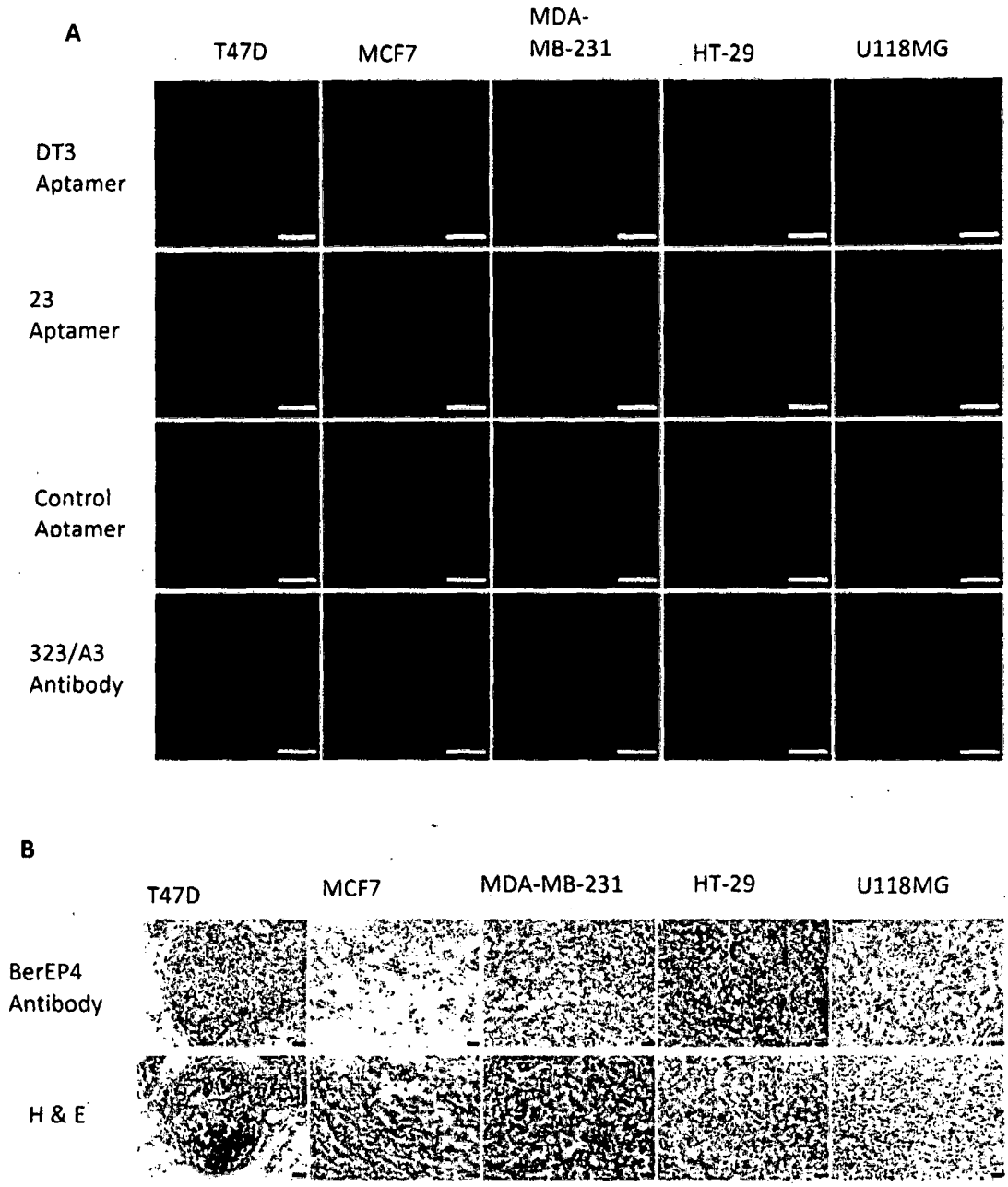

A
T47D
MCF7
MDA-MB-231
HT-29
U118MG
DT3 Aptamer
23 Aptamer
Control Aptamer
323/A3 Antibody
B
T47D
MCF7
MDA-MB-231
HT-29
U118MG
BerEP4 Antibody
H & E

