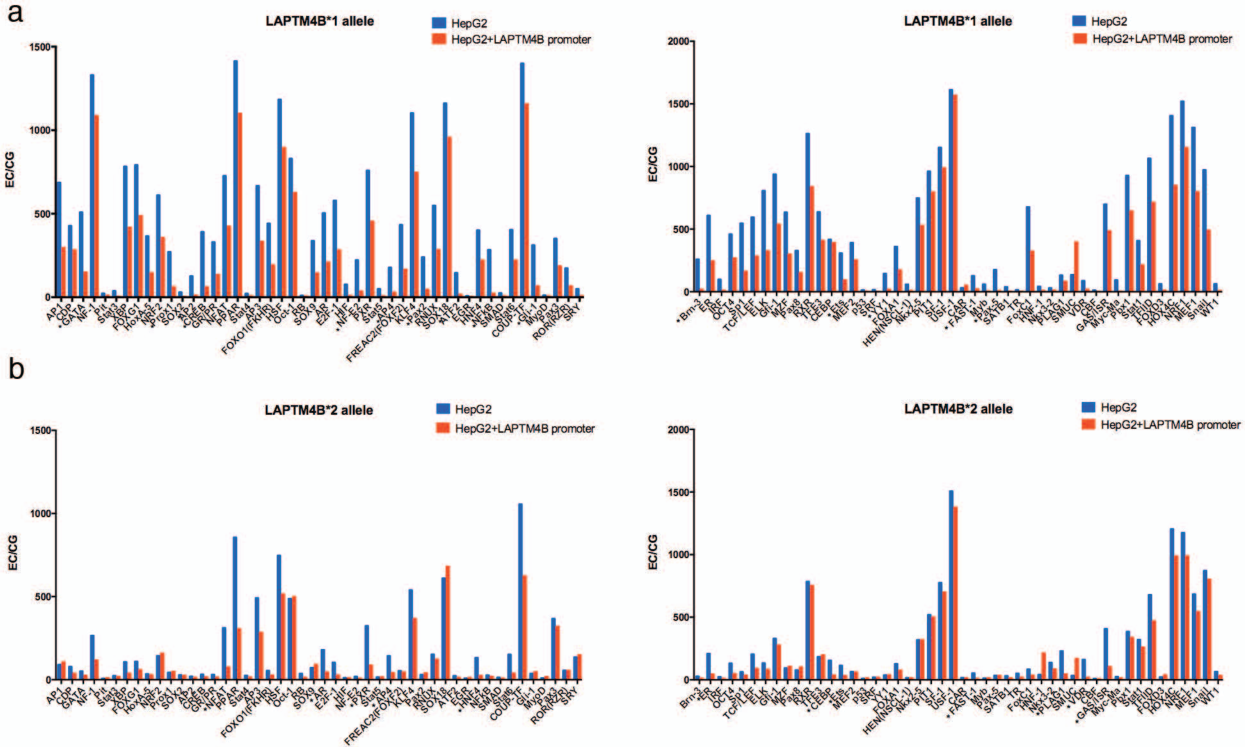
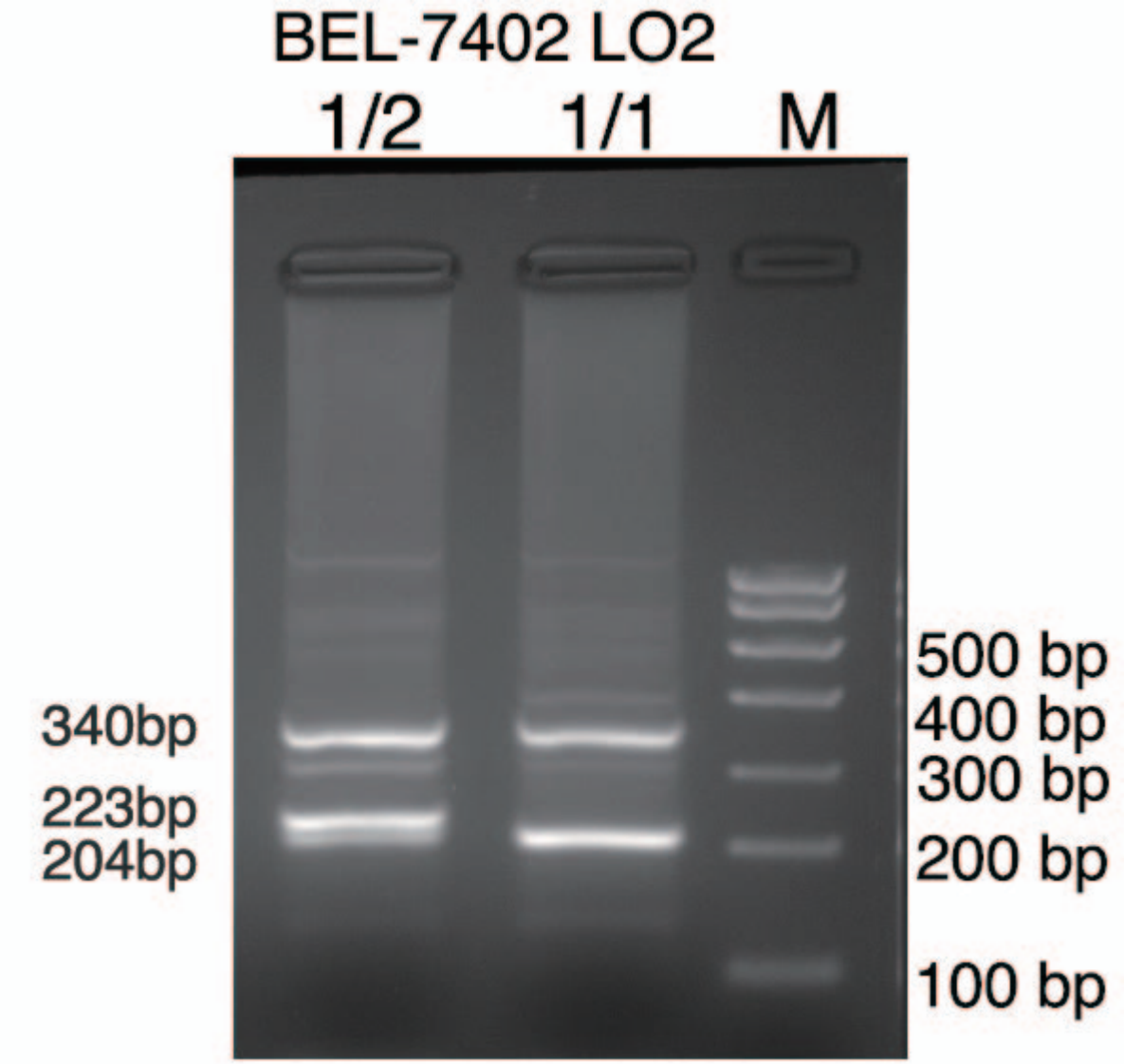


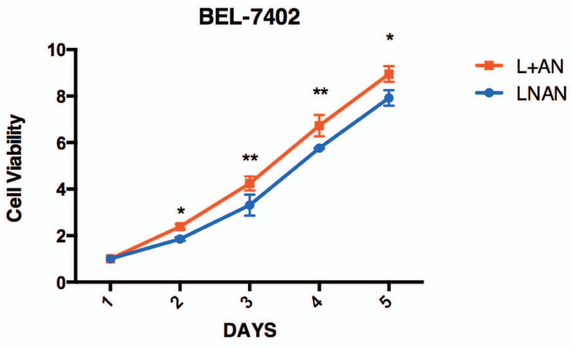
a
LAPTM4B*1 allele
HepG2
HepG2+LAPTM4B promoter
EC/CG
LAPTM4B*1 allele
HepG2
HepG2+LAPTM4B promoter
EC/CG
b
LAPTM4B*2 allele
HepG2
HepG2+LAPTM4B promoter
EC/CG
LAPTM4B*2 allele
HepG2
HepG2+LAPTM4B promoter
EC/CG

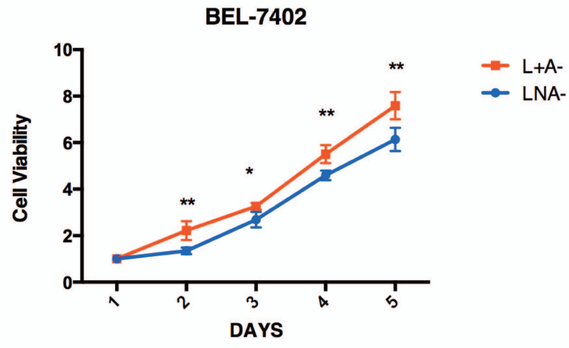
FigureS1. The result of TF activation profiling plate assay. (a) The result of TF activation profiling plate assay in LAPTM4B*1 promoter. (b) The result of TF activation profiling plate assay in LAPTM4B*1 promoter. The factors with asterisk represent binding factors，which means the HepG2 nuclear protein+LAPTM4B promoter group compete more than 3-folds protein than HepG2 nuclear protein group and each factor’s value of chemiluminescence must be above 100.

