

Polymorphisms of *CCNBI* associated with the clinical outcomes of platinum-based chemotherapy in advanced Chinese NSCLC patients

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Table S1. A part of Features and functions of *CCNBI*

Gene	Features	Functions
<i>CCNBI</i>	Form maturation-promoting factor with CDK1	Control mitosis (from G2 to M phase)
	Switch like-all or none behavior (positive feedback)	Commit to mitosis
	Fluctuating protein expression in normal cells	Break down the nuclear envelope
	Overexpression in many cancers [#]	Tumor antigen

[#]Including lung cancer, breast cancer, cervical, gastric, colorectal, head and neck squamous cell, oral and esophageal¹⁻⁵.

Table S2. Haplotype information of four tagSNPs of *CCNBI*

No.	Haplotype	Freq
1	GAAA	0.180*
2	GAAG	0.000
3	GAGA	0.038
4	GGGA	0.313*
5	GGGG	0.000
6	AAAA	0.000
7	AAGA	0.415*
8	AAGG	0.000

Abbreviations: No.: number, Freq: frequency

*Haplotype requery more than 10% were analyzed.

Table S3. Univariate analysis of four tagSNPs of *CCNBI* with PFS in 972 advanced NSCLC patients

SNP ID	genotype	N(%)	mPFS(95%CI)	X ²	P _{L-G}	HR(95%CI)	P _{COX}
Rs352626				0.771	0.680	R	0.681
	AG	452(50.4%)	8.1(6.8-9.4)				
	GG	256(28.6%)	9.5(7.4-11.6)	0.93(0.77-1.13)	0.465		
	genotype	AA	188(21.0%)	9.5(6.8-12.2)	0.93(0.75-1.15)	0.485	

	AA +AG	640(71.4%)	8.7(7.5-10.0)	0.275	0.600		
Dominant(A)	GG	256(28.6%)	9.5(7.4-11.6)			0.95 (0.80-1.14)	0.601
	AA	188(21.0%)	9.5(6.8-12.2)	0.228	0.633		
Recessive(A)	GG+AG	708(79.0%)	9.1(7.9-10.3)			1.05(0.86-1.28)	0.633
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Rs2069429				1.804	0.406		0.409
	GG	596(66.5%)	9.1(7.7-10.5)			R	
	AG	271(30.2%)	8.7(6.7-10.8)			1.06(0.89-1.27)	0.511
genotype	AA	29(3.3%)	10.1(3.0-17.2)			0.76(0.46-1.25)	0.279
	AA+AG	300(32.7%)	9.1(7.5-10.8)	0.095	0.758		
Dominant(A)	GG	596(66.5%)	9.1(7.7-10.5)			0.97(0.82-1.16)	0.759
	AA	29(3.3%)	10.1(3.0-17.2)	1.365	0.243		
Recessive(A)	GG+AG	867(96.7%)	9.1(8.0-10.2)			1.34(0.82-2.21)	0.245
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Rs2069433				0.249	0.883		0.885
	A/A	804(89.7%)	9.1(7.8-10.3)			R	
	A/G	90(10.0%)	9.6(7.4-11.8)			1.01(0.77-1.33)	0.927
genotype	G/G	2(0.3%)	8.0(NA)			0.62(0.09-4.38)	0.629
	AA+AG	894(99.7%)	9.1(8.0-10.2)	0.241	0.624	1.63(0.23-11.56)	0.628
Recessive(G)	GG	2(0.3%)	8.0(NA)				
	AA	804(89.7%)	9.1(7.8-10.3)	0.0002	0.990	1.00(0.76-1.31)	0.990
Dominant(G)	GG+AG	92(10.3%)	9.6(7.4-11.9)				
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Rs350104				2.29	0.319		0.321
	A/A	421(47.0%)	9.4(7.7-11.2)			R	
	A/G	381(42.5%)	7.7(6.5-9.0)			1.09(0.92-1.30)	0.309
genotype	G/G	94(10.5%)	10.8(4.9-16.7)			0.90(0.67-1.19)	0.449
	AA +AG	802(89.5%)	9.0(7.9-10.1)	1.226	0.268	1.17(0.89-1.53)	0.270
Recessive(G)	GG	94(10.5%)	10.8(4.9-16.7)				
	AA	421(47.0%)	9.4(7.7-11.2)	0.349	0.554	0.95(0.81-1.12)	0.555
Dominant(G)	GG+AG	475(53.0%)	8.8(7.4-10.2)				