FIGURE 1

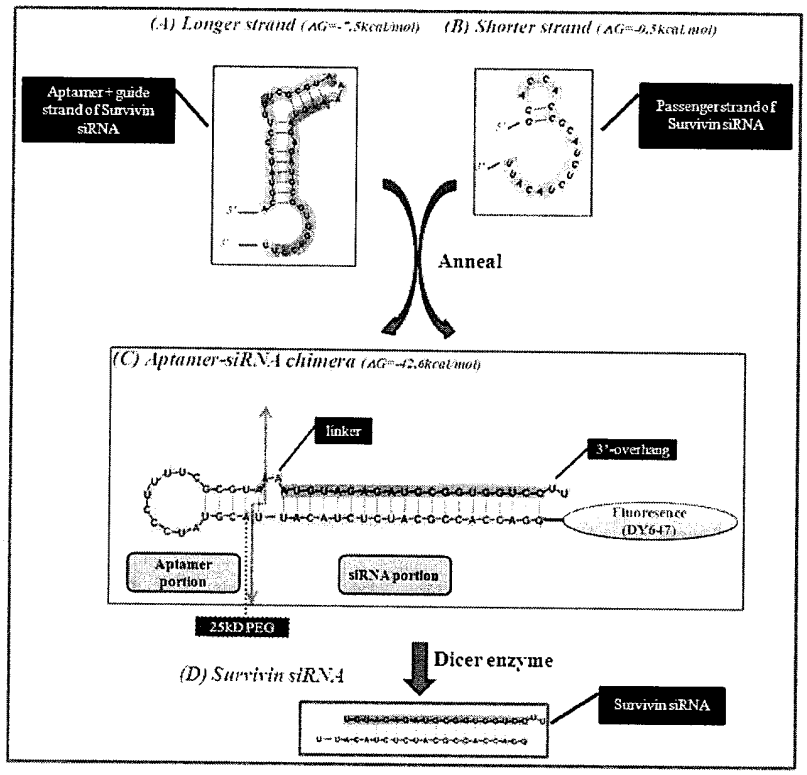

(A) Longer strand
(B) Shorter strand
Aptamer+guide strand of Survivin siRNA
Passenger strand of Survivin siRNA
Anneal
(C) Aptamer-siRNA chimera
linker
3'-overhang
Fluoresence (DY647)
Aptamer portion
siRNA portion
25KD PEG
(D) Survivin siRNA
Dicer enzyme
Survivin siRNA

