FIGURE 1A

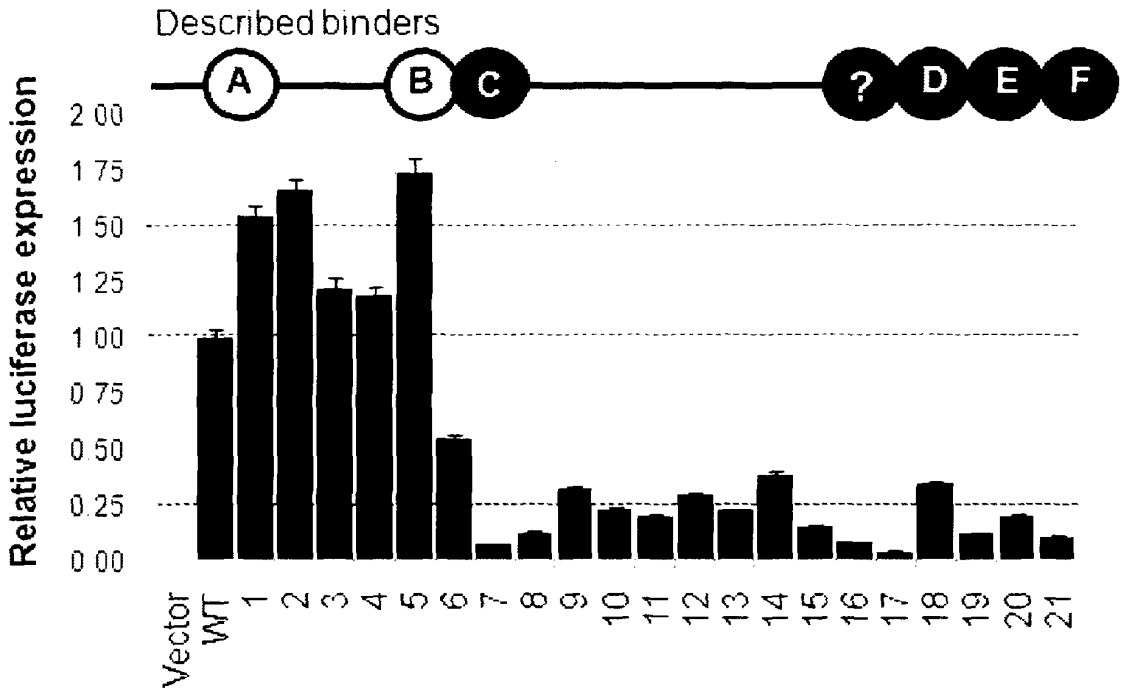

Described binders
A
B
C
?
D
E
F
Relative luciferase expression
2 00
1 75
1 50
1 25
1 00
0 75
0 50
0 25
0 00
Vector
WT
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21

FIGURE 1B

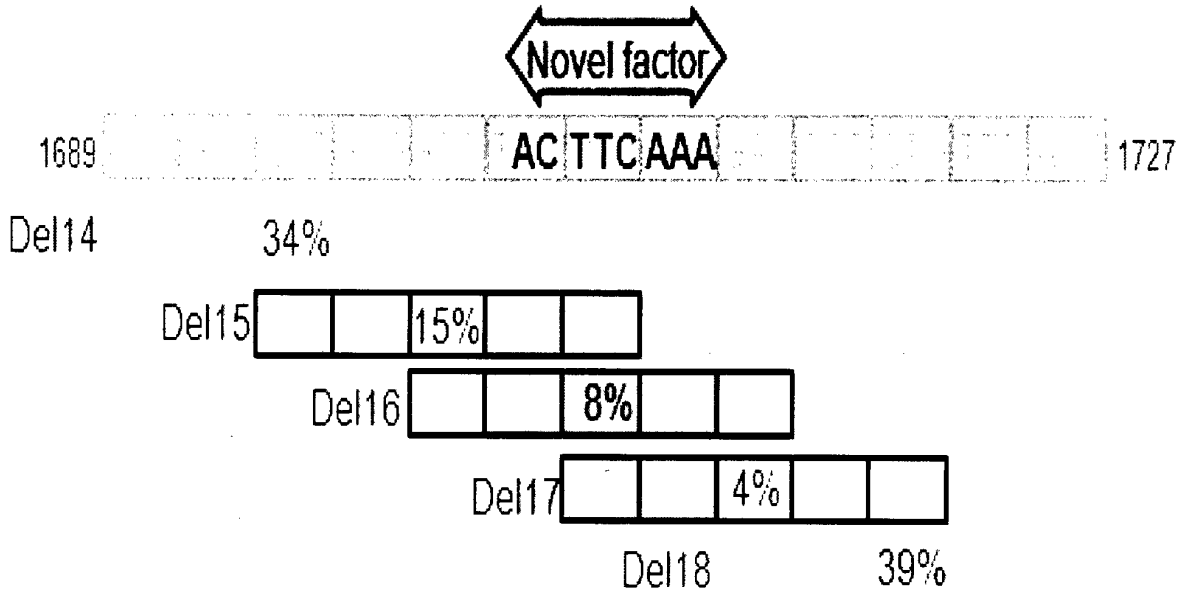
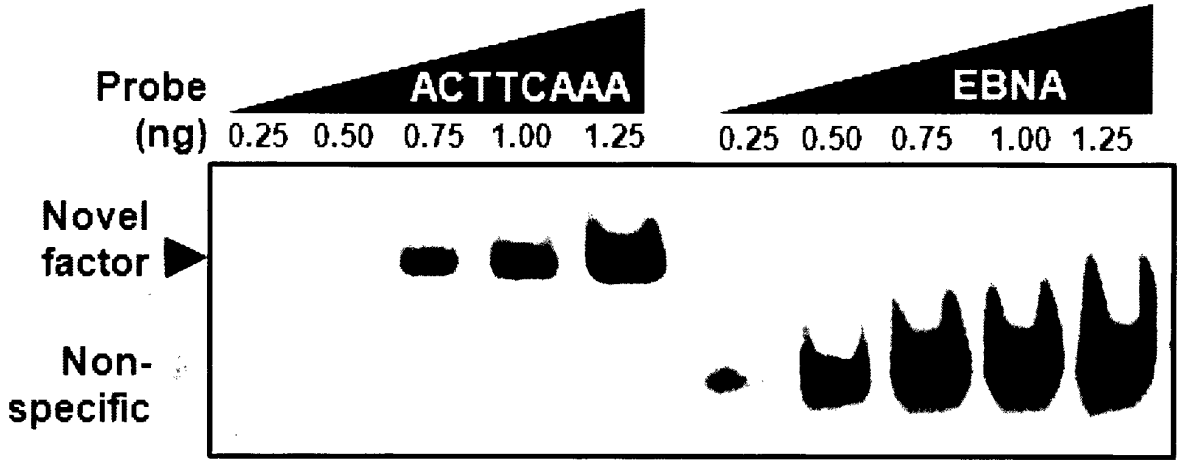

Novel factor
1689
AC TTC AAA
1727
Del14
34%
Del15
15%
Del16
8%
Del17
4%
Del18
39%

FIGURE 2A


Probe
(ng)
ACTTCAAA
0.25 0.50 0.75 1.00 1.25
EBNA
0.25 0.50 0.75 1.00 1.25
Novel factor
Non-specific

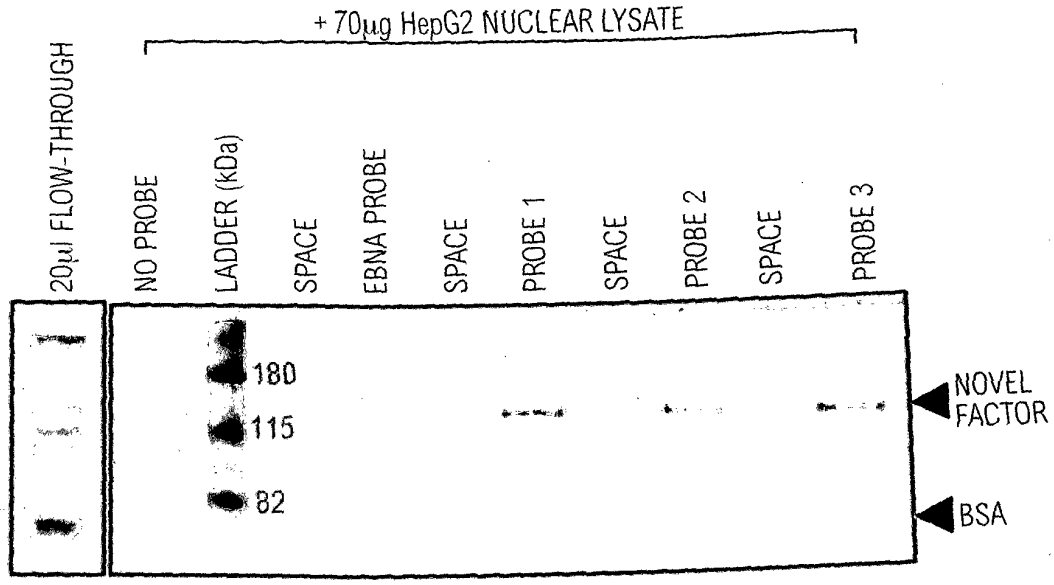

+ 70µg HepG2 NUCLEAR LYSATE
20µl FLOW-THROUGH
NO PROBE
LADDER (kDa)
SPACE
EBNA PROBE
SPACE
PROBE 1
SPACE
PROBE 2
SPACE
PROBE 3
180
115
82
NOVEL FACTOR
BSA

FIG. 2B

FIGURE 2C

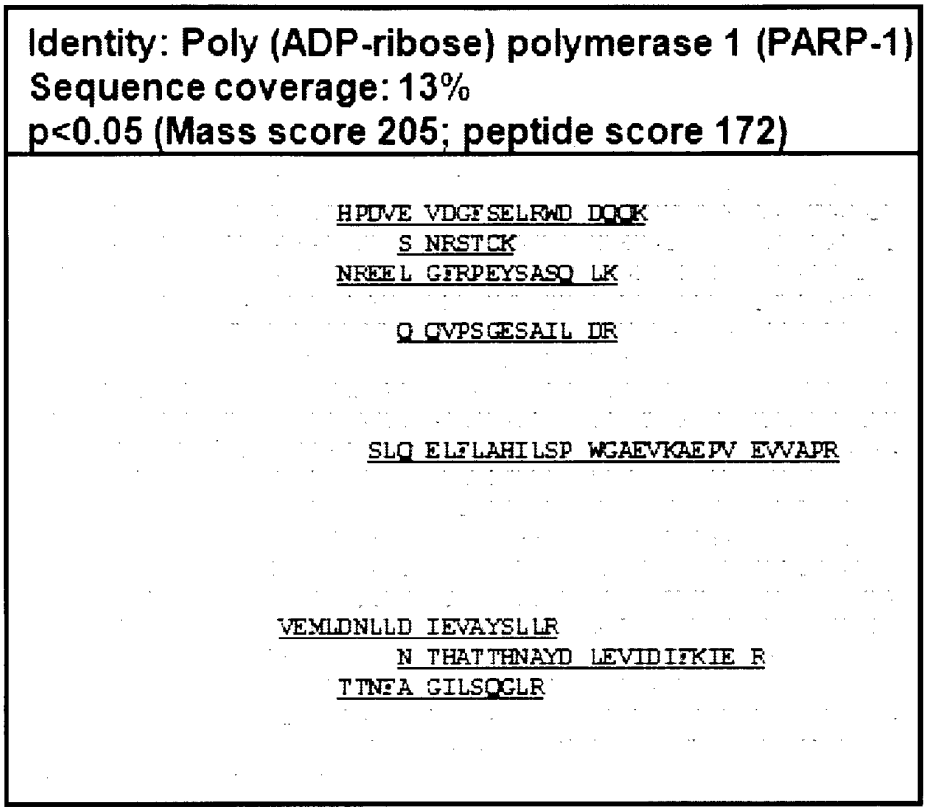

Identity: Poly (ADP-ribose) polymerase 1 (PARP-1)
Sequence coverage: 13%
p<0.05 (Mass score 205; peptide score 172)
HPDVE VDGFSELRWD DQQK
S NRSTCK
NREEL GFRPEYSASQ LK
Q GVPSGESAIL DR
SLQ ELFLAHILSP WGAEVKAEPV EVVAPR
VEMLDNLLD IEVAYSLLR
N THATTHNAYD LEVIDIFKIE R
TTNFA GILSQGLR

