, CT or TT alleles, and

the corresponding sequencing results are shown below with black arrows. 2-1: CC genotype, 2-2: CT genotype, 2-3: TT genotype. **C.** Real-time ARMS-PCR amplification plots and sequencing results for HNF1A-rs1169310 (C/T). ARMS-PCR was performed using two reactions. C: Amplification curves of C allele; T: amplification curves of T allele. The different Δ cycle thresholds ($\Delta Ct = Ct \text{ value of C allele} - Ct \text{ value of T allele}$) were used to determine the CC, CT or TT alleles, and the corresponding sequencing results are shown below with black arrows. 3-1: CC genotype, 3-2: CT genotype, 3-3: TT genotype.

Supplementary Table 2 Basic characteristics of apparently healthy subjects compared among the HNF1A genotypes

	Total	rs1169288			<i>P</i>	rs2464196			<i>P</i>	rs1169310			<i>P</i>
		AA (n=311)	AC (n=483)	CC (n=216)		GG (n=290)	GA (n=473)	AA (n=247)		CC (n=282)	CT (n=478)	TT (n=250)	
Gender	1010	189/122	294/189	132/84	0.997	173/117	282/191	160/87	0.355	166/116	287/191	162/88	0.327
(male/female)													
Age (years)	48.22±7.80	47.77±0.44	48.31±0.36	48.69±0.51	0.387	47.68±7.63	48.45±7.78	48.43±8.05	0.378	47.55±7.63	48.49±7.79	48.48±8.00	0.230
BMI (kg/m ²)	24.56±2.58	24.63±0.14	24.51±0.12	24.56±0.19	0.828	24.69±2.46	24.42±2.57	24.67±2.74	0.288	24.67±2.50	24.45±2.54	24.66±2.73	0.414
Systolic pressure (mmHg)	116.80±15.34	115.99±0.89	116.79±0.70	118.00±1.03	0.334	117.39±16.27	116.25±14.75	117.17±15.37	0.557	117.18±16.36	116.28±14.75	117.37±15.30	0.589
Diastolic pressure (mmHg)	75.74±9.85	75.11±0.55	75.80±0.46	76.50±0.63	0.280	76.04±10.30	75.62±9.27	75.60±10.42	0.827	75.99±10.12	75.64±9.40	75.64±10.42	0.879
LDL (mmol/L)	2.65±0.69	2.69±0.04	2.64±0.03	2.62±0.05	0.437	2.70±0.68	2.66±0.68	2.57±0.70	0.076	2.72±0.70	2.65±0.67	2.57±0.70	0.054
HDL (mmol/L)	0.96±0.23	0.96±0.01	0.95±0.01	0.96±0.02	0.824	0.97±0.26	0.96±0.22	0.94±0.23	0.282	0.97±0.26	0.96±0.22	0.94±0.23	0.255
TC (mmol/L)	4.98±0.88	5.00±0.05	4.97±0.04	4.97±0.06	0.890	5.04±0.89	4.97±0.86	4.92±0.88	0.275	5.06±0.91	4.97±0.85	4.92±0.88	0.172
AST (U/L)	20.40	20.50	20.50	20.30	0.189	20.85	20.10	20.60	0.056	20.85	20.15	20.60	0.107
	(17.40, 24.80)	(17.50, 25.00)	(17.60, 25.20)	(16.90, 24.68)		(17.88, 25.70)	(17.30, 24.30)	(17.60, 25.70)		(17.88, 25.35)	(17.27, 24.33)	(17.60, 25.63)	
FPG (mmol/L)	5.23±0.90	5.17±0.05	5.26±0.04	5.26±0.06	0.376	5.21±0.99	5.23±0.81	5.27±0.93	0.792	5.23±1.00	5.22±0.81	5.26±0.93	0.832
ALT (U/L)	18.50	18.50	18.60	17.40	0.199	19.25	18.10	18.80	0.165	19.15	18.15	18.95	0.333
	(13.10, 26.83)	(12.80, 26.9)	(13.40, 27.9)	(12.40, 25.1)		(13.40, 27.40)	(13.00, 25.60)	(13.10, 27.20)		(13.33, 27.40)	(13.00, 26.10)	(13.10, 26.98)	
TG (mmol/L)	1.27	1.28	1.24	1.31	0.843	1.28	1.23	1.33	0.067	1.28	1.23	1.33	0.092
	(0.88, 1.89)	(0.89, 1.90)	(0.85, 1.89)	(0.88, 1.86)		(0.90, 1.97)	(0.84, 1.82)	(0.91, 1.93)		(0.86, 1.94)	(0.84, 1.82)	(0.91, 1.94)	
GGT (U/L)	21.50	22.70	21.30	21.00	0.368	23.70	20.70	21.40	0.190	23.10	20.85	21.40	0.320
	(14.78, 35.73)	(14.90, 36.20)	(14.70, 36.80)	(14.68, 33.40)		(15.18, 36.95)	(14.10, 35.75)	(15.50, 33.60)		(15.05, 36.33)	(14.10, 36.35)	(15.48, 34.15)	
CRP (mg/L)	1.08	1.13	1.08	0.98	0.023	1.11	1.05	1.06	0.276	1.12	1.05	1.06	0.143
	(0.68, 1.81)	(0.72, 1.95)	(0.69, 1.78)	(0.57, 1.58)		(0.67, 2.09)	(0.67, 1.74)	(0.68, 1.61)		(0.70, 2.09)	(0.67, 1.73)	(0.69, 1.67)	
Fatty liver (%)	44.70	43.40	45.30	44.90	0.864	43.10	44.20	47.40	0.588	43.30	44.10	47.20	0.629