FIGURE 2

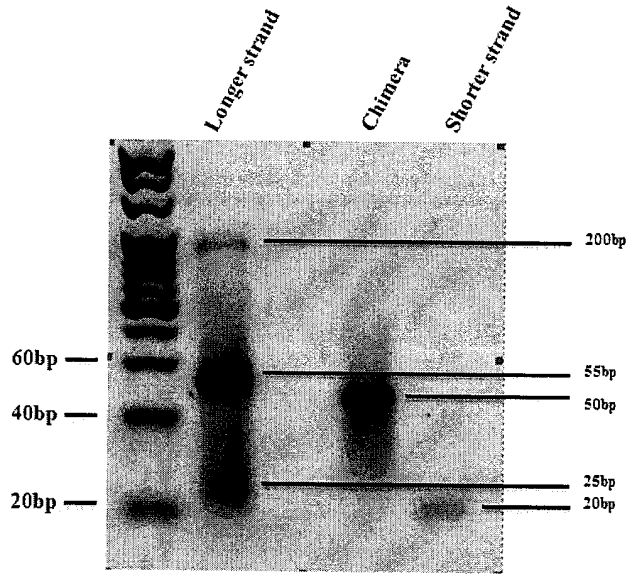

Longer strand
Chimera
Shorter strand
200bp
60bp
55bp
40bp
50bp
25bp
20bp
20bp

FIGURE 3

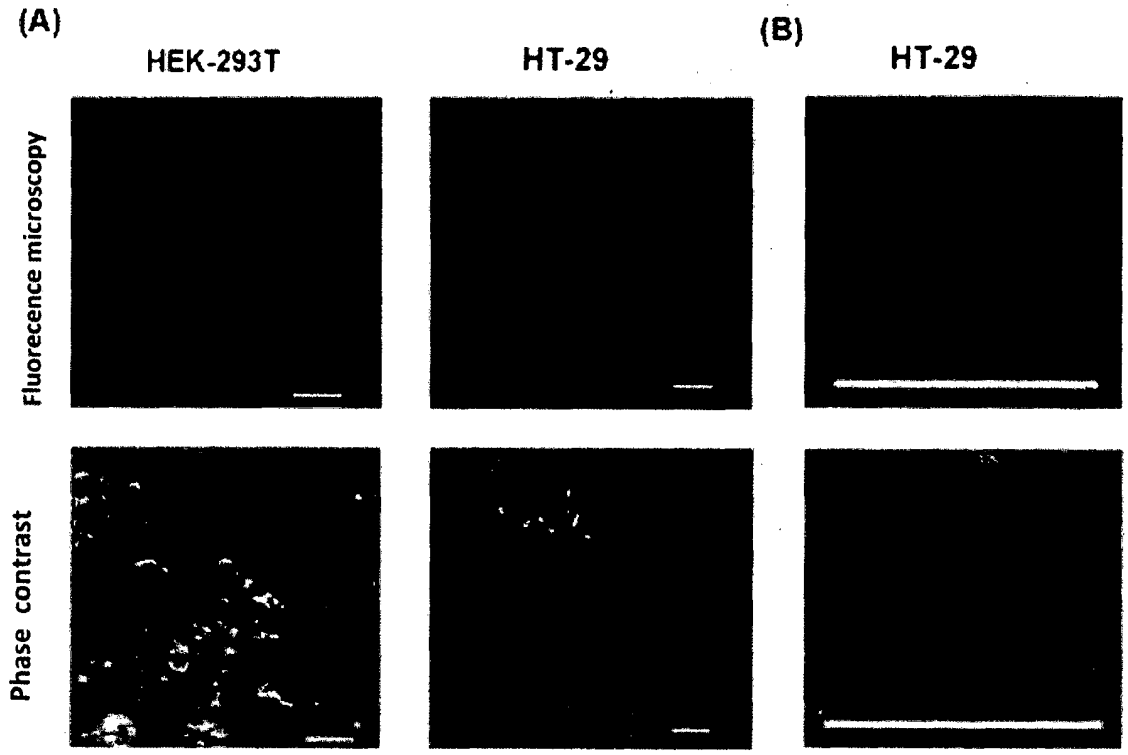

(A)
HEK-293T
HT-29
(B)
HT-29
Fluorecence microscopy
Phase contrast

FIGURE 4

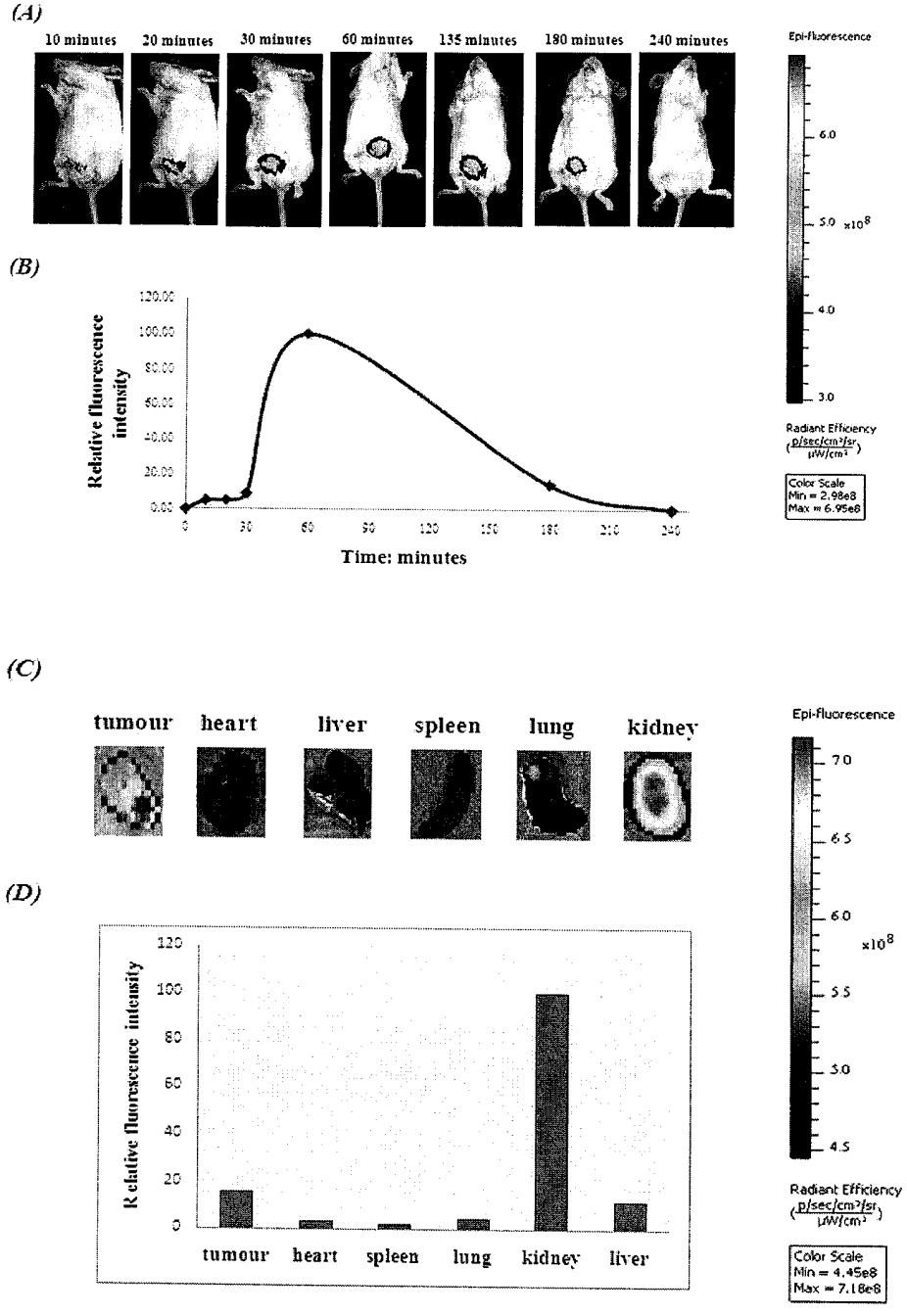
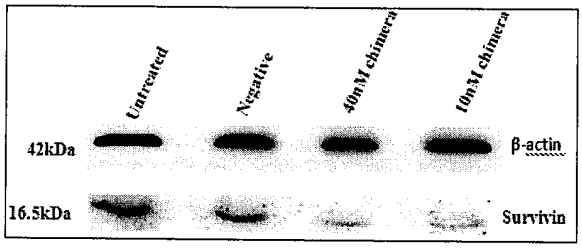