FIGURE 2D

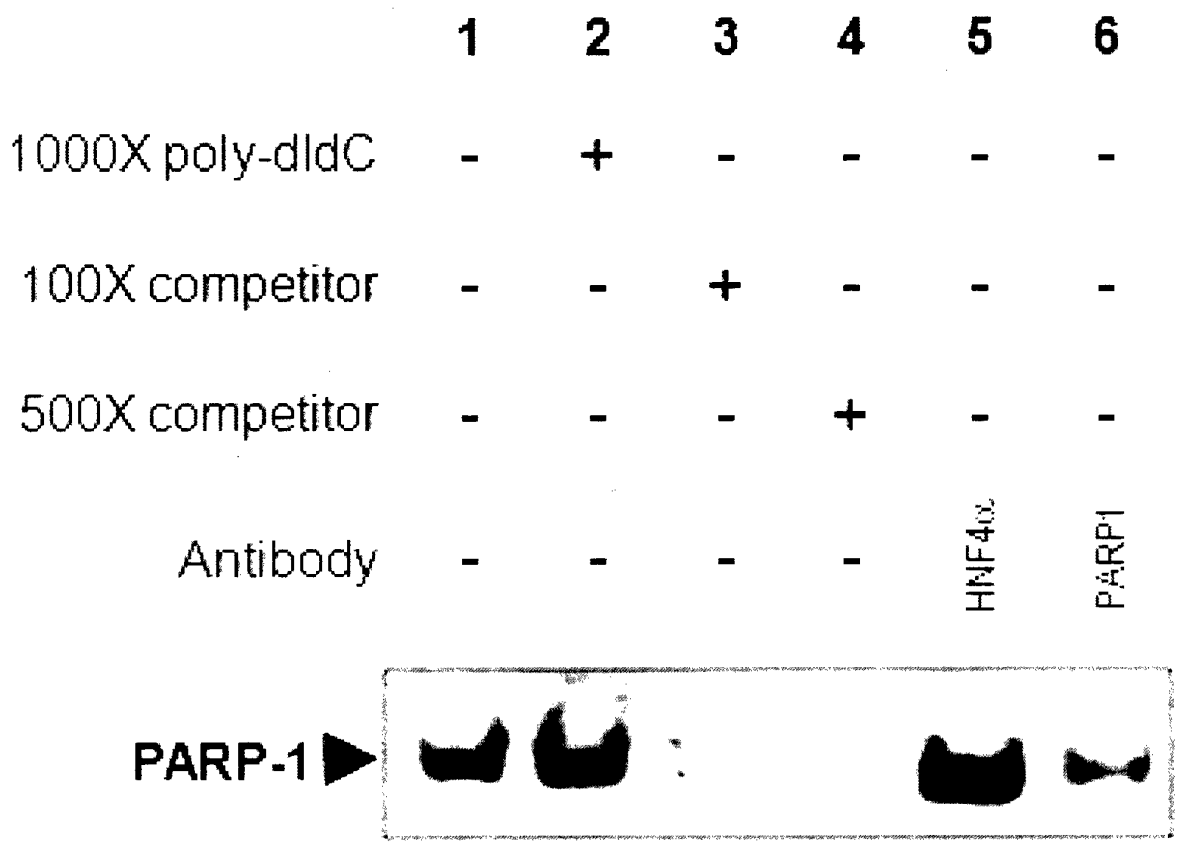

1 2 3 4 5 6
1000X poly-dIdC - + - - - -
100X competitor - - + - - -
500X competitor - - - + - -
Antibody - - - - HNF4α PARP1
PARP-1

FIGURE 3A

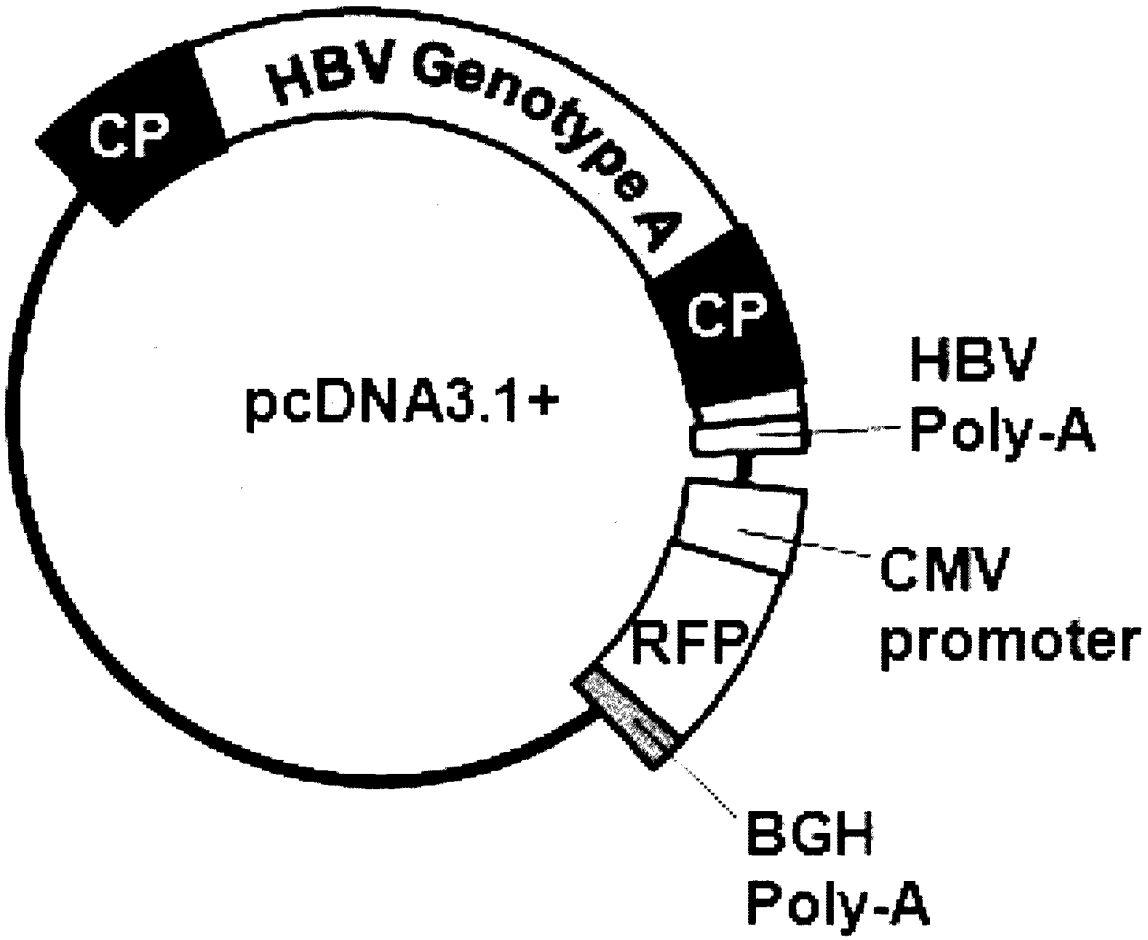
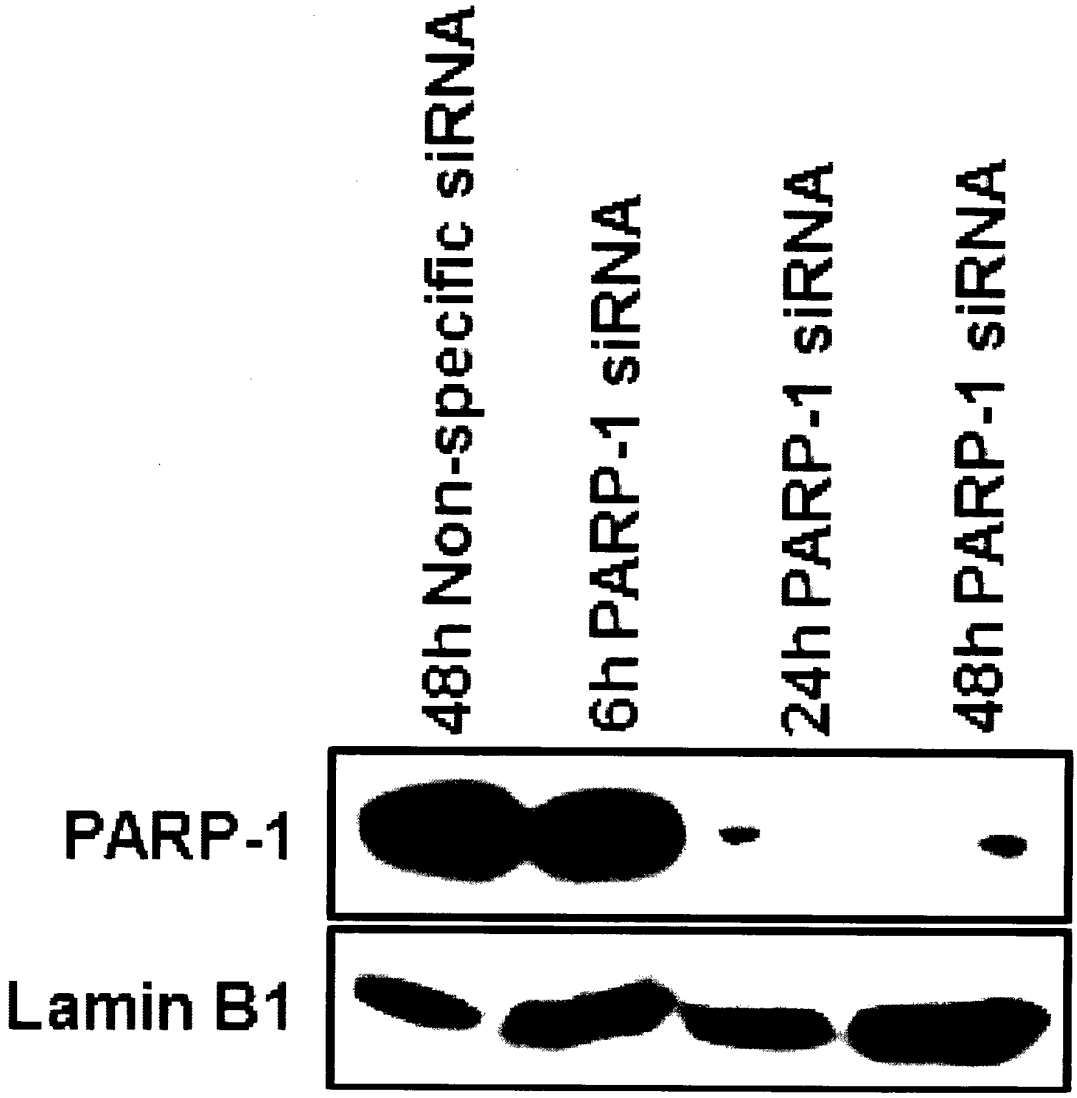