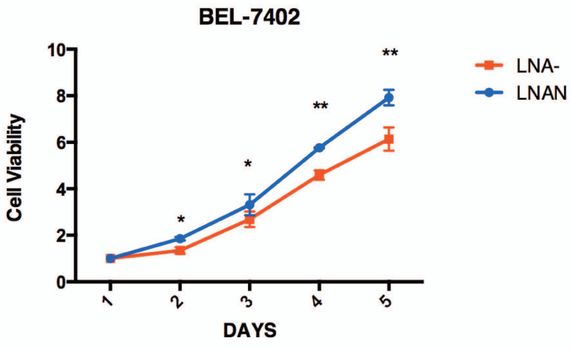

BEL-7402 LO2
1/2
1/1
M
340bp
223bp
204bp
500 bp
400 bp
300 bp
200 bp
100 bp

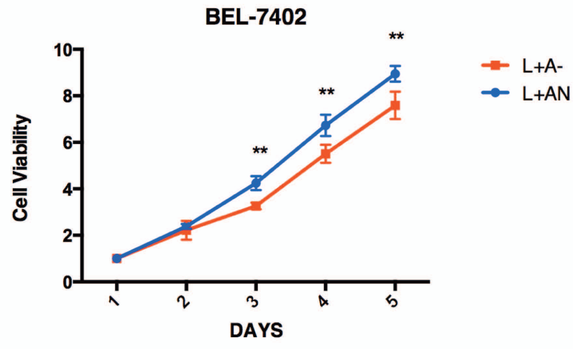
FigureS2. Genotyping of LAPTM4B. M is DNA marker. LO2 gennotype is LAPTM4B*1/1. BEL-7402 genotype is LAPTM4B*1/2. 204bp is the LAPTM4B*1 allele sequence, 223bp is the LAPTM4B*2 allele sequence, 340bp is the β-actin sequence.

