Figure S1. ROC curves were constructed to test the ability of differential diagnosis. (A) ROC curves were constructed to test the ability to differentiate between DN and HCC. (B) ROC curves were constructed to test the ability to differentiate between non-tumorous tissue and HCC. (C) ROC curves were constructed to test the ability to differentiate between DN and well-differentiated HCC. (D) ROC curves were constructed to test the ability to differentiate between HGDN and well-differentiated HCC. hepatocellular carcinoma; ROC, receiver operator characteristic; HGDN, high-grade dysplastic nodule; DN, dysplastic nodule.



Test Result Variable(s): IHC

Α

			Asymptotic 95% Confidence		
		Asymptotic	Interval		
Area	Std. Error	Sig."	Lower Bound	Upper Bound	
. 822	.067	.004	.690	.954	

The test result variable(s): IHC has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

- a. Under the nonparametric assumption
- b. Null hypothesis: true area = 0.5

С





Test Result Variable(s): IHC

			Asymptotic 95% Confidence Interval		
Area	Std. Error'	Asymptotic Sig. <sup>b</sup>	Lower Bound	Upper Bound	
.819	.099	.023	.624	1.000	

The test result variable(s): IHC has at least one tie between the positive actual

state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5



Test Result Variable(s): IHC

			Asymptotic 95% Confidence		
		Asymptotic	Interval		
Area	Std. Error'	Sig. <sup>b</sup>	Lower Bound	Upper Bound	
.923	.030	.000	.863	.983	

The test result variable(s): IHC has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

- a. Under the nonparametric assumption
- b. Null hypothesis: true area = 0.5

D



## Area Under the Curve

Test Result Variable(s): IHC

			Asymptotic 95% Co	nfidence Interval
Area	Std. Error	Asymptotic Sig.	Lower Bound	Upper Bound
. 808	.110	.045	. 593	1.000

The test result variable(s): IHC has at least one tie between the positive actual

state group and the negative actual state group. Statistics may be biased.

- a. Under the nonparametric assumption
- b. Null hypothesis: true area = 0.5

Figure S2. AUC values from HNRNPA3<sup>+</sup>, GPC3<sup>+</sup>, HNRNPA3<sup>+</sup>/GPC3<sup>+</sup>. (A) AUC values for diagnosis of HCC, HNRNPA3<sup>+</sup> (AUC=0.729), GPC3<sup>+</sup> (AUC=0.844) and HNRNPA3<sup>+</sup>/GPC3<sup>+</sup> (AUC=0.854), HNRNPA3<sup>+</sup>/GPC3<sup>+</sup> two-marker set showed a specificity of 100%. (B) AUC values for diagnosis of well-differentiated HCC, HNRNPA3<sup>+</sup> (AUC=0.713), GPC3<sup>+</sup> (AUC=0.838) and HNRNPA3<sup>+</sup>/GPC3<sup>+</sup> (AUC=0.850), HNRNPA3<sup>+</sup>/GPC3<sup>+</sup> two-marker set showed a specificity of 100%. (C) AUC values for diagnosis of early HCC, HNRNPA3<sup>+</sup> (AUC=0.741), GPC3<sup>+</sup> (AUC=0.795) and HNRNPA3<sup>+</sup>/GPC3<sup>+</sup> (AUC=0.857), HNRNPA3<sup>+</sup>/GPC3<sup>+</sup> two-marker set showed a specificity of 100%. HNRNPA3<sup>+</sup> (AUC=0.795) and HNRNPA3<sup>+</sup>/GPC3<sup>+</sup> (AUC=0.857), HNRNPA3<sup>+</sup>/GPC3<sup>+</sup> two-marker set showed a specificity of 100%. HNRNPA3<sup>+</sup> (AUC=0.900) and HNRNPA3<sup>+</sup>/GPC3<sup>+</sup> (AUC=0.900) and HNRNPA3<sup>+</sup> (AUC=0.900) and HNRNPA3<sup>+</sup> (AUC=0.900) and



Case no.	Sex	Age, years	HBV	HBsAg	HBsAb	HBeAg	HBeAb	HBcAb
1	М	62	+	+	+	+	_	+
2	М	65	-	-	-	-	+	+
3	М	56	+	+	+	-	+	+
4	М	63	+	+	+	-	+	+
5	М	55	-	-	-	+	+	+
6	F	76	+	+	+	-	-	+
7	М	49	+	+	+	-	+	+
8	М	52	+	+	+	-	+	+
9	М	61	+	+	+	-	+	+
10	F	62	+	+	+	+	-	+
11	F	61	+	+	-	-	+	+
12	М	60	-	-	-	-	+	+
13	Μ	63	+	+	-	-	+	+
14	М	58	+	+	-	-	+	+
15	М	81	-	-	+	-	-	-
16	М	50	+	+	-	_	+	+
17	F	50	+	+	-	+	-	+
18	М	71	+	+	-	_	+	+
19	М	51	+	+	-	-	+	+
20	М	67	+	+	-	+	-	+
21	М	59	+	+	-	+	-	+
22	М	55	+	+	-	-	+	+
23	М	59	+	+	-	+	+	+
24	М	66	-	-	+	-	+	+
25	М	69	+	+	-	+	-	+
26	F	59	+	+	-	-	+	+
27	М	43	+	+	-	-	+	+
28	М	63	+	+	+	-	+	+
29	М	61	+	+	-	+	-	+
30	М	60	+	+	-	-	+	+
31	F	43	+	+	-	-	+	+
32	F	61	+	+	-	+	+	+
33	М	67	+	+	-	_	+	+
34	М	78	+	+	-	_	+	+
35	М	67	+	+	_	_	+	+
36	М	47	+	+	_	_	+	+
37	М	64	+	+	_	_	+	+
38	M	72	+	+	+	_	+	+
39	M	59	-	-	-	_	-	-
40	M	54	+	+	_	+	+	+
41	M	89	-	-	+	-	-	+
42	M	70	+	+	+	_	+	' +
43	M	67	-	-	+	_	+	' +
44	M	46	+	+	-	_	' +	т +
45	M	- <del>1</del> 0	т -	т -	_	_	T L	т 
46	M	61	τ +	-T -	-	-	т +	т 
47	M	54	Missing	Missing	Missing	Missing	Missing	Missing
48	M	60	Missing	Missing	Missing	Missing	Missing	Missing