Data are presented as mean ± standard deviation (SD) or n (%). Non-normally distributed data are presented as median (interquartile range [IQR]). The TG, CRP, ALT, AST and GGT data were

In-transformed before analysis. *P* value indicates the comparison among the genotypes of each SNP locus of HNF1A using ANOVA for continuous variables and Chi-square test for categorical variables and SNP distribution frequencies.

Supplementary Table 3 HNF1A rs2464196-rs1169310 haplotype frequencies in healthy Chinese subjects and HCC patients.

	rs2464196	rs1169310	Frequency (%)	
			Healthy subjects	HCC patients
H1	G	C	50.98	48.65
H2	G	T	1.15	0.54
H3	A	C	0.60	0.27
H4	A	T	47.27	50.54

Supplementary Table 4 Associations of HNF1A rs2464196 and rs1169310 haplotypes with AFP level in healthy Chinese subjects.

	R ²	Haplotype	β	95% CI	SE	<i>P</i>
Model 1	0.010	GC	0			
		AT	-0.080	-0.117, -0.043	0.019	<0.001
		Other	0.072	-0.071, 0.214	0.072	0.324
Model 2	0.023	GC	0			
		AT	-0.081	-0.118, -0.044	0.019	<0.001
		Other	0.069	-0.072, 0.21	0.072	0.339
Model 3	0.073	GC	0			
		AT	-0.074	-0.111, -0.038	0.018	<0.001
		Other	0.056	-0.083, 0.194	0.071	0.430

Model 1: no adjustment; Model 2: adjusted for age, gender, and BMI; Model 3: adjusted for age, gender, BMI, blood pressure, HDL, TC, lnAST, lnALT, lnTG, lnGGT, lnCRP, FPG, and fatty liver. β means the unstandardized beta coefficients (β) for the effects of HNF1A polymorphisms on the AFP levels. *P* values for the associations of the haplotypes of rs2464196 and rs1169310 with the lnAFP level in healthy subjects.

Supplementary Table 5 Associations of HNF1A rs2464196- rs1169310 haplotypes with AFP level in Chinese HCC patients.

	R ²	Haplotype	β	95% CI	SE	<i>P</i>
Model 1	0.022	GC	0			
		AT	-1.033	-1.744, -0.321	0.362	0.005
		Other	-0.437	-4.403, 3.529	2.017	0.829
Model 2	0.073	GC	0			
		AT	-0.899	-1.6, -0.199	0.356	0.012
		Other	-0.432	-4.306, 3.441	1.970	0.826
Model 3	0.603	GC	0			
		AT	-0.474	-0.948, 0	0.241	0.049
		Other	-0.477	-3.046, 2.092	1.306	0.715

Model 1: no adjustment; Model 2: adjusted for age and gender; Model 3: adjusted for age, gender, lnALT, lnAST, HBV and HCV infection status, tumor size, clinical stage, and differentiation degree. β means the unstandardized beta coefficients (β) for the effects of HNF1A polymorphisms on the AFP levels. *P* values for the associations of the haplotypes of rs2464196 and rs1169310 with the lnAFP level in HCC patients.