a

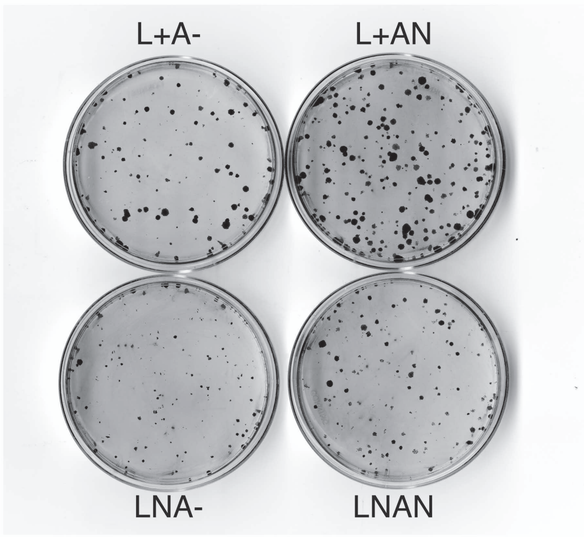

BEL-7402
Cell Viability
DAYS
L+AN
LNAN

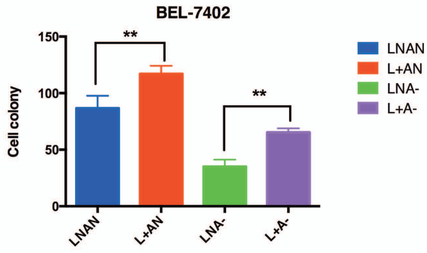

BEL-7402
Cell Viability
DAYS
L+A-
LNA-

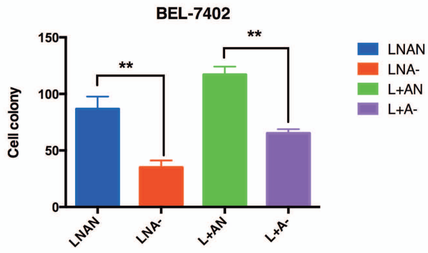

BEL-7402
Cell Viability
DAYS
LNA-
LNAN


BEL-7402
Cell Viability
DAYS
L+A-
L+AN

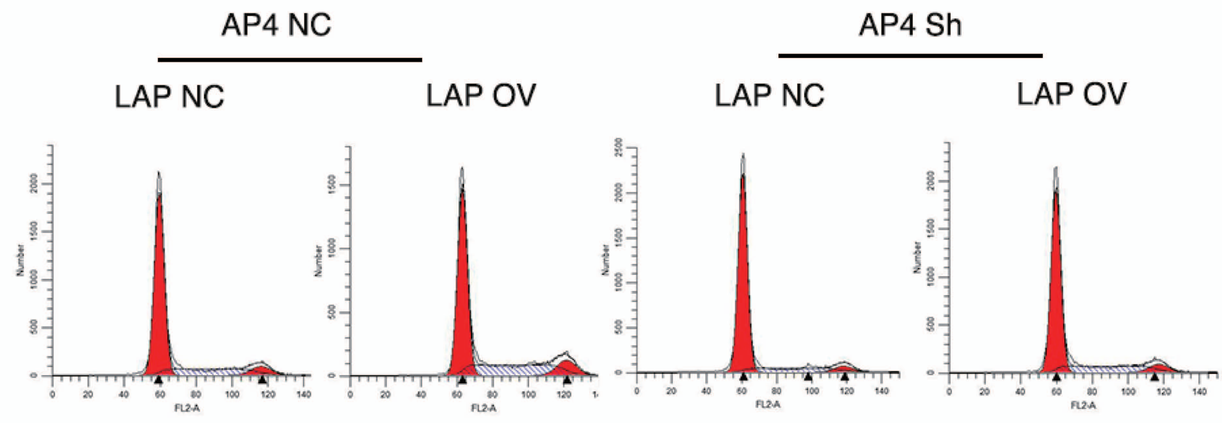
b


L+A-
L+AN
LNA-
LNAN

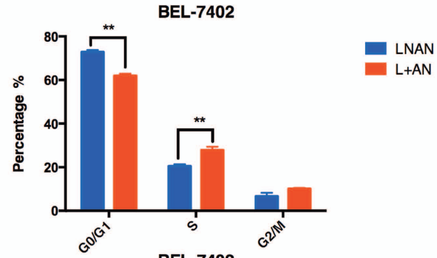

BEL-7402
Cell colony
LNAN
L+AN
LNA-
L+A-

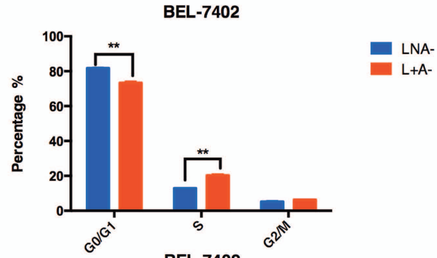

BEL-7402
Cell colony
LNAN
LNA-
L+AN
L+A-

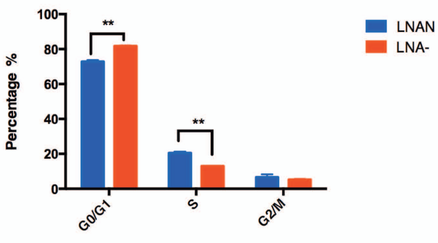
c

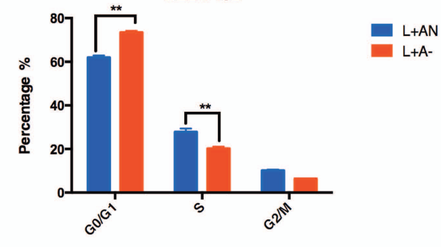

AP4 NC
AP4 Sh
LAP NC
LAP OV
LAP NC
LAP OV
Number
FL2-A

BEL-7402


BEL-7402
Percentage %
G0/G1
S
G2/M
LNAN
L+AN

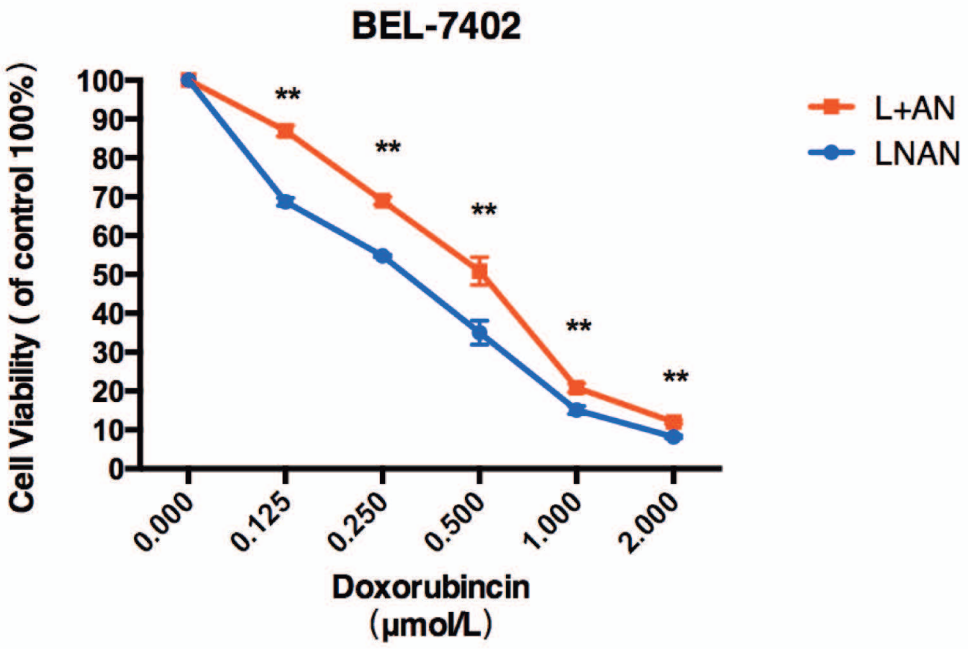

BEL-7402
Percentage %
G0/G1
S
G2/M
LNA-
L+A-

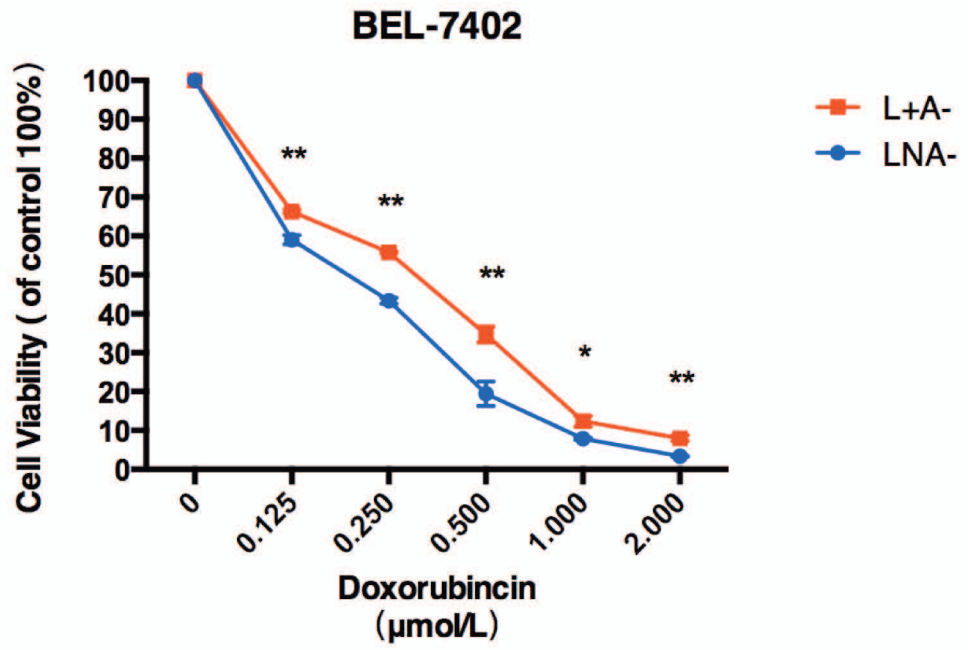

BEL-7402
Percentage %
G0/G1
S
G2/M
LNAN
LNA-

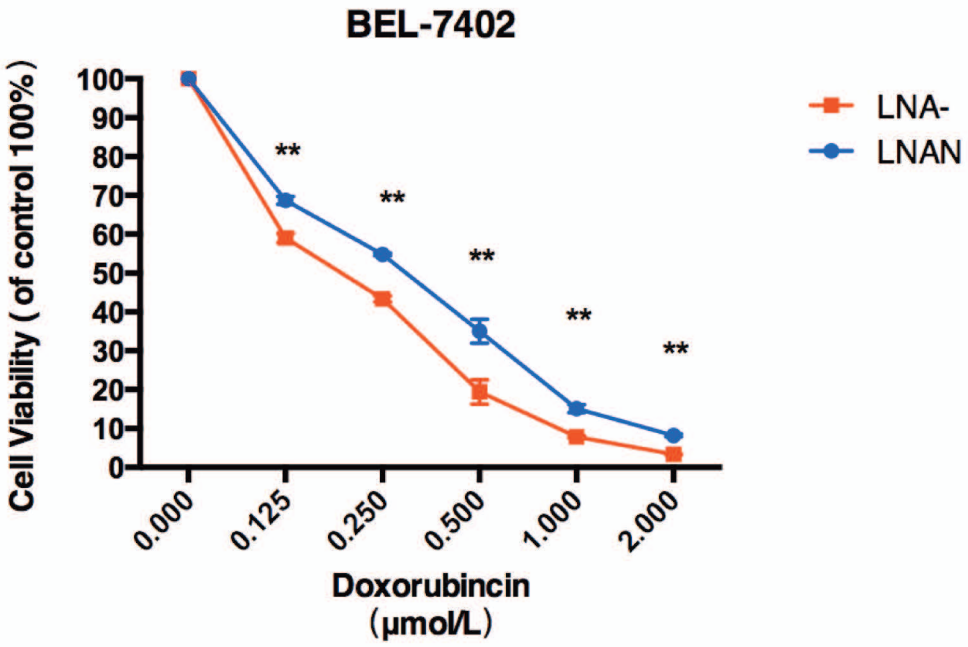

BEL-7402
Percentage %
G0/G1
S
G2/M
L+AN
L+A-

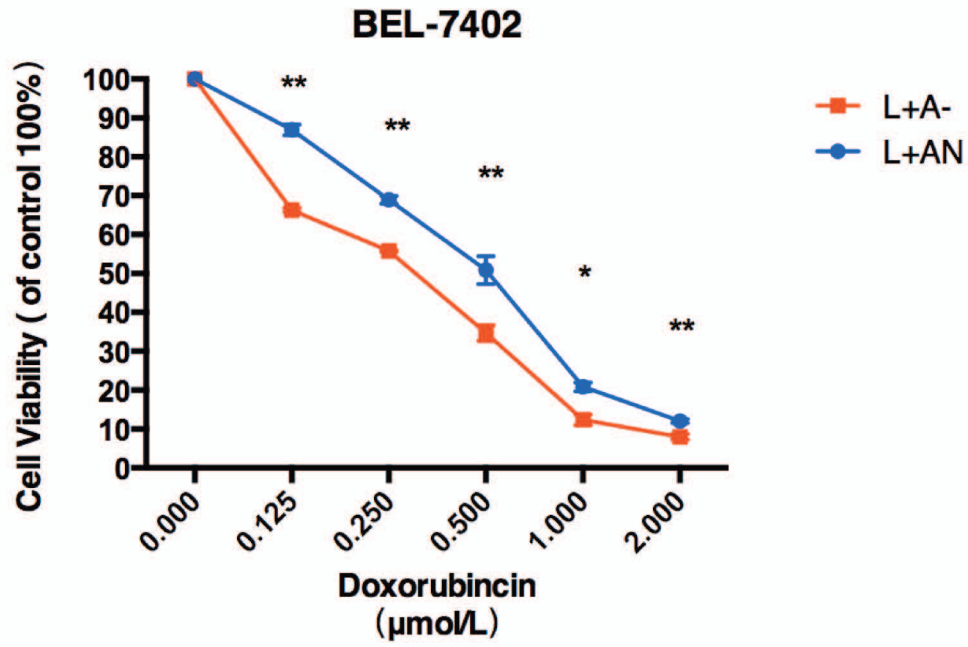
FigureS3. AP4 promotes HCC cell growth via LAPTM4B by affecting cell proliferation and cell cycle *in vitro* and *in vivo*. **(a-b)** Overexpression of LAPTM4B partially but significantly rescued the cell growth arrest induced by TFAP4 knockdown in BEL-7402 cells, as measured by the cell viability assay and colony formation (*P<0.05, ** P<0.01). **(c)** Restoration of LAPTM4B significantly reversed the cycle arrest at G1 phase induced by AP4 knockdown in BEL-7402 cells. (n=3, mean ± s.d.).