CP
HBV Genotype A
CP
pcDNA3.1+
HBV
Poly-A
CMV
promoter
RFP
BGH
Poly-A

FIGURE 3B


48h Non-specific siRNA
6h PARP-1 siRNA
24h PARP-1 siRNA
48h PARP-1 siRNA
PARP-1
Lamin B1

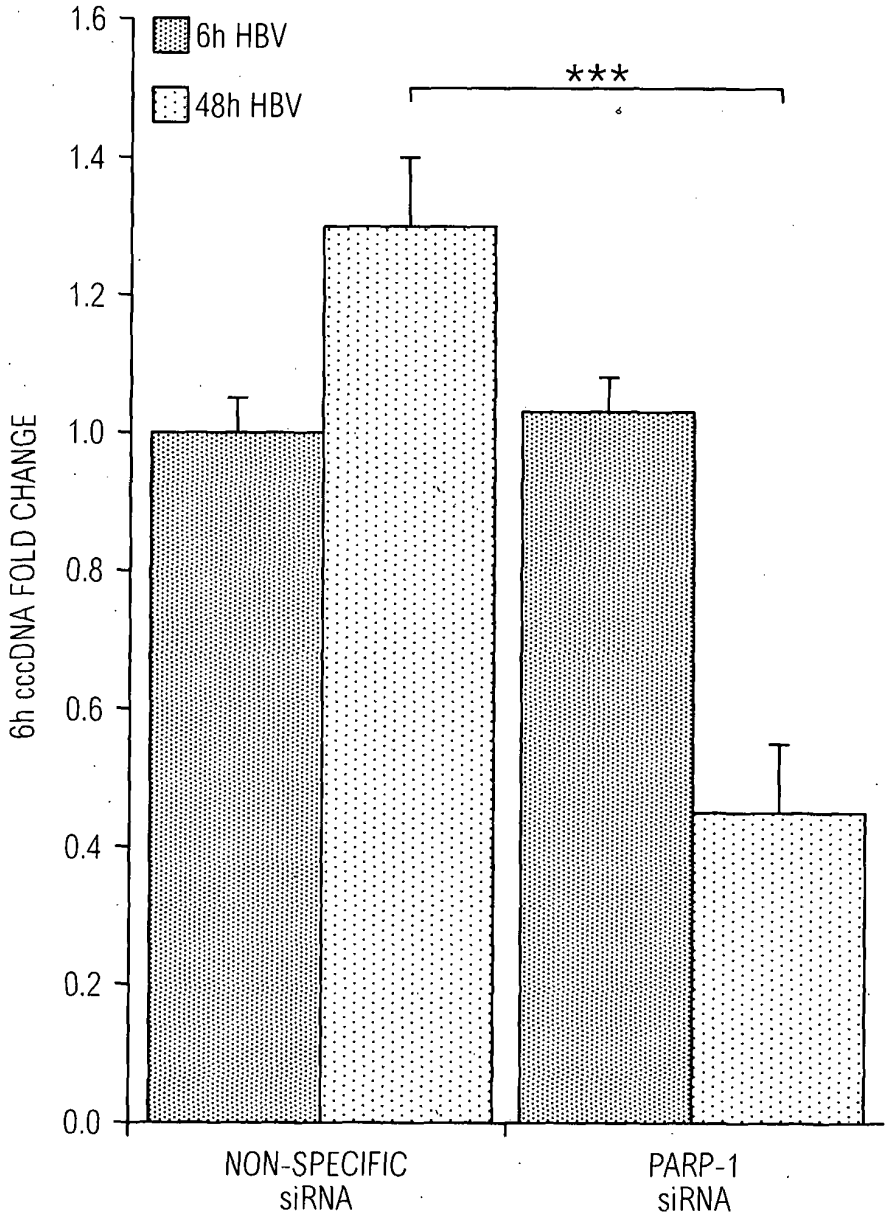

1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
6h HBV
48h HBV
***
6h cccDNA FOLD CHANGE
NON-SPECIFIC siRNA
PARP-1 siRNA

FIG. 3C

FIGURE 4A

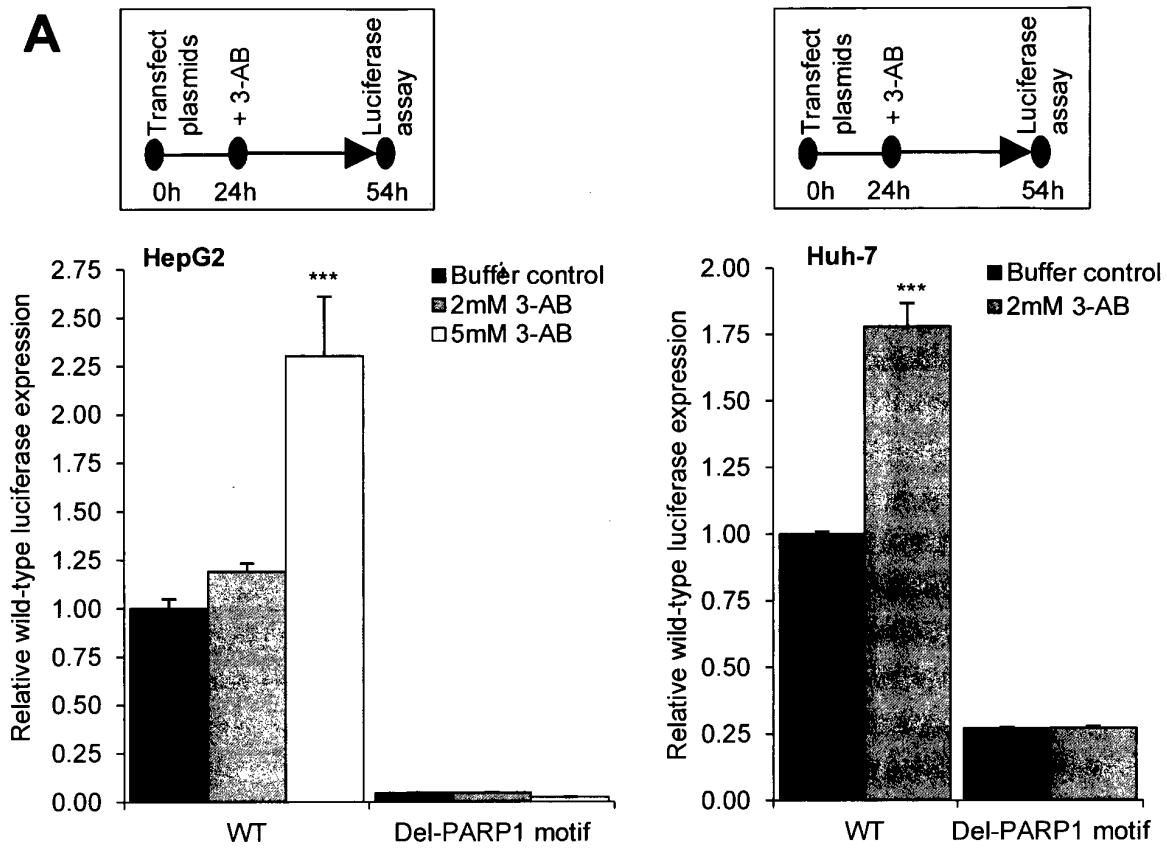

A
Transfect plasmids
+ 3-AB
Luciferase assay
0h
24h
54h
HepG2
Buffer control
2mM 3-AB
5mM 3-AB
***
Relative wild-type luciferase expression
2.75
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
WT
Del-PARP1 motif
Huh-7
Buffer control
2mM 3-AB
***
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
WT
Del-PARP1 motif

FIGURE 4B

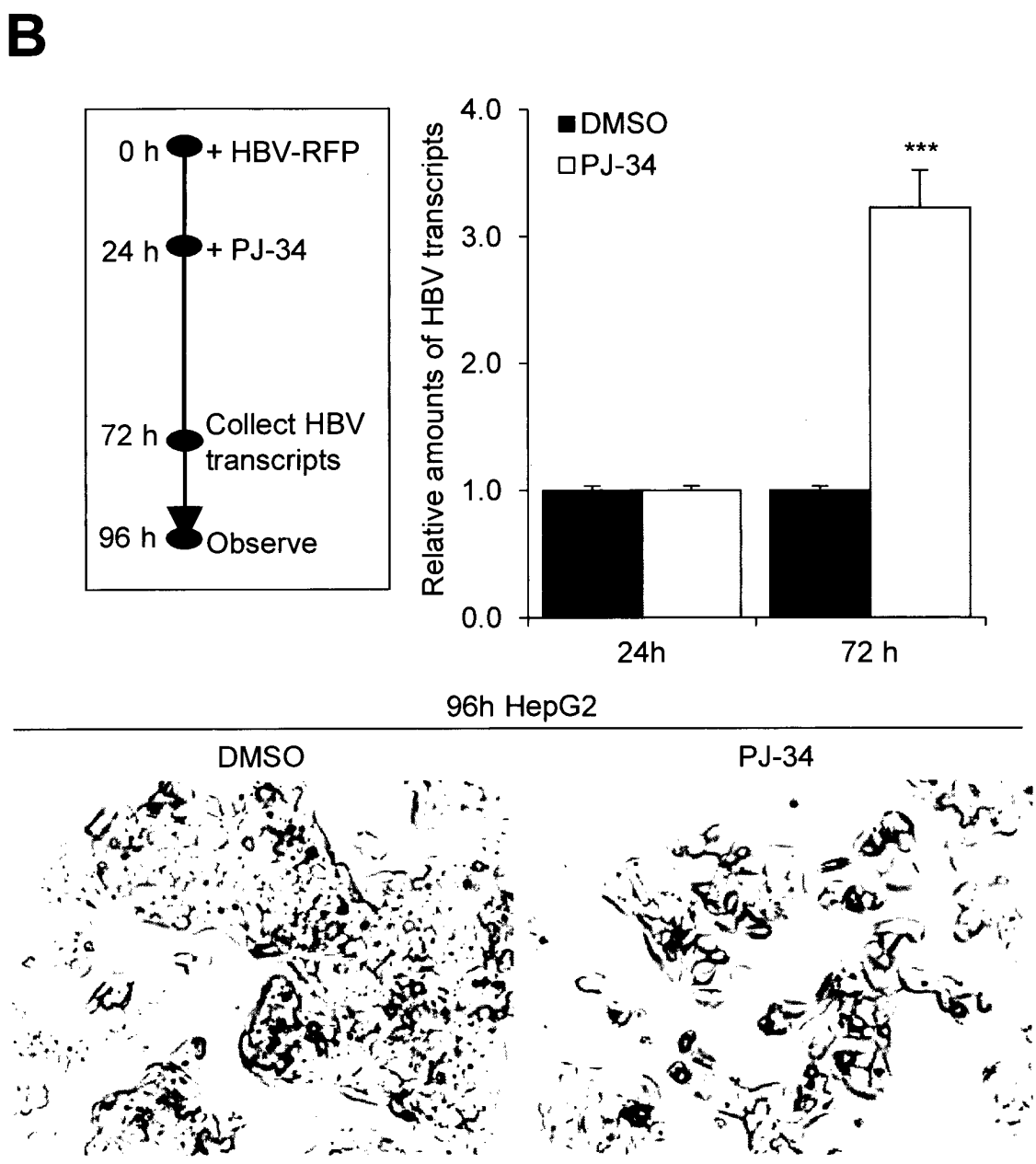
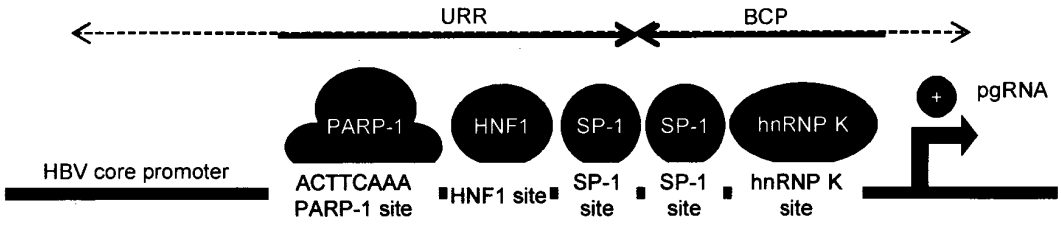