* $p < 0.05$. Abbreviations: mPFS: median progression free survival, HR: hazard ratio, CI: confidence interval, NA: Not available, R: Reference

P_{LG} : p value was calculated by log-rank test; P_{COX} : p value was calculated by univariate cox regression analysis.

Table S4. Multivariate Cox's regression analysis of clinical factors and *CCNB1* tagSNPs for PFS in the 972 advanced NSCLC patients treated with platinum-based chemotherapy

Variables	HR (95% CI)	P
Age (≥ 60 vs. < 60)	0.97(0.82-1.15)	0.725
Sex (male vs. female)	1.07(0.89-1.29)	0.476
TNM(IV vs. IIIa vs. IIIb)	1.14(1.00-1.30)	0.057
ECOG PS(2 vs. 1)	1.54(1.15-2.06)	0.003*
Smoking (ever vs. never)	1.03(0.81-1.33)	0.790
Histology		0.744
adenocarcinoma	R	

squamous	1.09(0.87-1.36)	0.471
adenosquamous	0.77(0.38-1.56)	0.462
others	0.99(0.75-1.30)	0.918
Treatment		0.103
DNA-damaging agents ^a	R	
Platinum-tubulin-targeting drugs ^b	1.13(0.93-1.36)	0.233
Other combination ^c	1.43(0.99-2.07)	0.056
Rs2069429 dominant (A)	0.93(0.77-1.12)	0.448
Rs2069429 recessive (A)	1.42(0.84-2.38)	0.188
Rs2069433 dominant (G)	1.08(0.81-1.44)	0.621
Rs2069433 recessive (G)	1.28(0.17-9.69)	0.810
Rs350104 dominant (G)	0.92(0.77-1.10)	0.372
Rs350104 recessive (G)	1.13(0.86-1.48)	0.175
Rs352626 dominant (A)	1.00(0.68-1.46)	0.989
Rs352626 recessive (A)	1.02(0.74-1.22)	0.888

a Others NSCLC included adenosquamous carcinoma, mixed-cell, neuroendocrine carcinoma, or undifferentiated carcinoma.

b Tubulin-targeting drugs includes paclitaxel, docetaxel or navelbine.

c Other combination included etoposide or bevacizumab.

* $p < 0.05$. Abbreviations: HR: hazard ratio, CI: confidence interval;

Table S5. Association between *CCNBI* haplotypes with OS/PFS in all with advanced NSCLC

Haplotype	N (%)	mOS (95% CI), mo	HR (95% CI)	P-value
GAAA				
Copy number 0	654 (67.3%)	19.5(18.0-21.2)	R	0.109
Copy number 1-2	318(32.7%)	18.2(16.0-20.5)	1.13(0.97-1.32)	
GGGA				
Copy number 0	462(47.5%)	18.8(17.0-20.6)	R	0.292
Copy number 1-2	510 (52.5%)	19.8(18.0-21.7)	0.93(0.80-1.07)	
AAGA				
Copy number 0	324(33.3%)	19.1(16.9-21.3)	R	0.682
Copy number 1-2	648 (66.7%)	19.3(17.6-20.9)	1.03(0.89-1.21)	
Haplotype	N (%)	mPFS (95% CI), mo	HR (95% CI)	P-value
GAAA				
Copy number 0	596 (66.5%)	9.1 (7.7-10.5)	R	0.759