(A)
10 minutes
20 minutes
30 minutes
60 minutes
135 minutes
180 minutes
240 minutes
Epi-fluorescence
6.0
5.0 x10^8
4.0
3.0
Radiant Efficiency
(p/sec/cm²/sr / µW/cm²)
Color Scale
Min = 2.98e8
Max = 6.95e8
(B)
Relative fluorescence intensity
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
30
60
90
120
150
180
210
240
Time: minutes
(C)
tumour
heart
liver
spleen
lung
kidney
Epi-fluorescence
7.0
6.5
6.0
x10^8
5.5
5.0
4.5
Radiant Efficiency
(p/sec/cm²/sr / µW/cm²)
Color Scale
Min = 4.45e8
Max = 7.18e8
(D)
Relative fluorescence intensity
120
100
80
60
40
20
0
tumour
heart
spleen
lung
kidney
liver

FIGURE 5

A


Untreated
Negative
40nM chimera
10nM chimera
42kDa
β-actin
16.5kDa
Survivin

B

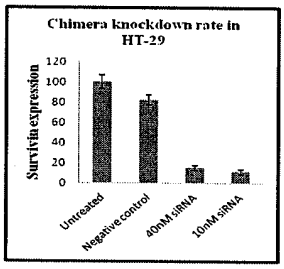

Chimera knockdown rate in HT-29
Survivin expression
120
100
80
60
40
20
0
Untreated
Negative control
40nM siRNA
10nM siRNA

FIGURE 6

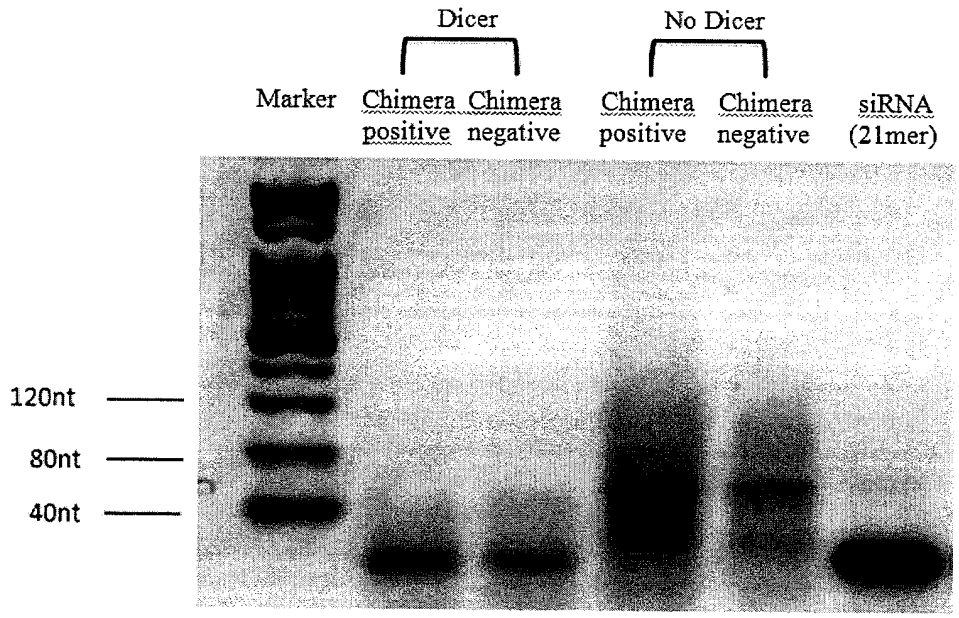

Dicer
No Dicer
Marker
Chimera positive
Chimera negative
Chimera positive
Chimera negative
siRNA (21mer)
120nt
80nt
40nt