a1

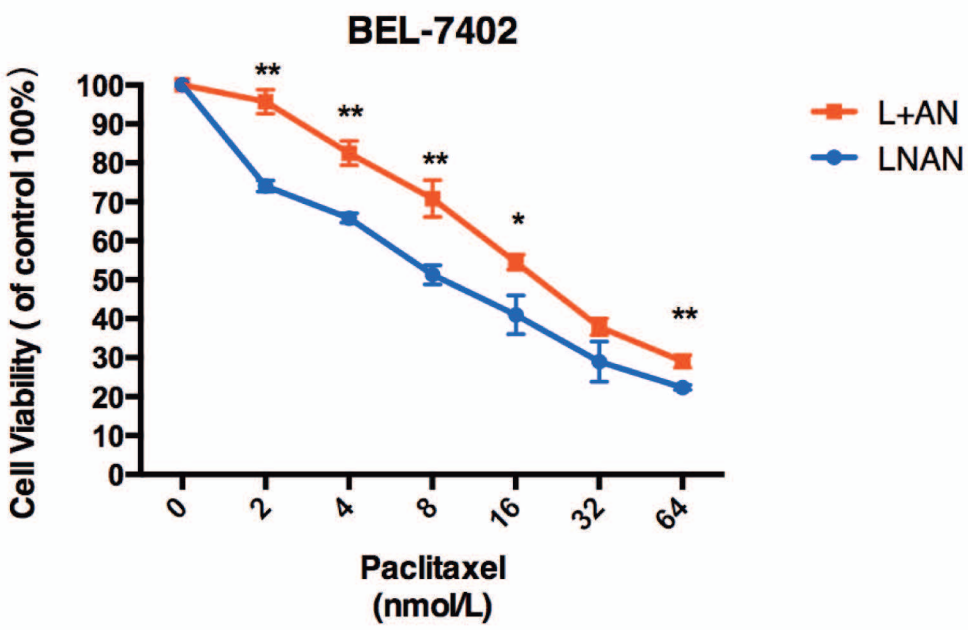

BEL-7402
Cell Viability (of control 100%)
100
90
80
70
60
50
40
30
20
10
0
**
**
**
**
**
0.000
0.125
0.250
0.500
1.000
2.000
Doxorubincin
(μmol/L)
L+AN
LNAN

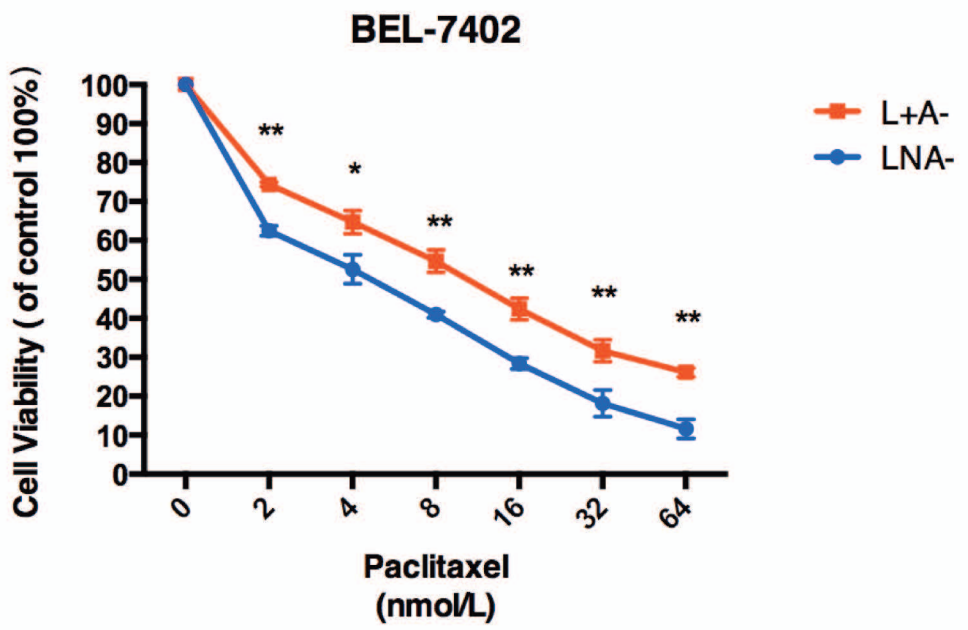

BEL-7402
Cell Viability (of control 100%)
100
90
80
70
60
50
40
30
20
10
0
**
**
**
*
**
0
0.125
0.250
0.500
1.000
2.000
Doxorubincin
(μmol/L)
L+A-
LNA-

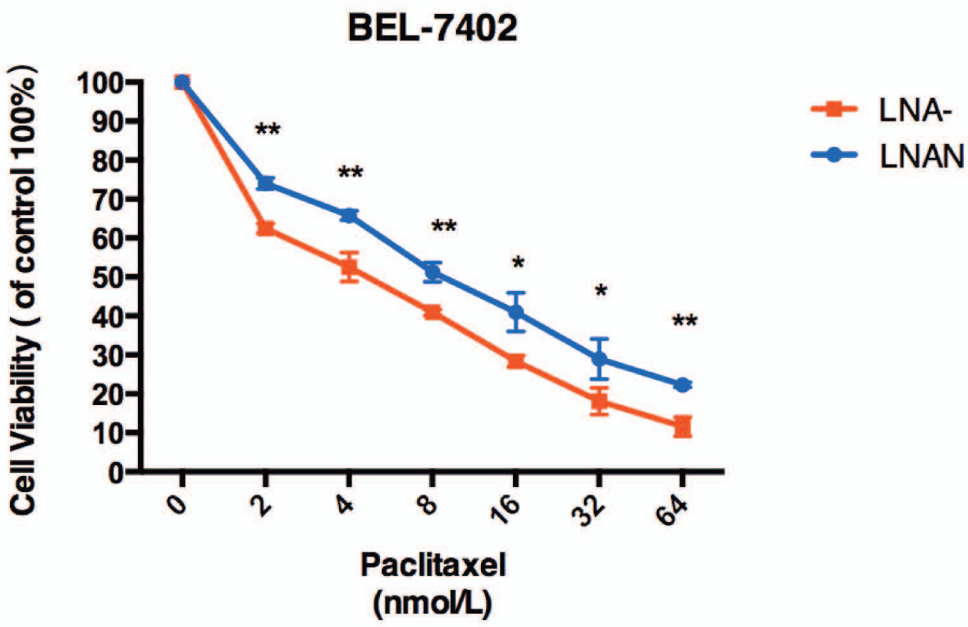

BEL-7402
Cell Viability (of control 100%)
100
90
80
70
60
50
40
30
20
10
0
**
**
**
**
**
0.000
0.125
0.250
0.500
1.000
2.000
Doxorubincin
(μmol/L)
LNA-
LNAN

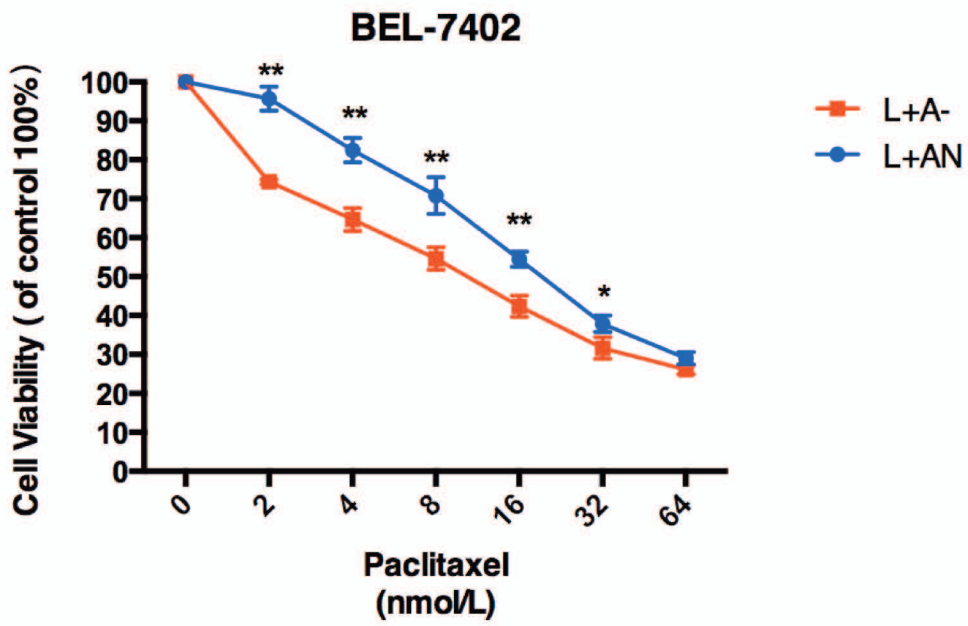

BEL-7402
Cell Viability (of control 100%)
100
90
80
70
60
50
40
30
20
10
0
**
**
**
*
**
0.000
0.125
0.250
0.500
1.000
2.000
Doxorubincin
(μmol/L)
L+A-
L+AN