B
0 h
+ HBV-RFP
24 h
+ PJ-34
72 h
Collect HBV transcripts
96 h
Observe
Relative amounts of HBV transcripts
4.0
3.0
2.0
1.0
0.0
DMSO
PJ-34
***
24h
72 h
96h HepG2
DMSO
PJ-34

FIGURE 4C

C



D

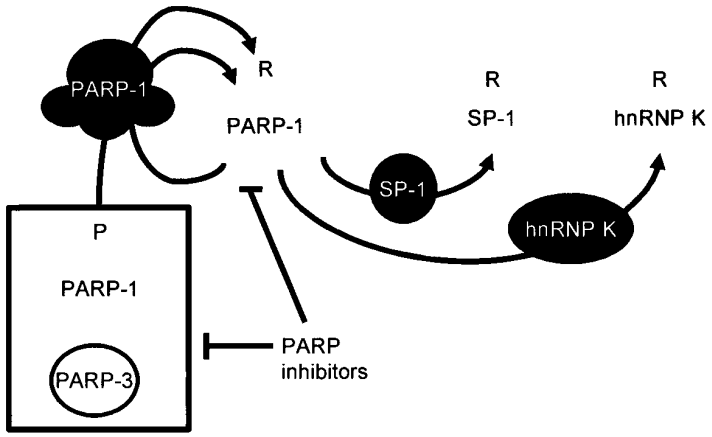


FIGURE 4D

FIGURE 5

FIGURE 5A

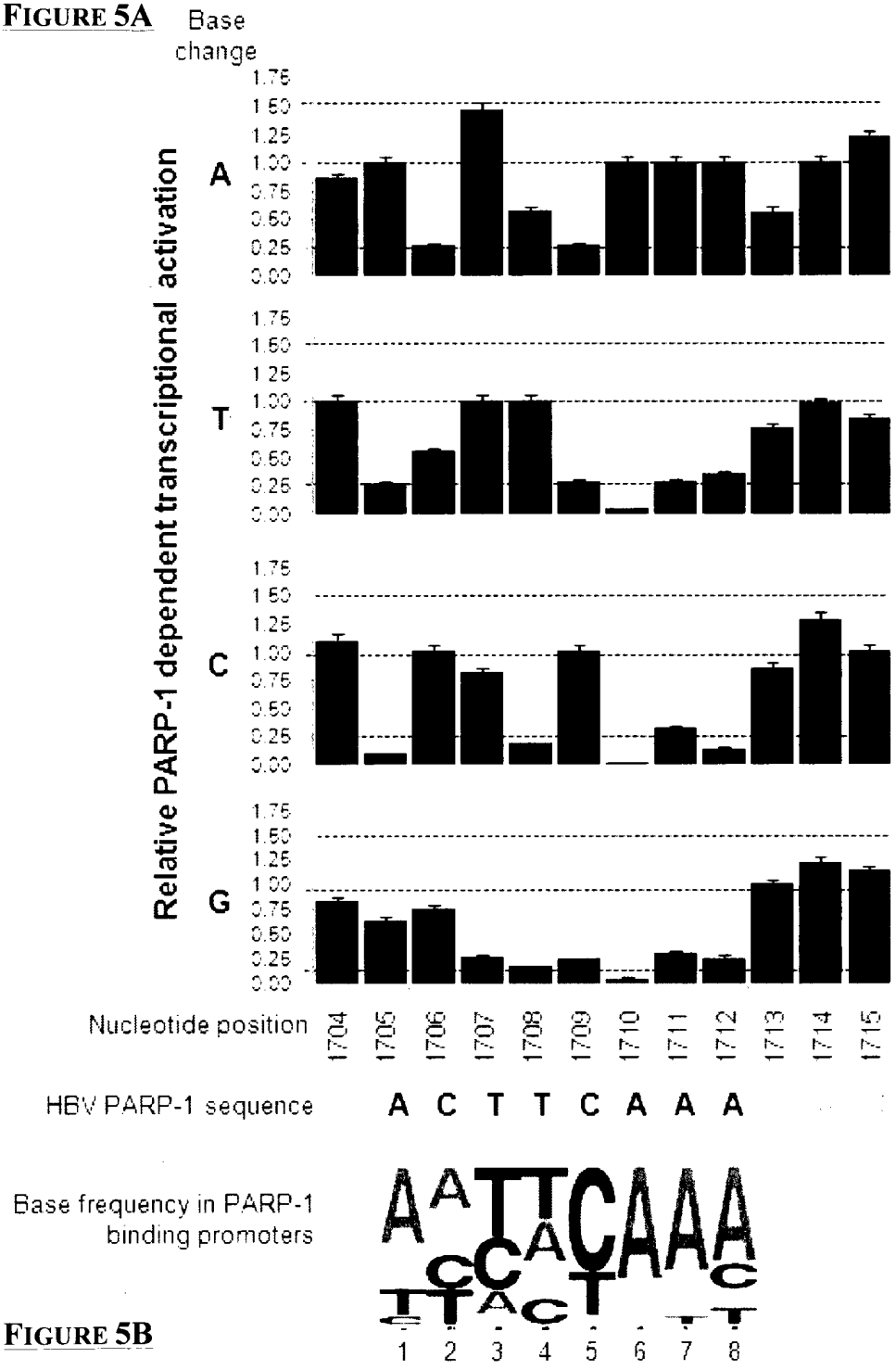


FIGURE 5B

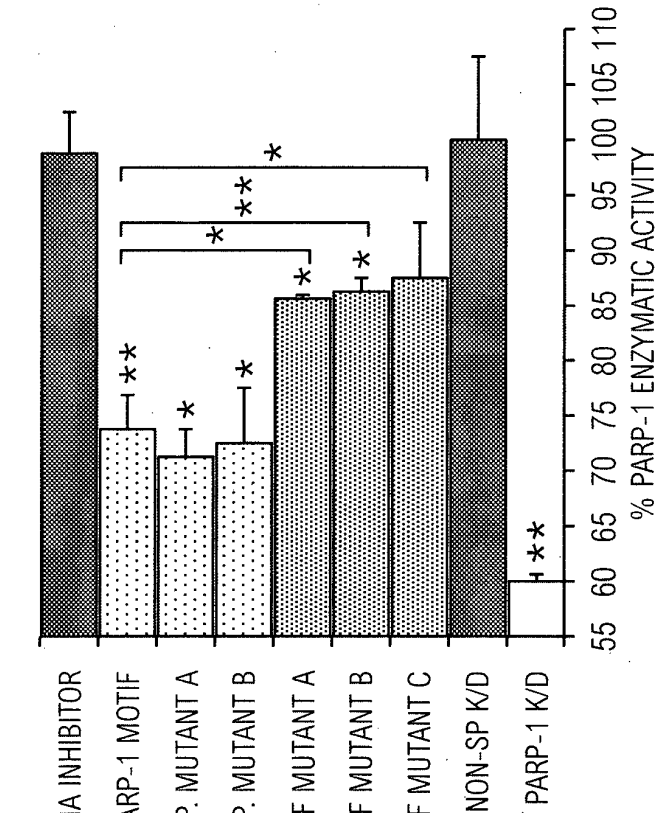

DNA SEQUENCE
-
ACGTCTACATCAAAGTTGCA
CCGTCTACATCAAAGTTGCA
CTATCTACATCAAAGTTGCA
ACGTCTACATCCAAGTTGCA
ACGTCTACATGCAAGTTGCA
ACGTCTACAGGCAAGTTGCA
-
-
NO DNA INHIBITOR
PARP-1 MOTIF
NON-SP. MUTANT A
NON-SP. MUTANT B
MOTIF MUTANT A
MOTIF MUTANT B
MOTIF MUTANT C
NON-SP K/D
PARP-1 K/D
55 60 65 70 75 80 85 90 95 100 105 110
% PARP-1 ENZYMATIC ACTIVITY

FIG. 6A

B

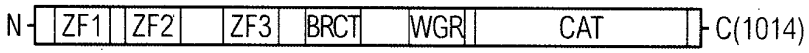


FIG. 6B

C

DOMAINS	ZINC FINGER 1		ZINC FINGER 2		ZINC FINGER 3			BRCT		WGR			CATALYTIC			VECTOR	WT
MUTATED RESIDUE	C24	H53	C125	W157	F289	C311	R330	K418	I430	K564	S606	T622	V762	H862	K893		
TRANSCRIPTION	-	-	-	-	+	+	+	+	-	+	+	+	+	+	+	-	+