FIGURE 7

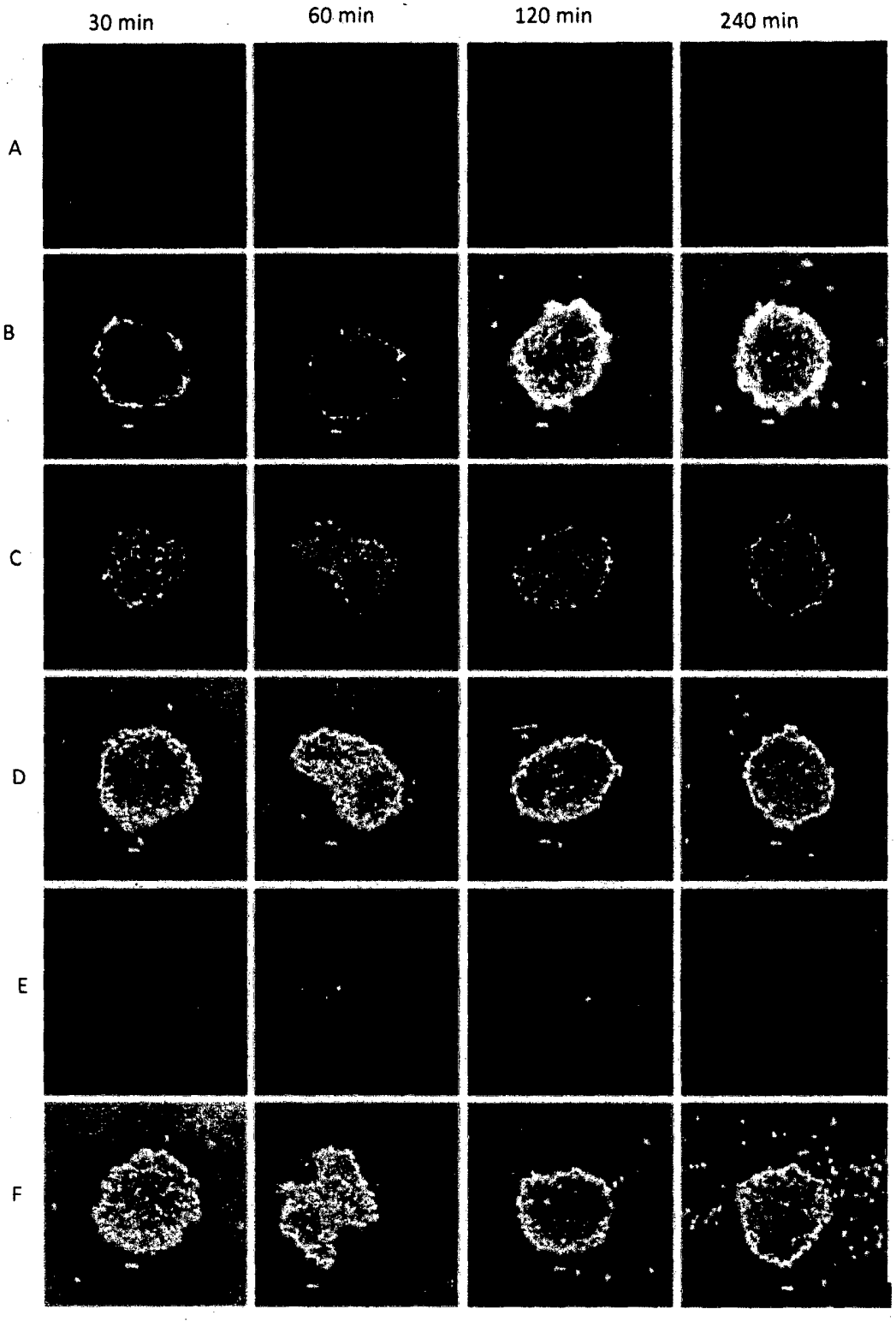


FIGURE 8

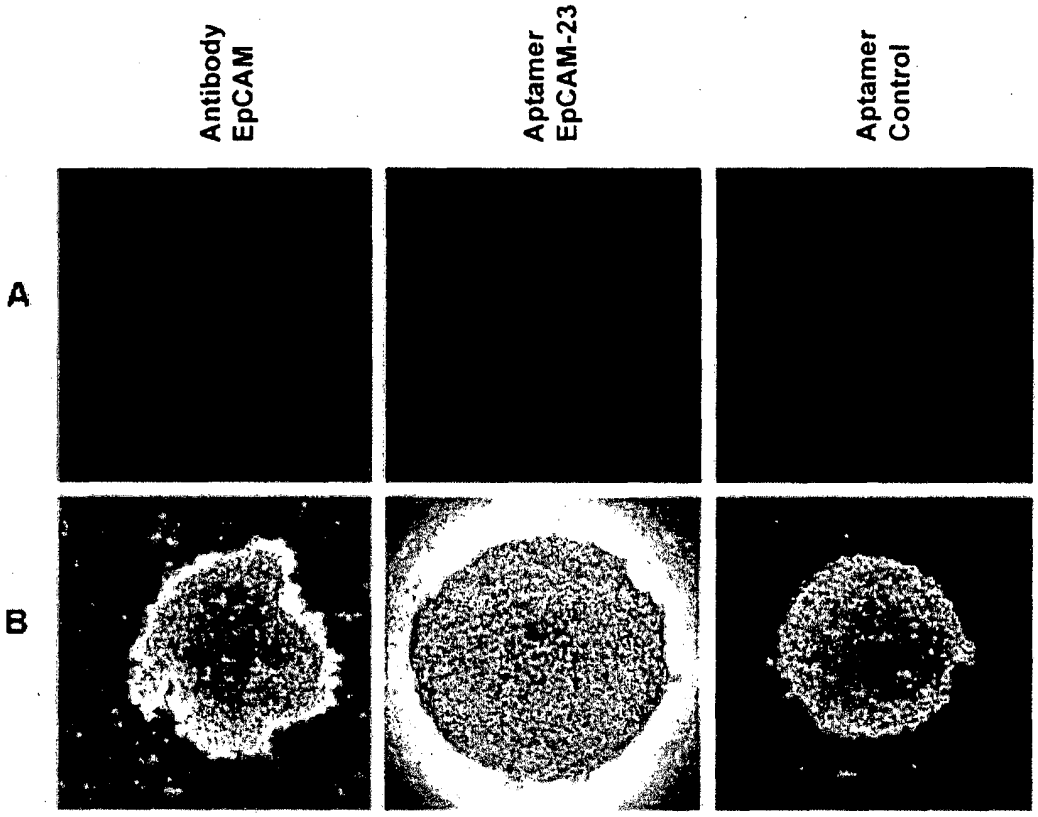