a2

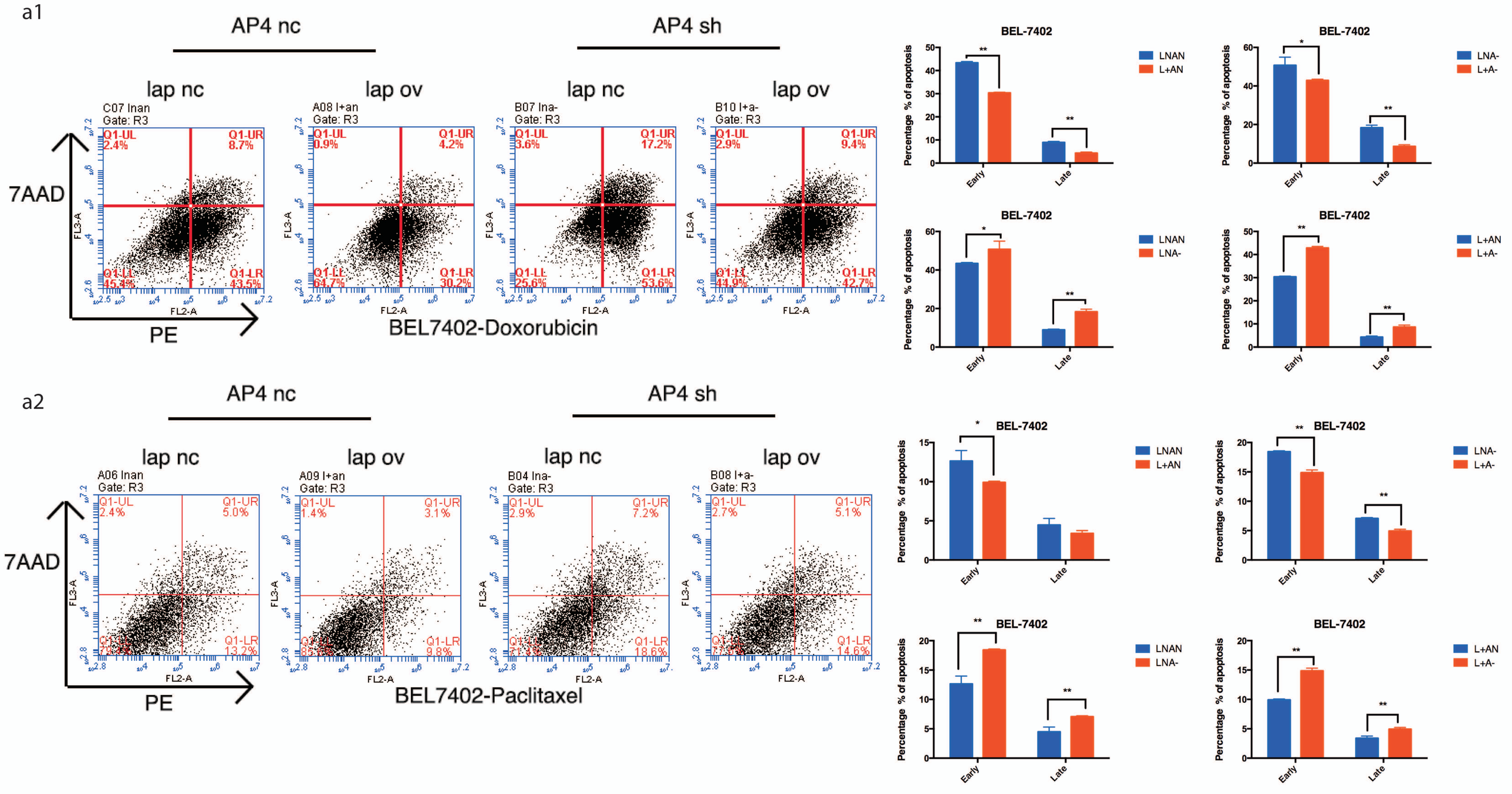

BEL-7402
Cell Viability (of control 100%)
100
90
80
70
60
50
40
30
20
10
0
**
**
**
*
**
0
2
4
8
16
32
64
Paclitaxel
(nmol/L)
L+AN
LNAN


BEL-7402
Cell Viability (of control 100%)
100
90
80
70
60
50
40
30
20
10
0
**
*
**
**
**
**
0
2
4
8
16
32
64
Paclitaxel
(nmol/L)
L+A-
LNA-


BEL-7402
Cell Viability (of control 100%)
100
90
80
70
60
50
40
30
20
10
0
**
**
**
*
*
**
0
2
4
8
16
32
64
Paclitaxel
(nmol/L)
LNA-
LNAN

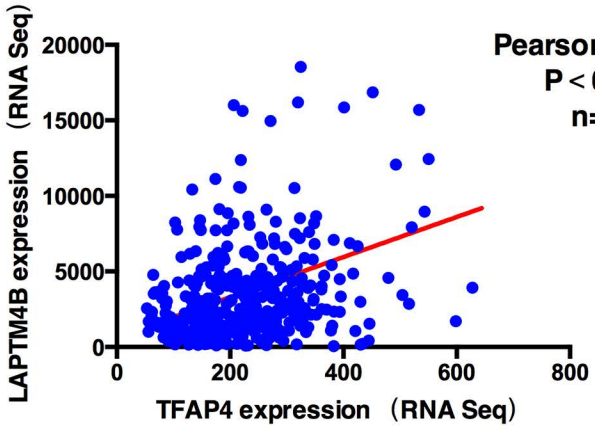

BEL-7402
Cell Viability (of control 100%)
100
90
80
70
60
50
40
30
20
10
0
**
**
**
**
*
0
2
4
8
16
32
64
Paclitaxel
(nmol/L)
L+A-
L+AN

FigureS4. AP4 reduce chemotherapy sensitivity via LAPTM4B. **(a)** Viability curves of cells in the presence of various anticancer chemotherapeutic drugs. The LNAN BEL-7402, L+AN BEL-7402, LNA- BEL-7402, L+A-BEL-7402 cells were exposed to increasing concentrations of doxorubicin **(a1)** or paclitaxel **(a2)** respectively, for 48 h. Cell viabilities were determined by cell viability assay as described in materials and methods. Results were expressed as a mean±s.d. of viable cell percentage in triplicates from three independent experiments. (*P<0.05; **P<0.01, Student' *t*-test).

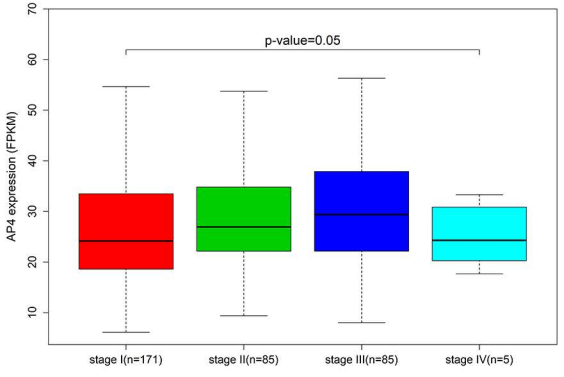

a1
AP4 nc
AP4 sh
lap nc
lap ov
lap nc
lap ov
C07 Inan
Gate: R3
A08 I+an
Gate: R3
B07 Ina-
Gate: R3
B10 I+a-
Gate: R3
Q1-UL 2.4%
Q1-UR 8.7%
Q1-LL 45.4%
Q1-LR 43.5%
Q1-UL 0.9%
Q1-UR 4.2%
Q1-LL 64.7%
Q1-LR 30.2%
Q1-UL 3.6%
Q1-UR 17.2%
Q1-LL 25.6%
Q1-LR 53.6%
Q1-UL 2.9%
Q1-UR 9.4%
Q1-LL 44.9%
Q1-LR 42.7%
7AAD
PE
FL2-A
FL3-A
BEL7402-Doxorubicin
BEL-7402
Percentage % of apoptosis
Early
Late
LNAN
L+AN
LNA-
L+A-
L+AN
L+A-
a2
AP4 nc
AP4 sh
lap nc
lap ov
lap nc
lap ov
A06 Inan
Gate: R3
A09 I+an
Gate: R3
B04 Ina-
Gate: R3
B08 I+a-
Gate: R3
Q1-UL 2.4%
Q1-UR 5.0%
Q1-LR 13.2%
Q1-UL 1.4%
Q1-UR 3.1%
Q1-LR 9.8%
Q1-UL 2.9%
Q1-UR 7.2%
Q1-LR 18.6%
Q1-UL 2.7%
Q1-UR 5.1%
Q1-LR 14.6%
7AAD
PE
FL2-A
FL3-A
BEL7402-Paclitaxel
BEL-7402
Percentage % of apoptosis
Early
Late
LNAN
L+AN
LNA-
L+A-
L+AN
L+A-