FIG. 6C

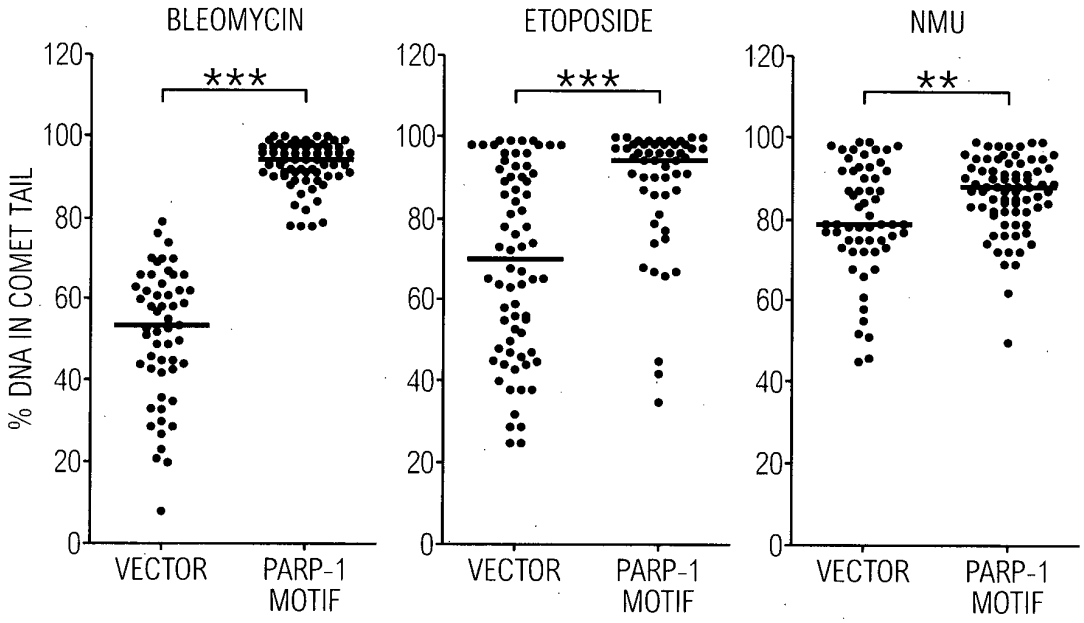

BLEOMYCIN
ETOPOSIDE
NMU
% DNA IN COMET TAIL
120
100
80
60
40
20
0
***
***
**
VECTOR
PARP-1 MOTIF
VECTOR
PARP-1 MOTIF
VECTOR
PARP-1 MOTIF

FIG. 7A

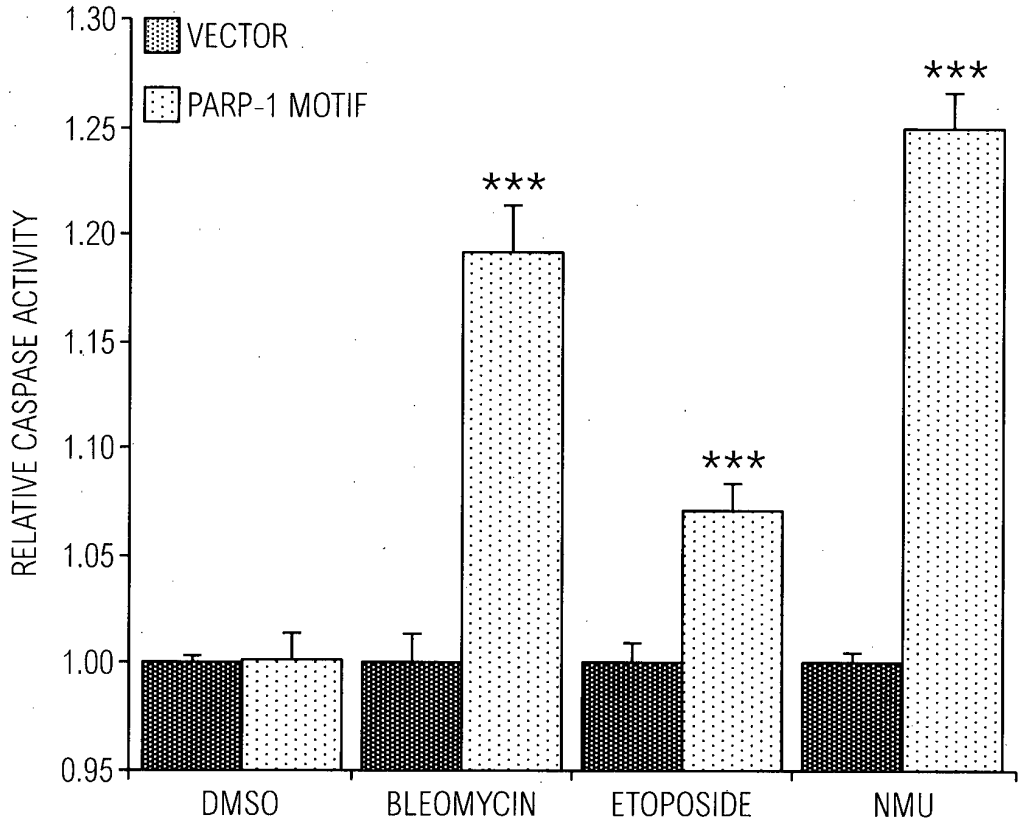

1.30
1.25
1.20
1.15
1.10
1.05
1.00
0.95
RELATIVE CASPASE ACTIVITY
VECTOR
PARP-1 MOTIF
***
***
***
DMSO
BLEOMYCIN
ETOPOSIDE
NMU

FIG. 7B

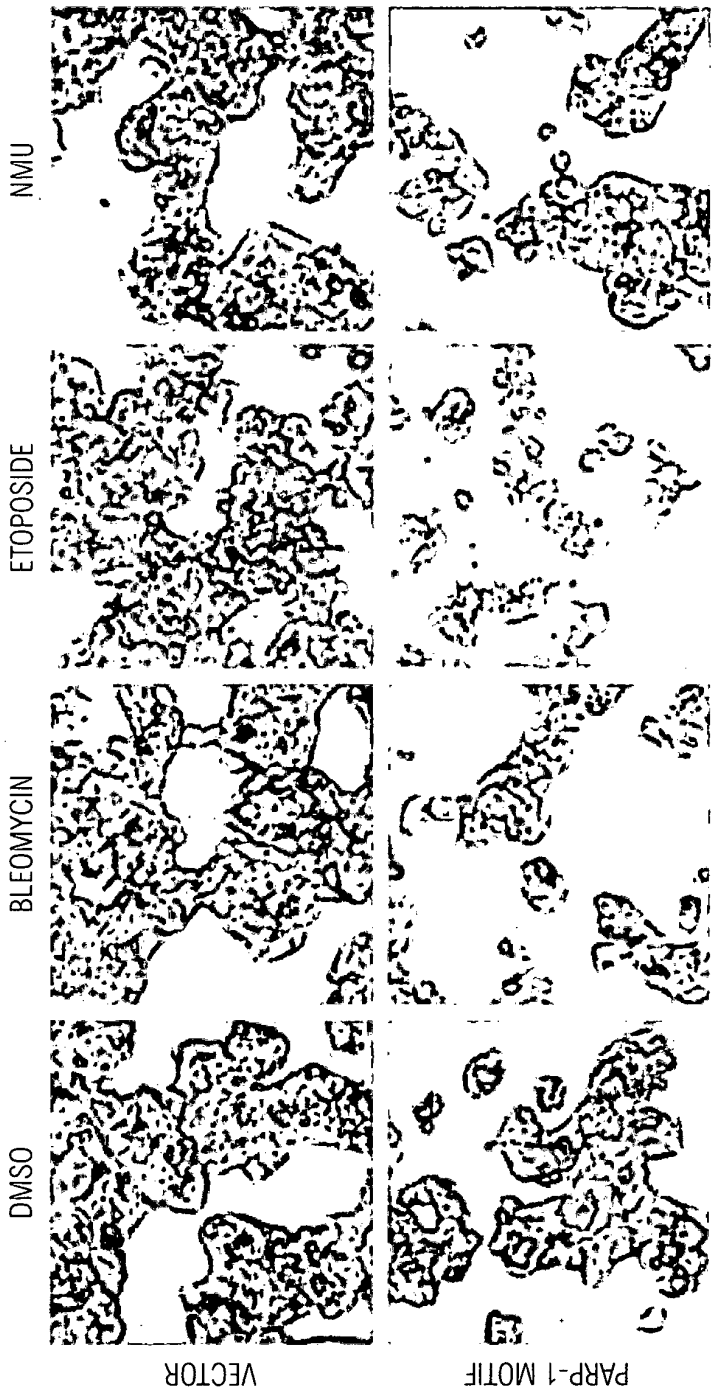
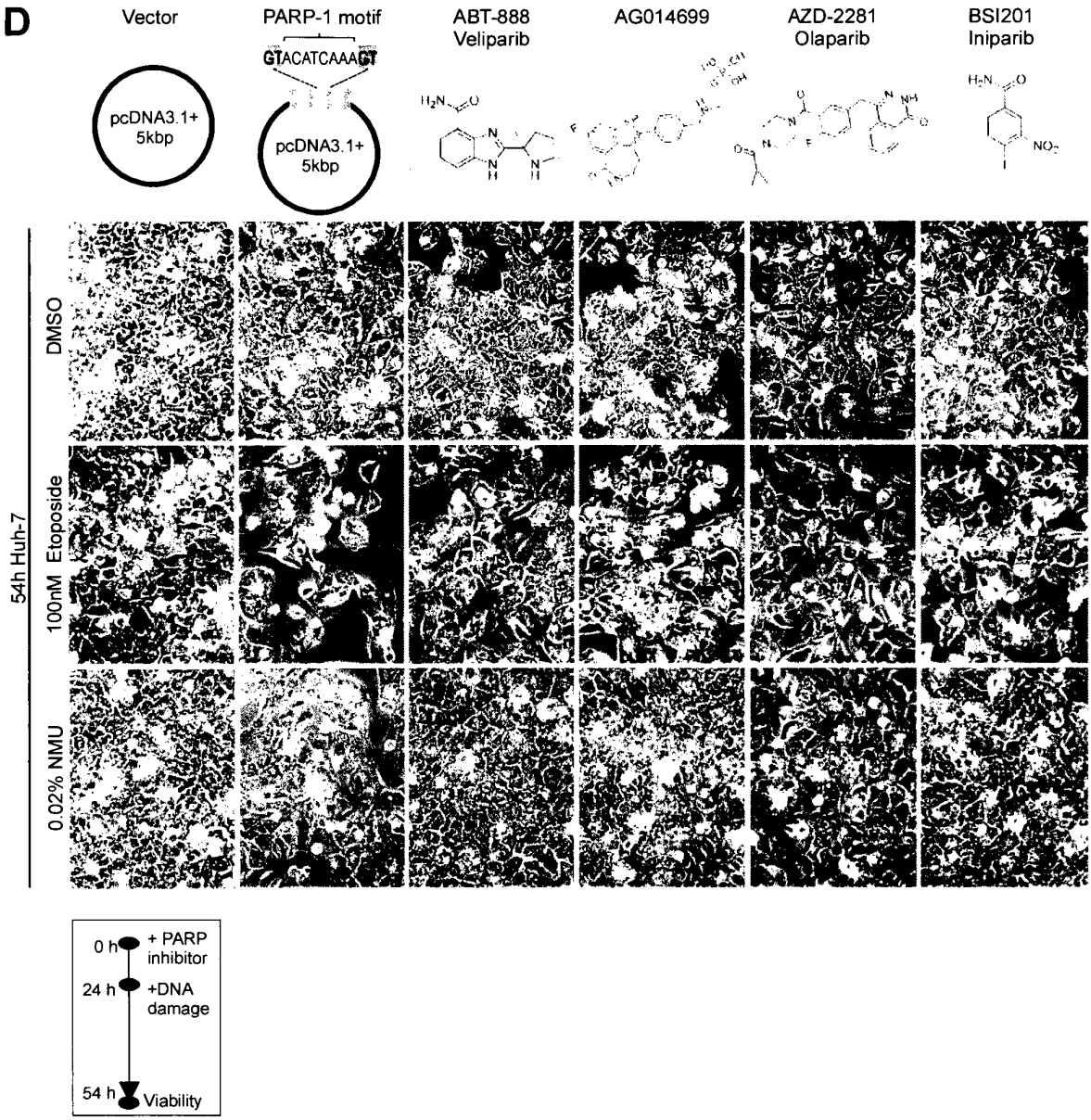