FIGURE 9

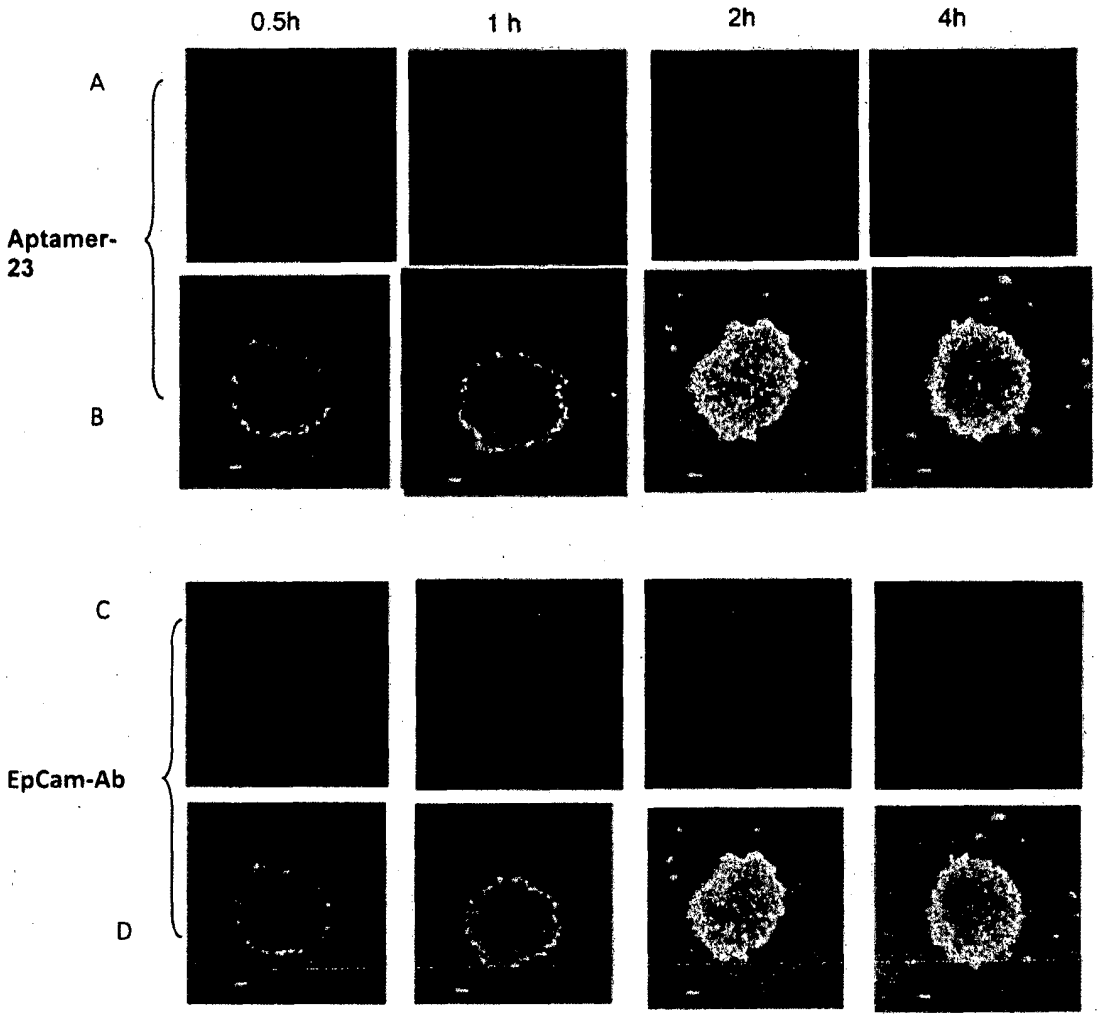
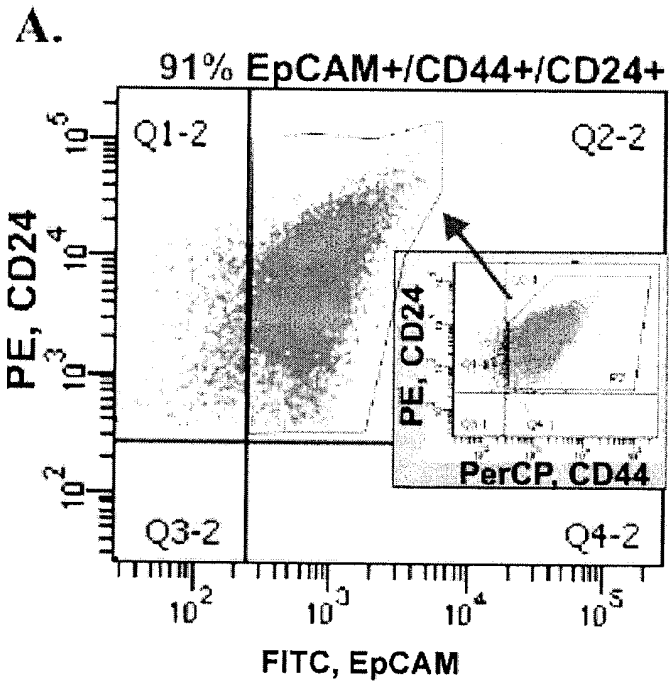