F, female patient; M, male patient; HPV, Hepatitis B Virus; +, positive; -, negative; HBsAg, Hepatitis B virus surface Antigen; HBeAg, Hepatitis B virus e antigen; HBeAb, Hepatitis B virus e antibody; HBcAb, Hepatitis B virus core antibody.

Table SII. Clinical HBV data of patients with dysplastic nodules.

Case no.	Sex	Age, years	HBV	HBsAg	HBsAb	HBeAg	HBeAb	HBcAb
1	М	61	+	+	-	-	+	+
2	М	63	+	+	-	+	-	+
3	М	50	+	+	-	-	+	+
4	М	48	+	+	-	-	+	+
5	М	32	-	-	-	-	-	-
6	F	65	+	+	-	-	+	+
7	F	60	+	+	-	-	+	+
8	М	72	-	-	-	-	+	+

F, female patient; M, male patient; HBV, Hepatitis B Virus; +, positive; -, negative; HBsAg, Hepatitis B virus surface Antigen; HBeAg, Hepatitis B virus e antigen; HBeAb, Hepatitis B virus e antibody; HBcAb, Hepatitis B virus core antibody.

Table SIII. Sensitivity, specificity, PPV and NPV for detection of HCC, well-differentiated HCC and early HCC using HNRNPA3<sup>+</sup>, GPC3<sup>+</sup> and combination.

A, HCC							
Phenotype	НСС	DN (n=8)	Sensitivity	Specificity	PPV	NPV	
HNRNPA3 <sup>+</sup>	40	3	83.33	62.50	93.0	38.5	
GPC3+	39	1	81.25	87.50	97.5	43.8	
HNRNPA3 <sup>+</sup> /GPC3 <sup>+</sup>	34	0	70.83	100.00	100.0	36.4	

## B, Well-differentiated HCC

Phenotype	Well-differentiated HCC	DN (n=8)	Sensitivity	Specificity	PPV	NPV
HNRNPA3+	8	3	80.00	62.50	72.7	71.4
GPC3+	8	1	80.00	87.50	88.9	77.8
HNRNPA3+/GPC3+	7	0	70.00	100.00	100.0	72.7
C, Early HCC						

Phenotype	Early HCC	DN (n=8)	Sensitivity	Specificity	PPV	NPV
HNRNPA3 <sup>+</sup>	6	3	85.71	62.50	66.7	83.3
GPC3+	5	1	71.43	87.50	83.3	77.8
HNRNPA3+/GPC3+	5	0	71.43	100.00	100.0	80.0

NPV, negative predictive value; PPV, positive predictive value; +, positive expression; HCC, hepatocellular carcinoma; HNRNPA3, heterogeneous nuclear ribonucleoprotein A3; GPC3, glypican 3; DN, dysplastic nodules.

		HNR expre	NPA3 ession	
Variable	n	Weak	Strong	P-value
AFP <sup>a</sup>				
≤20 ng/ml	15	4	11	
>20 ng/ml	24	3	21	
Missing	9	1	8	0.4538
CEA <sup>a</sup>				
≤5 ng/ml	28	6	22	
>5 ng/ml	2	0	2	
Missing	18	16	2	0.5334
CA-125 <sup>a</sup>				
≤35 U/ml	28	3	25	
>35 U/ml	3	1	2	
Missing	17	4	13	0.3885
ALT <sup>a</sup>				
≤40 U/l	17	1	16	
>40 U/l	22	6	16	
Missing	9	1	8	0.1822
AST <sup>a</sup>				
≤35 U/l	18	2	16	
>35 U/l	21	5	16	
Missing	9	1	8	0.5037

Table SIV. Association between HNRNPA3 expression, serum enzymes and tumor biomarkers in hepatocellular carcinoma.

HNRNPA3, heterogeneous nuclear ribonucleoprotein A3; AFP,  $\alpha$ -fetoprotein; CEA, carcinoembryonic antigen; CA-125, cancer antigen 125; ALT, alanine aminotransferase; AST, aspartate aminotransferase.  ${}^{a}\chi^{2}$  test was used to investigate the association between HNRNPA3 expression and indicators that were subdivided into three groups.

		HNR expre		
Variable	Ν	Weak	Strong	P-value
Age <sup>a</sup>				
≤55	3	2	1	
>55	5	3	2	>0.9999
Gender <sup>a</sup>				
Male	6	4	2	
Female	2	1	1	>0.9999
Tumor size <sup>a</sup>				
≤5	6	4	2	
>5	2	1	1	>0.9999
Cirrhosis <sup>a</sup>				
Yes	7	3	4	
No	1	1	0	>0.9999

Table SV. Association between HNRNPA3 expression and clinicopathological factors in patients with dysplastic nodule.

HNRNPA3, heterogeneous nuclear ribonucleoprotein A3. <sup>a</sup>Fisher's exact test was applied to find the association between HNRNPA3 expression and indicators that were subdivided into two groups.