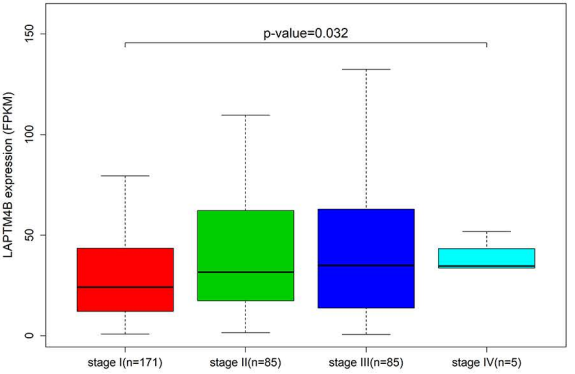
FigureS5 (a) Flow cytometry analysis of apoptosis by APC and 7AAD staining. The LNAN BEL-7402, L+AN BEL-7402, LNA- BEL-7402, L+A- BEL-7402 cells were incubated with 0.25μmol/l doxorubicin **(a1)**, 8 nmol/l paclitaxel **(a2)** After 48 h incubation, the cells were harvested and analyzed by flow cytometer. Column diagrams of apoptotic cells in percentage. (*P<0.05; **P<0.01).

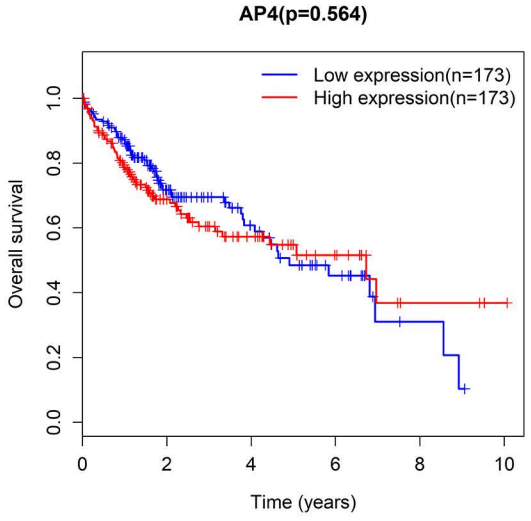
a

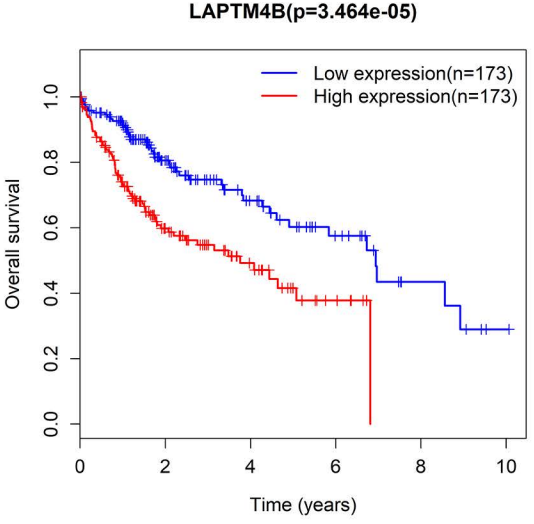

LAPTM4B expression (RNA Seq)
20000
15000
10000
5000
0
0
200
400
600
800
TFAP4 expression (RNA Seq)
Pearson r=0.3137
P < 0.0001
n=373

b

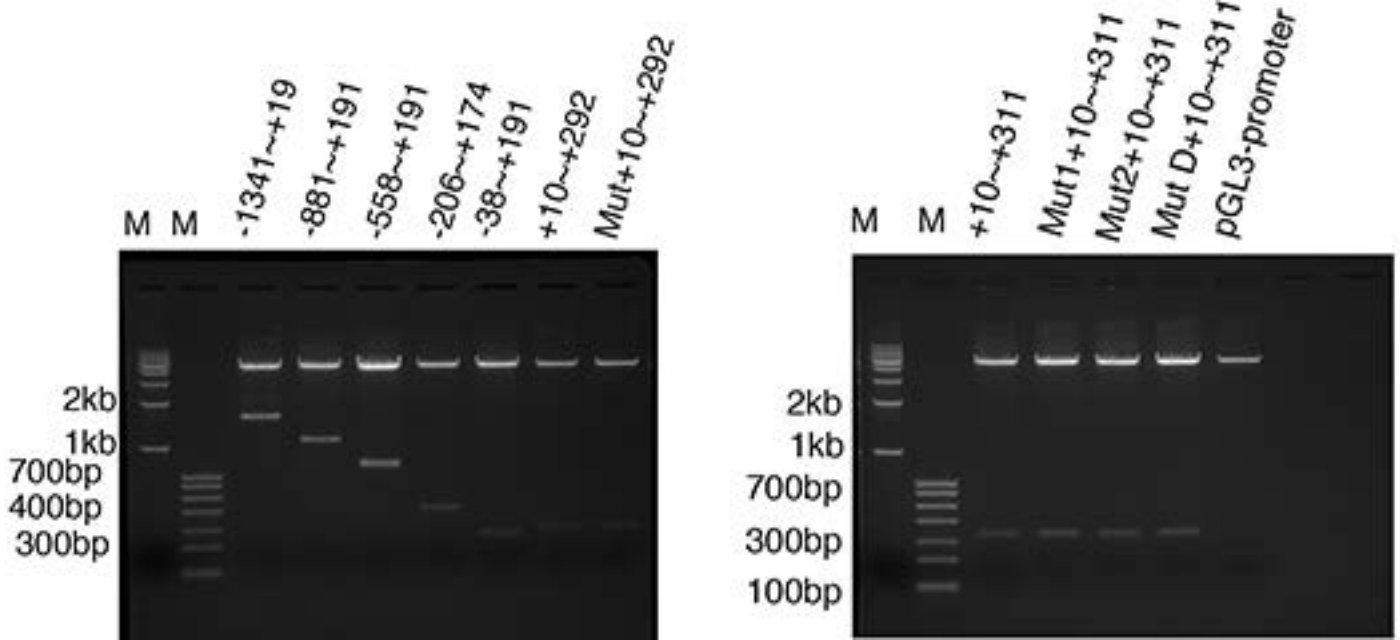

AP4 expression (FPKM)
p-value=0.05
stage I(n=171)
stage II(n=85)
stage III(n=85)
stage IV(n=5)


LAPTM4B expression (FPKM)
p-value=0.032
stage I(n=171)
stage II(n=85)
stage III(n=85)
stage IV(n=5)


AP4(p=0.564)
Low expression(n=173)
High expression(n=173)
Overall survival
Time (years)