FIG. 7C

FIGURE 7D


D
Vector
PARP-1 motif
ABT-888
Veliparib
AG014699
AZD-2281
Olaparib
BSI201
Iniparib
pcDNA3.1+
5kbp
GTACATCAAAGT
pcDNA3.1+
5kbp
54h Huh-7
DMSO
100nM Etoposide
0.02% NMU
0 h
+ PARP
inhibitor
24 h
+DNA
damage
54 h
Viability

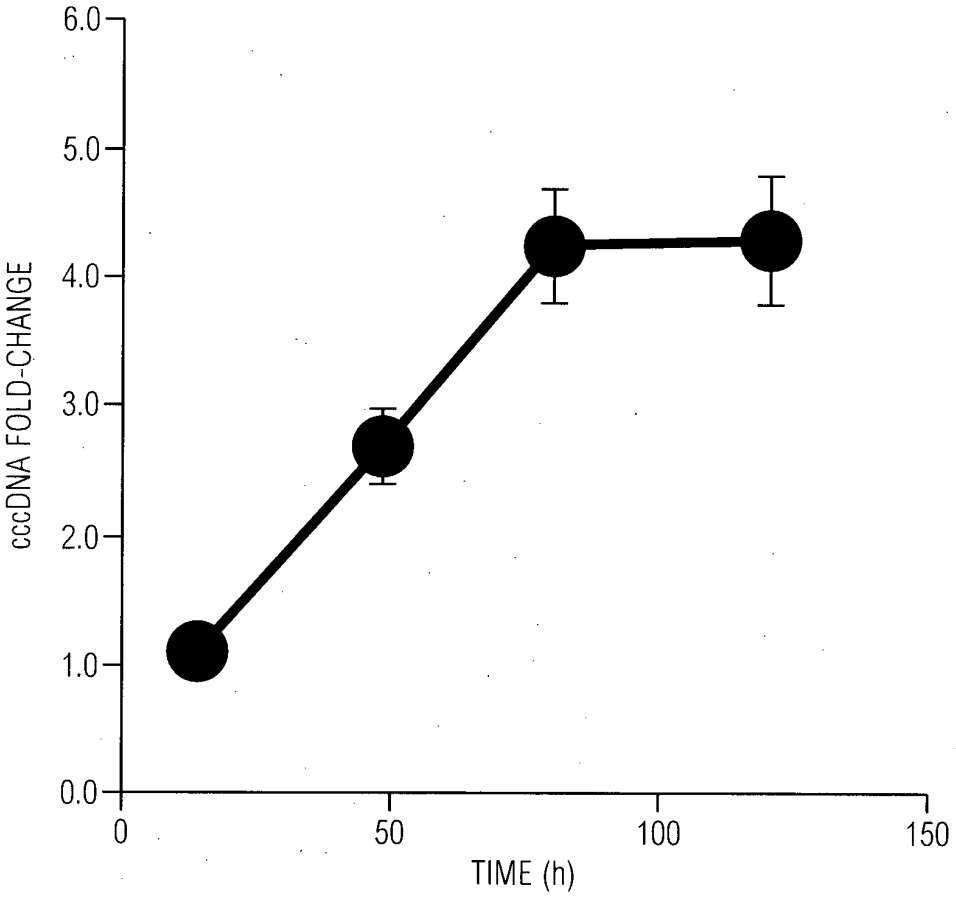


FIG. 8A

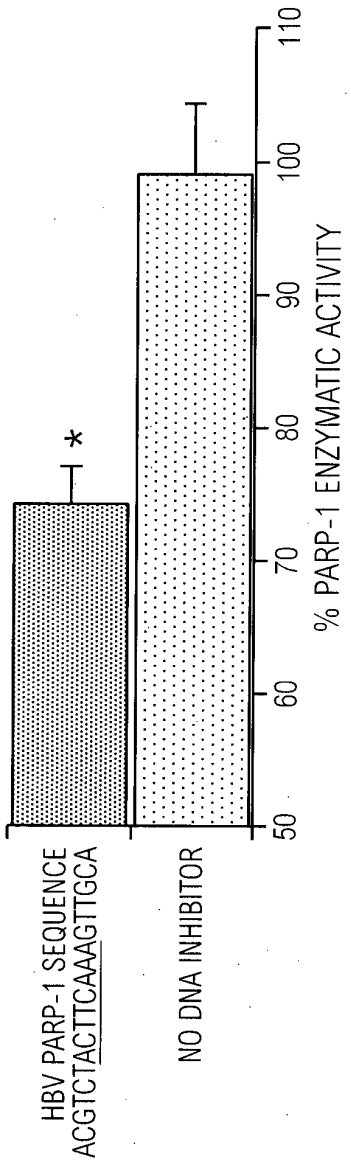

110
100
90
80
70
60
50
% PARP-1 ENZYMATIC ACTIVITY
*
HBV PARP-1 SEQUENCE
ACGTCTACTTCAAGTTGCA
NO DNA INHIBITOR

FIG. 8B

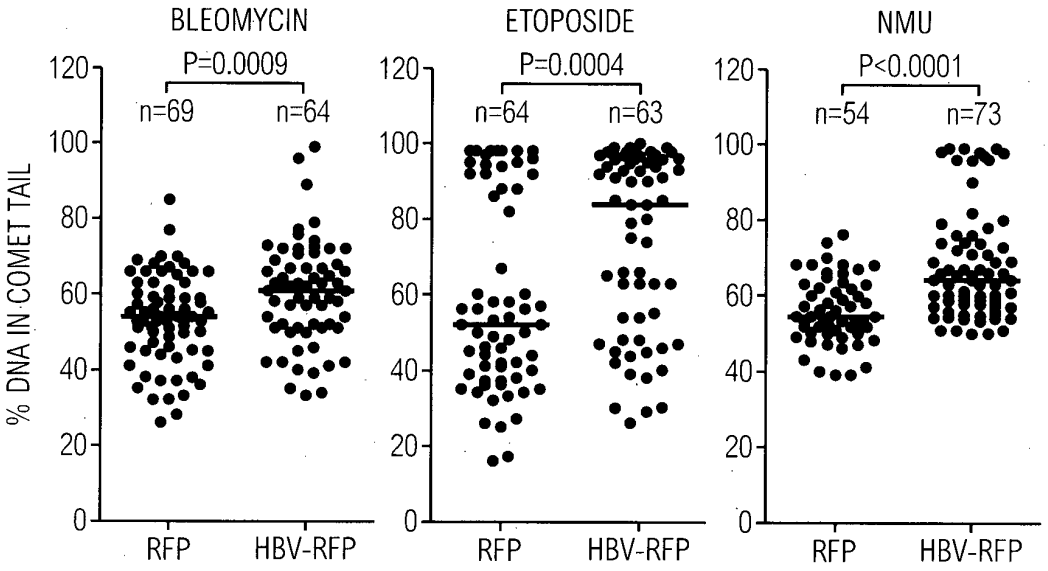

BLEOMYCIN
P=0.0009
n=69
n=64
ETOPOSIDE
P=0.0004
n=64
n=63
NMU
P<0.0001
n=54
n=73
% DNA IN COMET TAIL
120
100
80
60
40
20
0
RFP
HBV-RFP

FIG. 8C

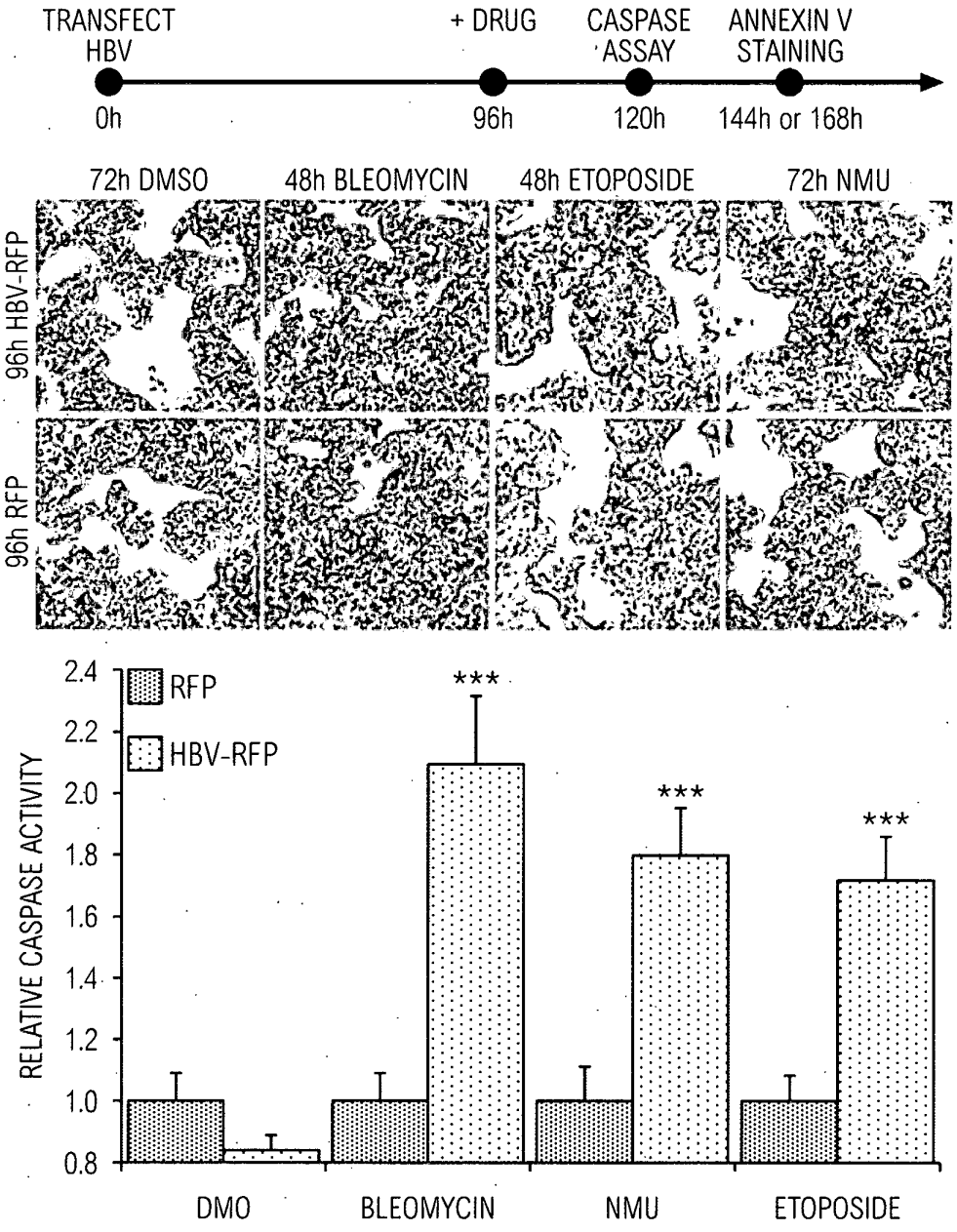
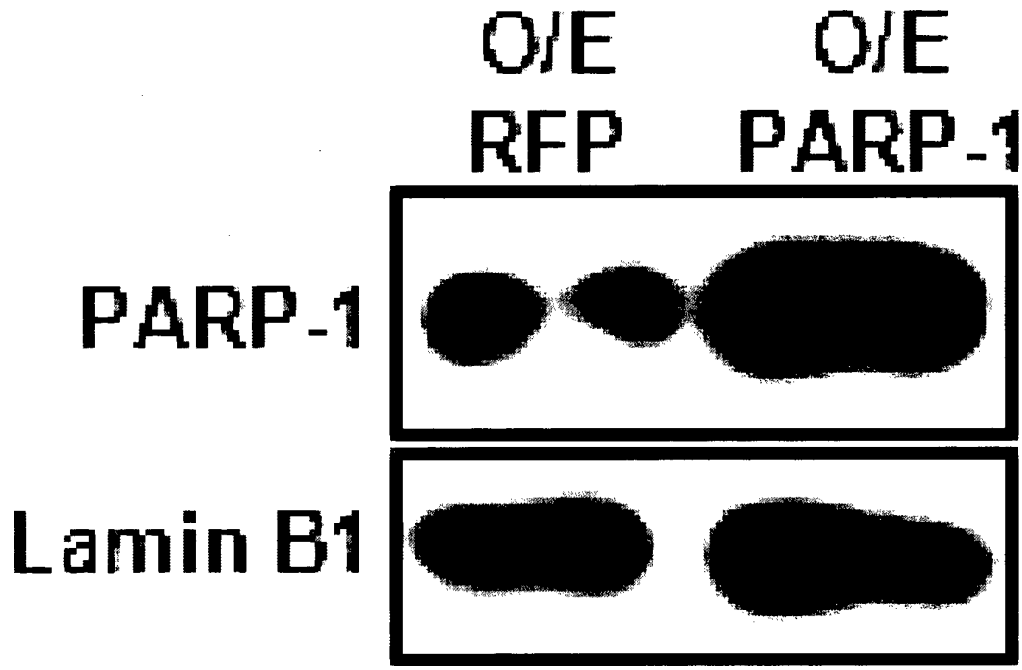