Copy number 1-2	300(33.5%)	9.1(7.5-10.8)	1.03(0.86-1.22)	
GGGA				
Copy number 0	421 (47.0%)	9.4(7.7-11.2)	R	0.555
Copy number 1-2	475(53.0%)	8.8(7.4-10.2)	1.05(0.89-1.24)	
AAGA				
Copy number 0	305 (34.0%)	9.5(7.7-11.3)	R	0.517
Copy number 1-2	591 (66.0%)	8.7(7.4-9.9)	1.06(0.89-1.26)	

* $p < 0.05$. Abbreviations: mOS: median overall survival, mo: months, HR: hazard ratio, CI: confidence interval

Table S6. Stratified analysis of association between *CCNBI* haplotypes with PFS in patients with clinical stage III and IV

Haplotype	Patients with clinical stage III				Patients with clinical stage IV			
	N (%)	mPFS(95% CI), mo	X ²	P-value	N (%)	mPFS(95% CI), mo	HR (95% CI)	P-value
GAAA								
Copy number 0	207(64.9%)	11.0 (7.8-14.2)	-	0.984	385(67.3%)	7.8(6.4-9.1)	-	0.625
Copy number 1-2	112 (35.1%)	9.5(5.9-13.0)	<0.001		187(32.7%)	8.1(6.0-10.2)	0.239	
GGGA								
Copy number 0	146 (45.8%)	10.1(8.1-12.0)	-	0.241	272(47.6%)	9.3(7.1-11.6)	-	0.062
Copy number 1-2	173(54.2%)	10.8(6.7-14.9)	1.377		300(52.4%)	7.4(5.8-9.1)	3.472	
AAGA								
Copy number 0	112(35.1%)	10.3(7.2-13.4)	-	0.486	191(33.3%)	8.8(6.8-10.9)	-	0.854
Copy number 1-2	207(64.9%)	9.7(6.4-12.9)	0.485		381(66.7%)	7.8(6.4-9.2)	0.034	

* $p < 0.05$. Abbreviations: mPFS: median progression free survival, mo: months, HR: hazard ratio, CI: confidence interval

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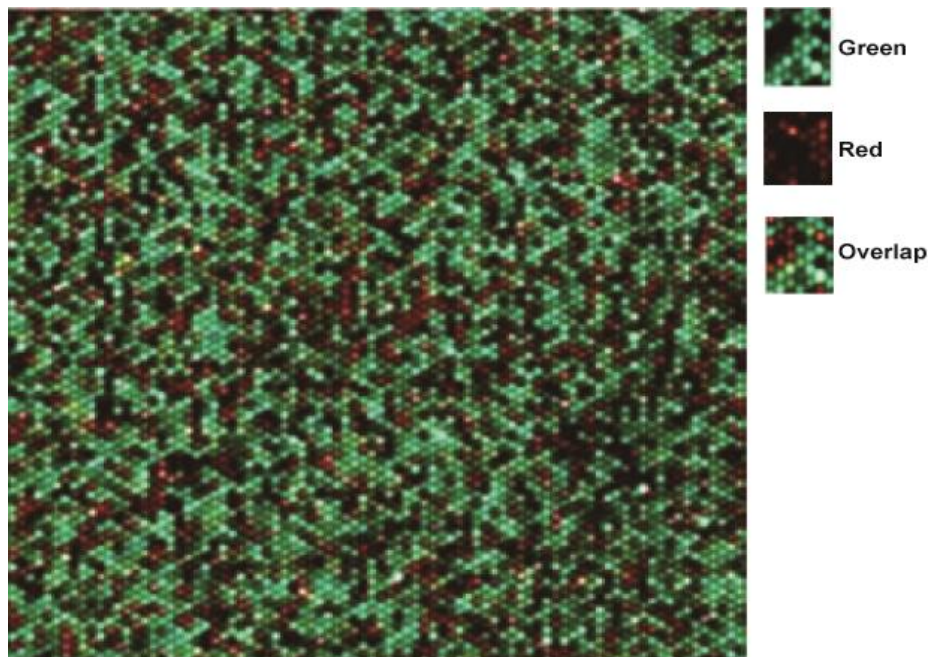


Figure S1

Figure S1: The tagSNPs of *CCNB1* with Illumina BeadScan Picture.

Reference

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