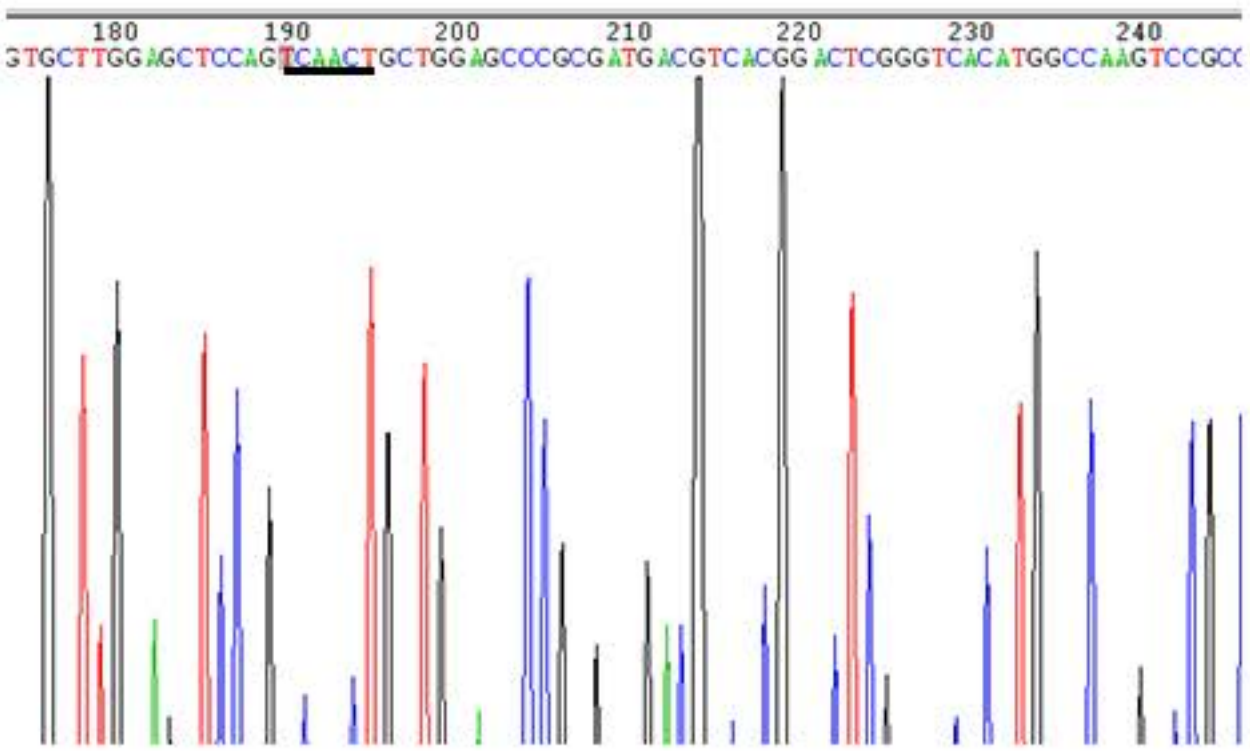

LAPTM4B(p=3.464e-05)
Low expression(n=173)
High expression(n=173)
Overall survival
Time (years)

FigureS6. TCGA dataset information about 373 HCC patients. **(a)** AP4 mRNA expression significantly correlated with LAPTM4B mRNA expression in 373 hepatoma cell carcinoma patients from TCGA. **(b-c)** The association of AP4 and LAPTM4B with tumour grades and HCC patients' survival.

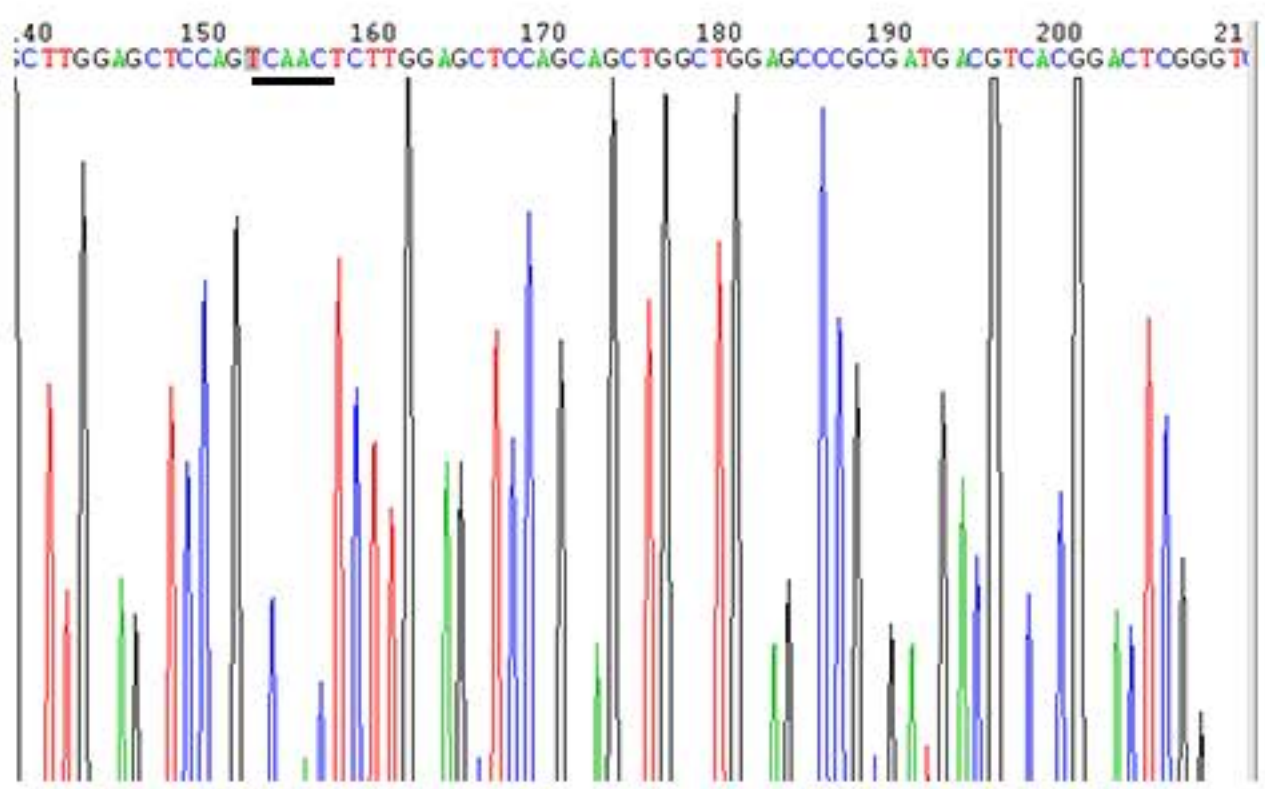

M
M
-1341~+19
-881~+191
-558~+191
-206~+174
-38~+191
+10~+292
Mut+10~+292
2kb
1kb
700bp
400bp
300bp
M
M
+10~+311
Mut1+10~+311
Mut2+10~+311
Mut D+10~+311
pGL3-promoter
2kb
1kb
700bp
300bp
100bp

FigureS7. All the plasmids digested by Xho1 and Hind3 enzyme. Mut+10~+292represents the LAPTM4B allele*1 promoter plasmid mutated the AP4 binding site. Mut1+10~+311 represents the LAPTM4B allele*2 promoter plasmid mutated the first AP4 binding site. Mut2+10~+311 represents the LAPTM4B allele*2 promoter plasmid mutated the second AP4 binding site. Mut D+10~+311 represents the LAPTM4B allele*2 promoter plasmid mutated both AP4 binding sites.

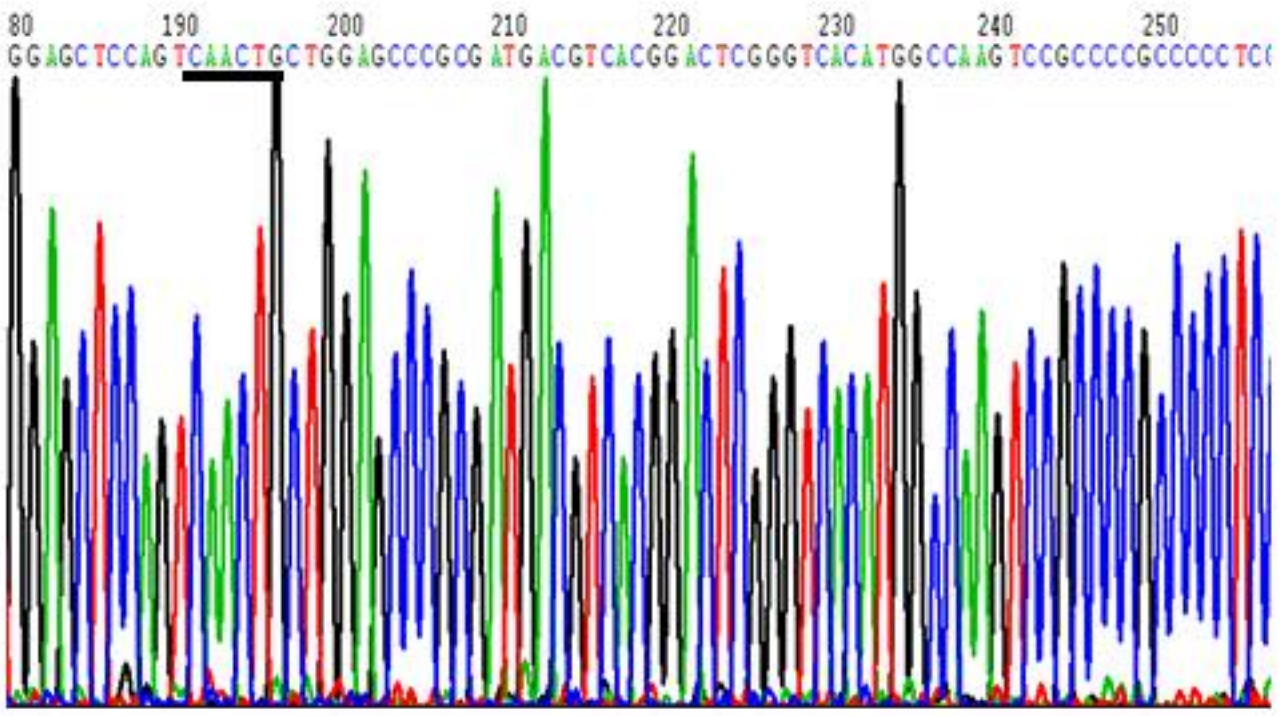
a.