TRANSFECT HBV
+ DRUG
CASPASE ASSAY
ANNEXIN V STAINING
0h
96h
120h
144h or 168h
72h DMSO
48h BLEOMYCIN
48h ETOPOSIDE
72h NMU
96h HBV-RFP
96h RFP
RFP
HBV-RFP
RELATIVE CASPASE ACTIVITY
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
***
***
***
DMO
BLEOMYCIN
NMU
ETOPOSIDE

FIG. 8D

FIGURE 9A



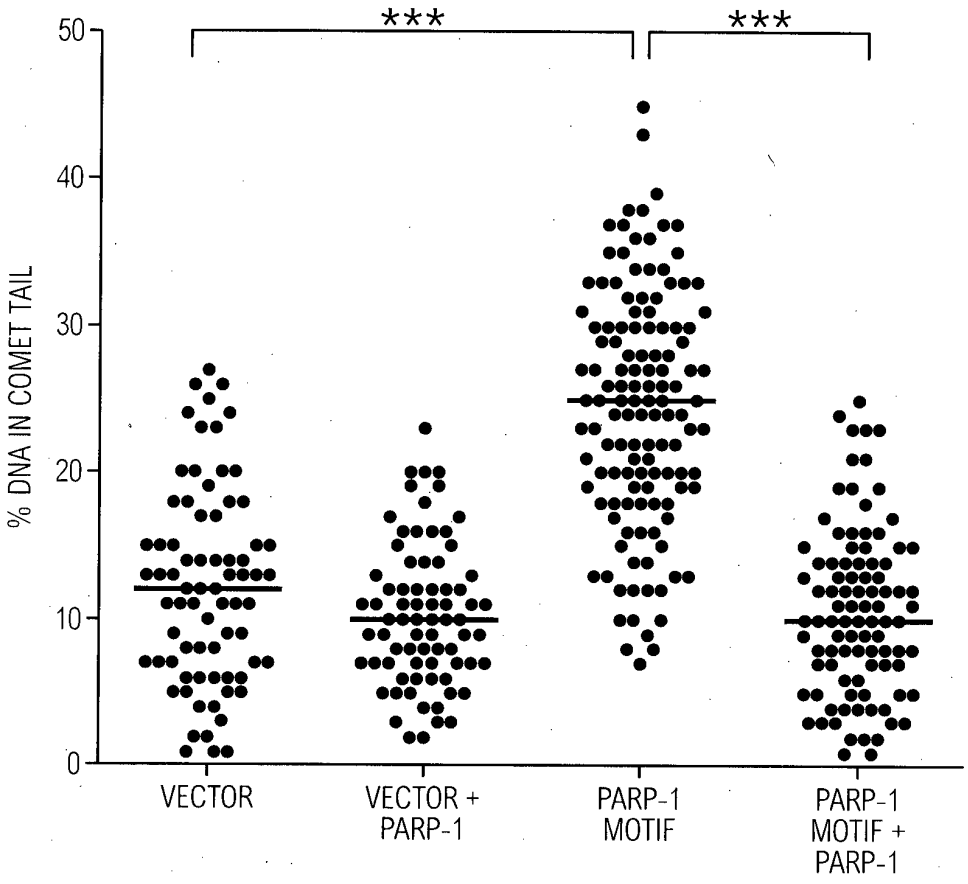

***
***
50
40
30
20
10
0
% DNA IN COMET TAIL
VECTOR
VECTOR + PARP-1
PARP-1 MOTIF
PARP-1 MOTIF + PARP-1

FIG. 9B

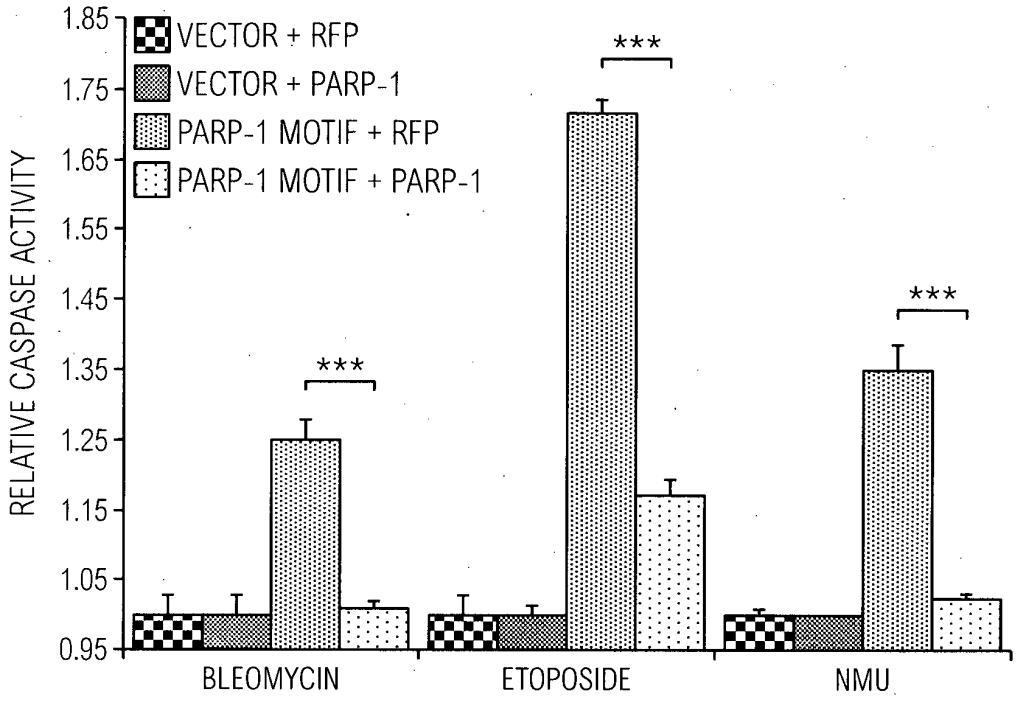

1.85
1.75
1.65
1.55
1.45
1.35
1.25
1.15
1.05
0.95
RELATIVE CASPASE ACTIVITY
VECTOR + RFP
VECTOR + PARP-1
PARP-1 MOTIF + RFP
PARP-1 MOTIF + PARP-1
***
***
***
BLEOMYCIN
ETOPOSIDE
NMU

FIG. 9C

FIGURE 10A

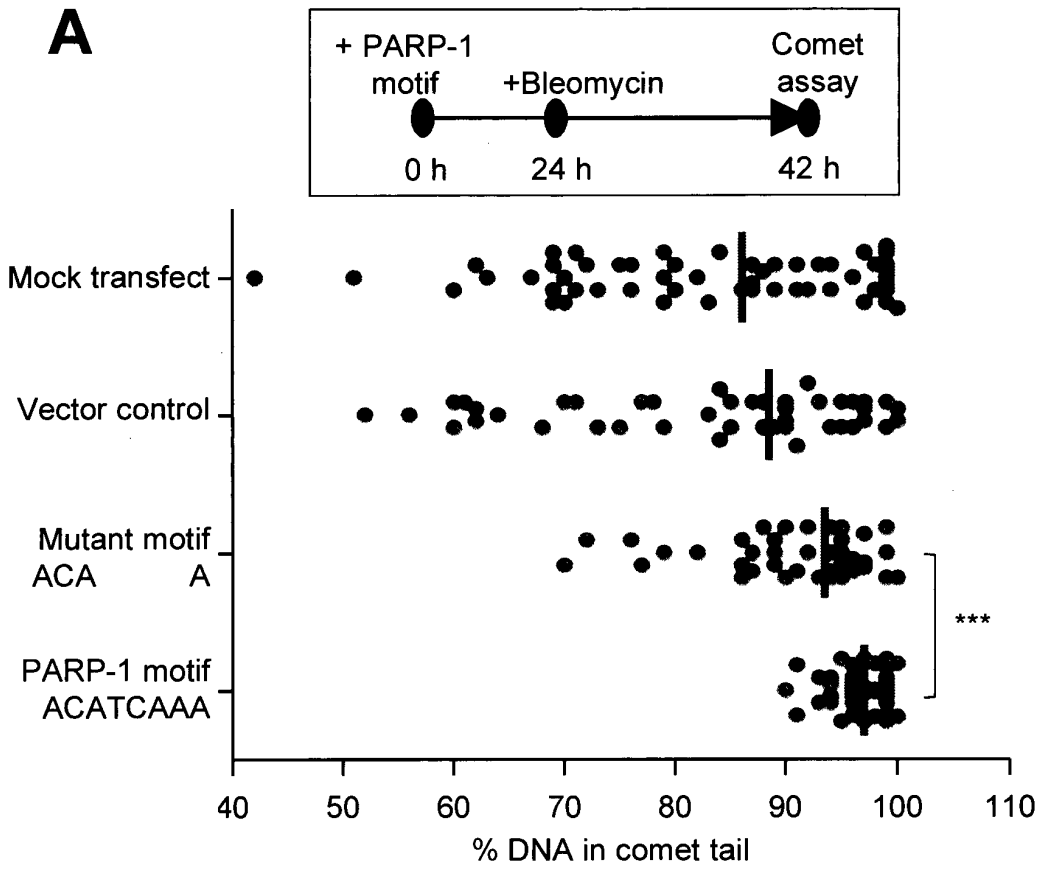

A
+ PARP-1 motif
+Bleomycin
Comet assay
0 h
24 h
42 h
Mock transfect
Vector control
Mutant motif ACA A
PARP-1 motif ACATCAAA
***
40
50
60
70
80
90
100
110
% DNA in comet tail