FIGURE 10


A.
91% EpCAM+/CD44+/CD24+
Q1-2
Q2-2
Q3-2
Q4-2
PE, CD24
FITC, EpCAM
PerCP, CD44

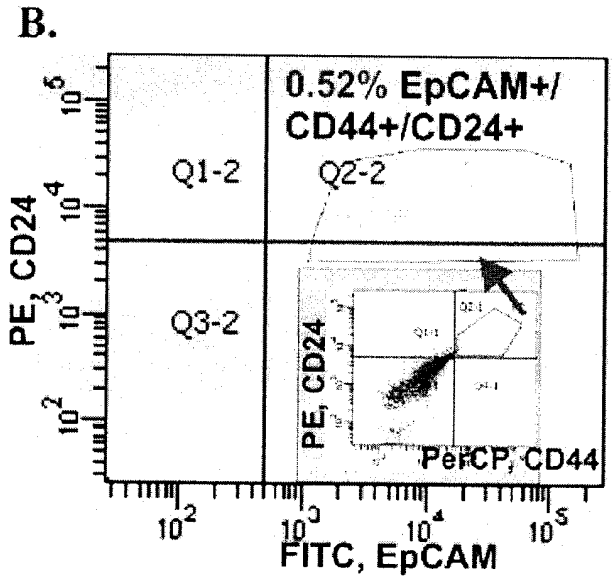

B.
0.52% EpCAM+/
CD44+/CD24+
Q1-2
Q2-2
Q3-2
PE, CD24
FITC, EpCAM
PerCP, CD44

FIGURE 11

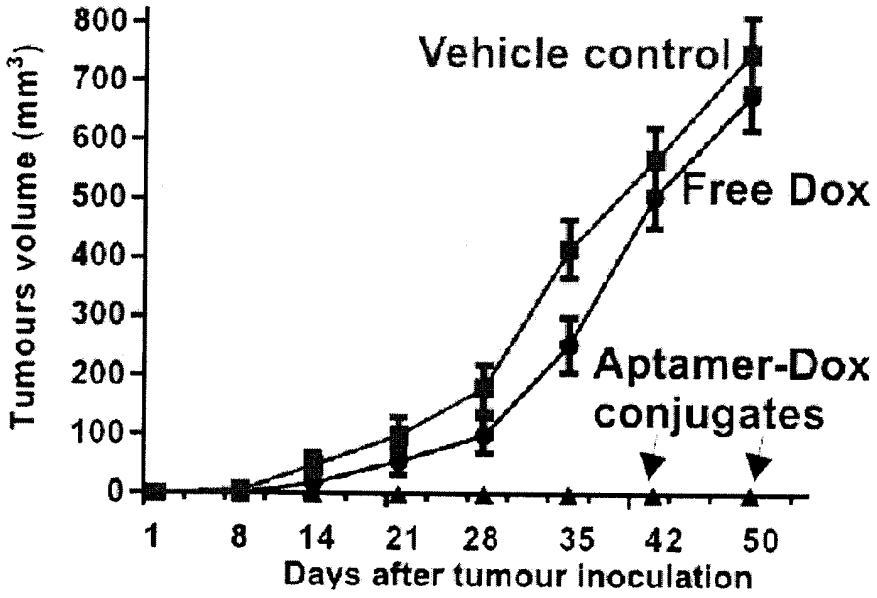

Tumours volume (mm3)
800
700
600
500
400
300
200
100
0
1
8
14
21
28
35
42
50
Days after tumour inoculation
Vehicle control
Free Dox
Aptamer-Dox conjugates