180
190
200
210
220
230
240

b.


150
160
170
180
190
200

c.


80
190
200
210
220
230
240
250

d.

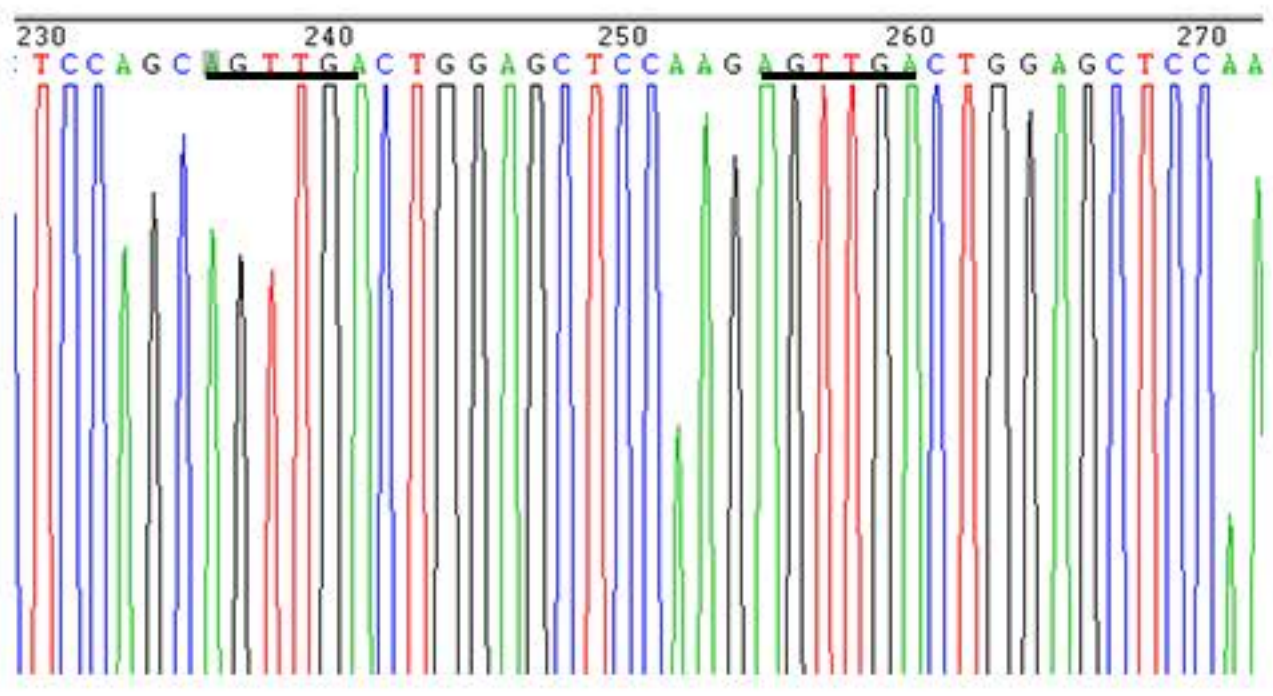
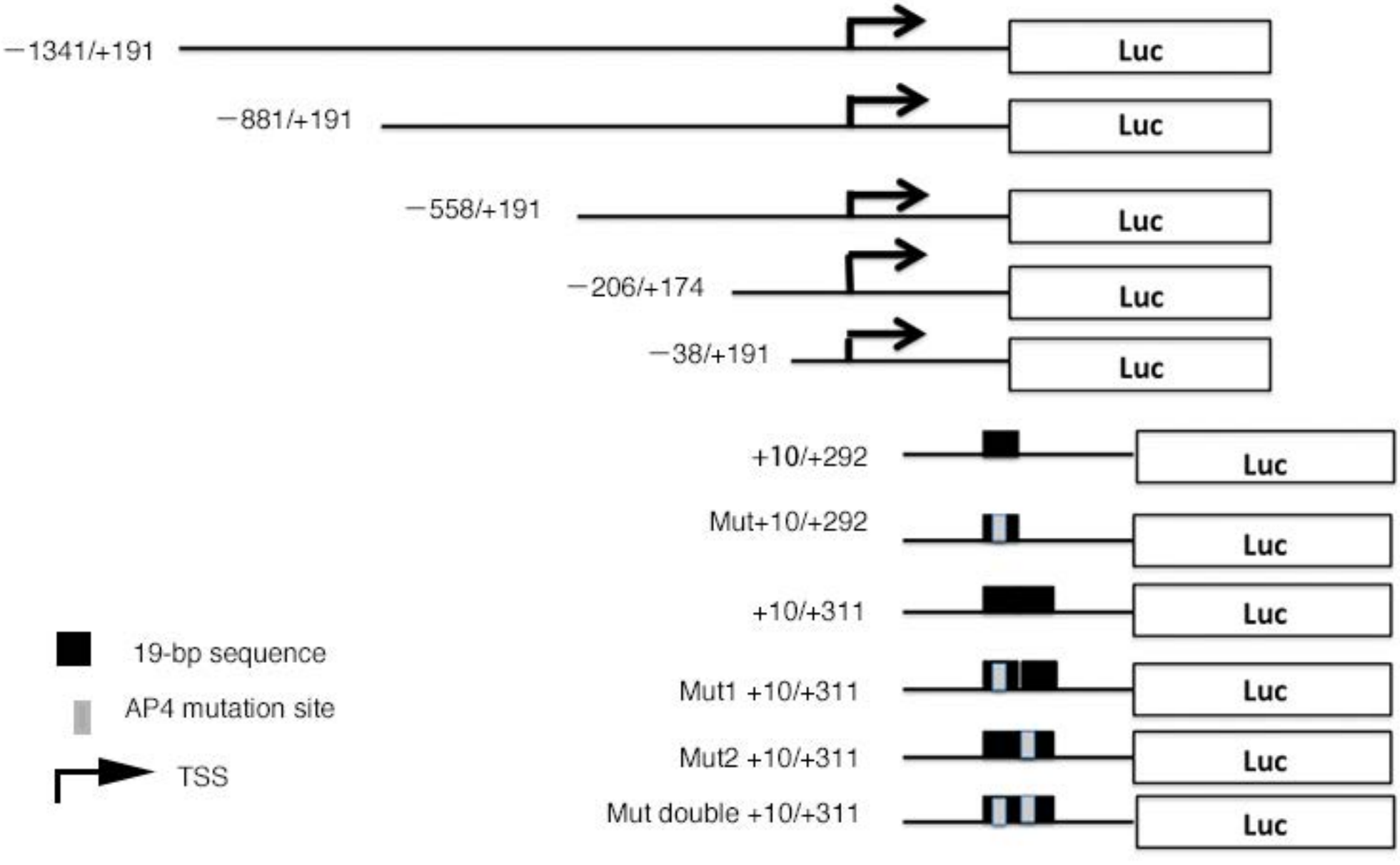

230
240
250
260
270

Figure S8. The sequenced results of mutation plasmids. TCAACT with underline were mutation sequence in **(a)** Mut +10-+292 plasmid, **(b)** Mut1 +10-+311 plasmid, **(c)** Mut2 +10-+311 plasmid and **(d)** Mut D +10-+311 plasmid.


−1341/+191
Luc
−881/+191
Luc
−558/+191
Luc
−206/+174
Luc
−38/+191
Luc
+10/+292
Luc
Mut+10/+292
Luc
+10/+311
Luc
19-bp sequence
AP4 mutation site
TSS
Mut1 +10/+311
Luc
Mut2 +10/+311
Luc
Mut double +10/+311
Luc

FigureS9. Eleven kinds of plasmids transfected into cells.