FIGURE 10B

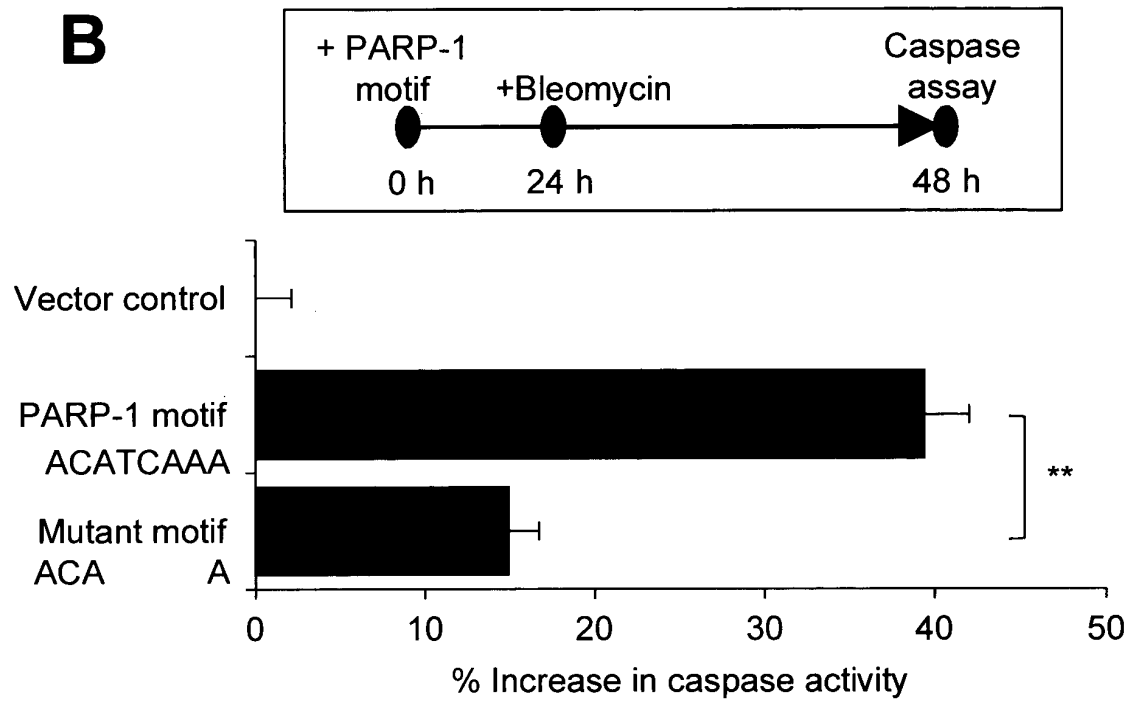
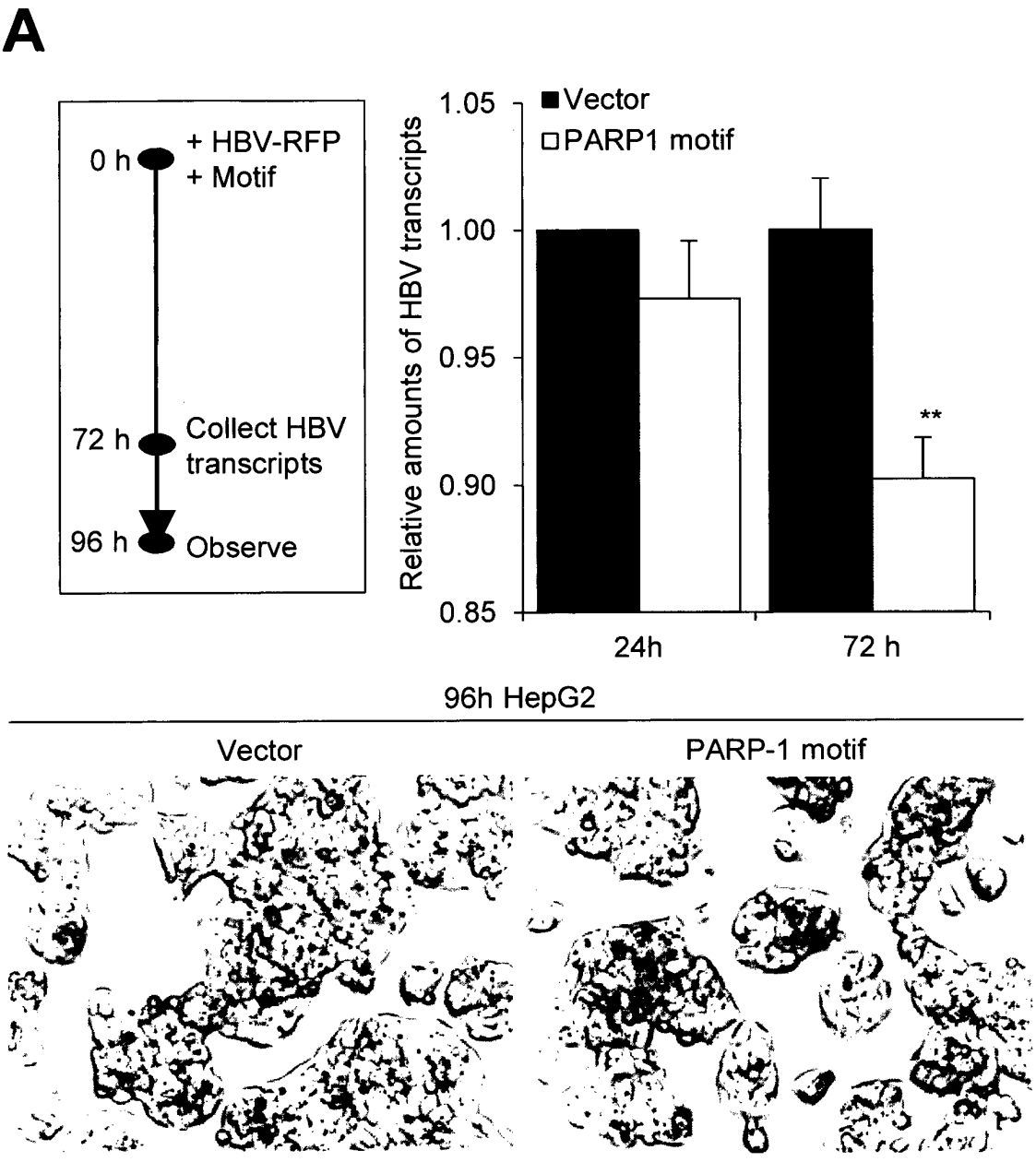

B
+ PARP-1 motif
+Bleomycin
Caspase assay
0 h
24 h
48 h
Vector control
PARP-1 motif ACATCAAA
Mutant motif ACA A
**
0
10
20
30
40
50
% Increase in caspase activity

FIGURE 11A


A
0 h
+ HBV-RFP
+ Motif
72 h
Collect HBV transcripts
96 h
Observe
Relative amounts of HBV transcripts
1.05
1.00
0.95
0.90
0.85
Vector
PARP1 motif
**
24h
72 h
96h HepG2
Vector
PARP-1 motif

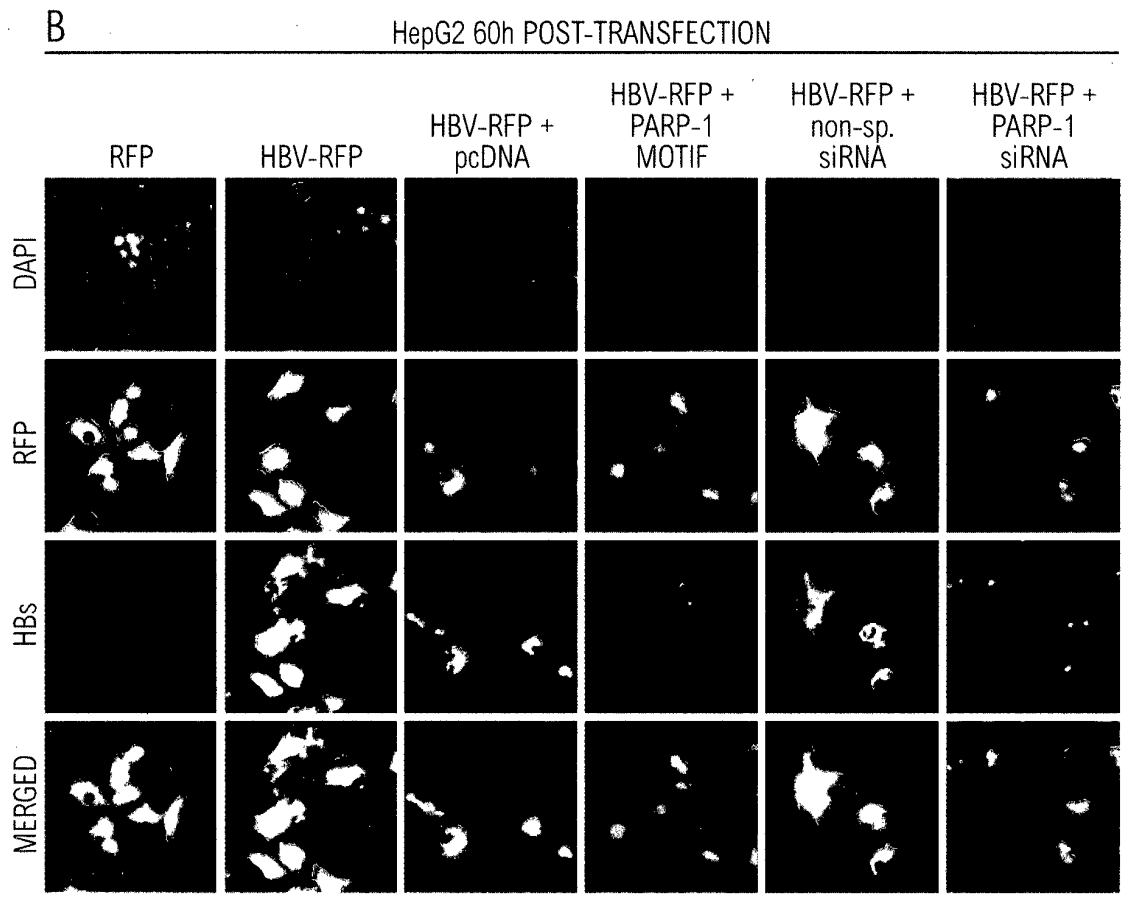

B
HepG2 60h POST-TRANSFECTION
RFP
HBV-RFP
HBV-RFP + pcDNA
HBV-RFP + PARP-1 MOTIF
HBV-RFP + non-sp. siRNA
HBV-RFP + PARP-1 siRNA
DAPI
RFP
HBs
MERGED

FIG. 11B