FIGURE 12

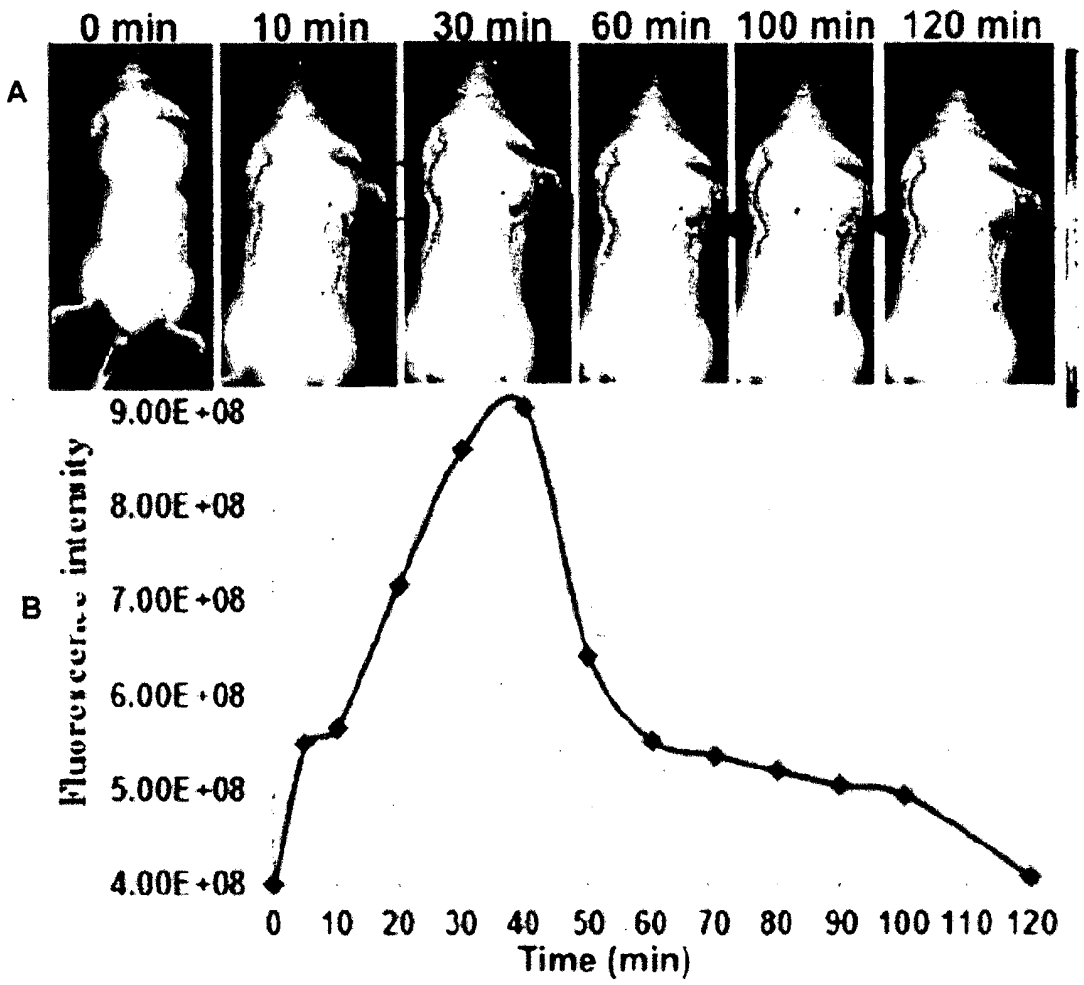

A
0 min
10 min
30 min
60 min
100 min
120 min
B
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
0 10 20 30 40 50 60 70 80 90 100 110 120
Time (min)

FIGURE 13

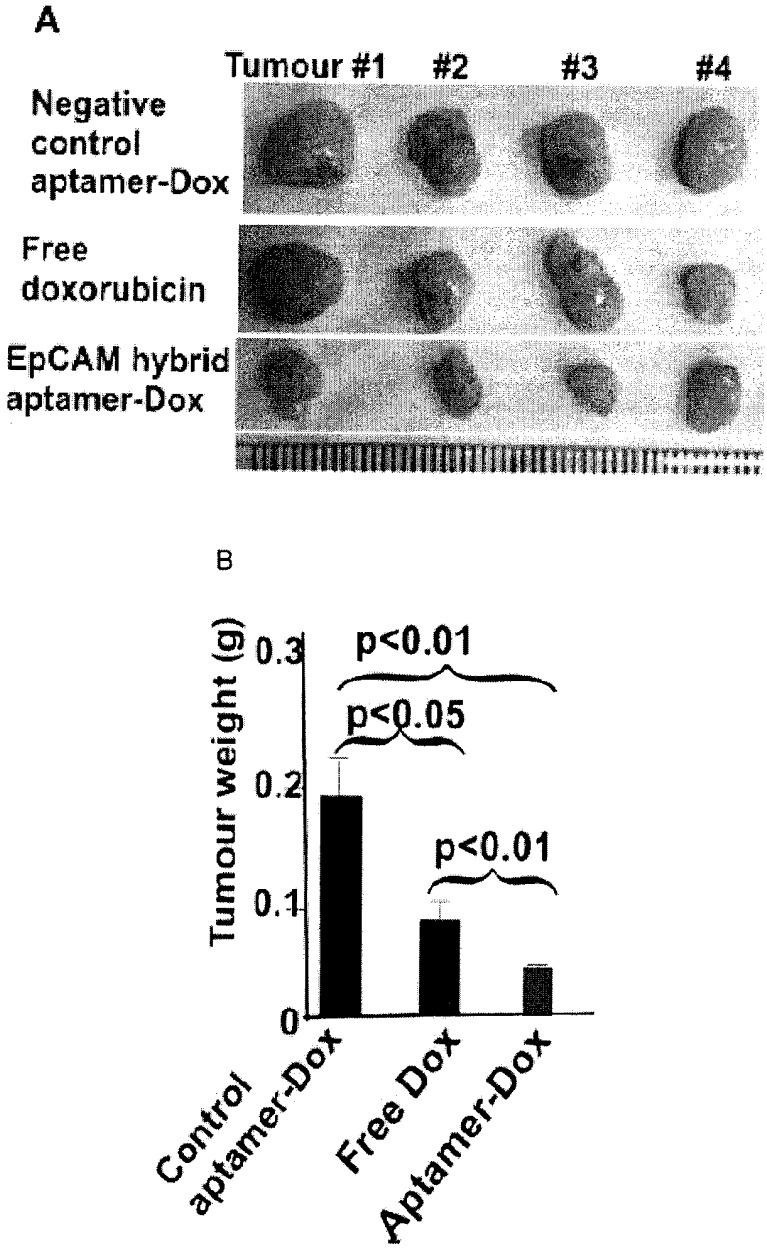

A
Tumour #1
#2
#3
#4
Negative control aptamer-Dox
Free doxorubicin
EpCAM hybrid aptamer-Dox
B
Tumour weight (g)
0.3
0.2
0.1
0
p<0.01
p<0.05
p<0.01
Control aptamer-Dox
Free Dox
Aptamer-Dox

FIGURE 14

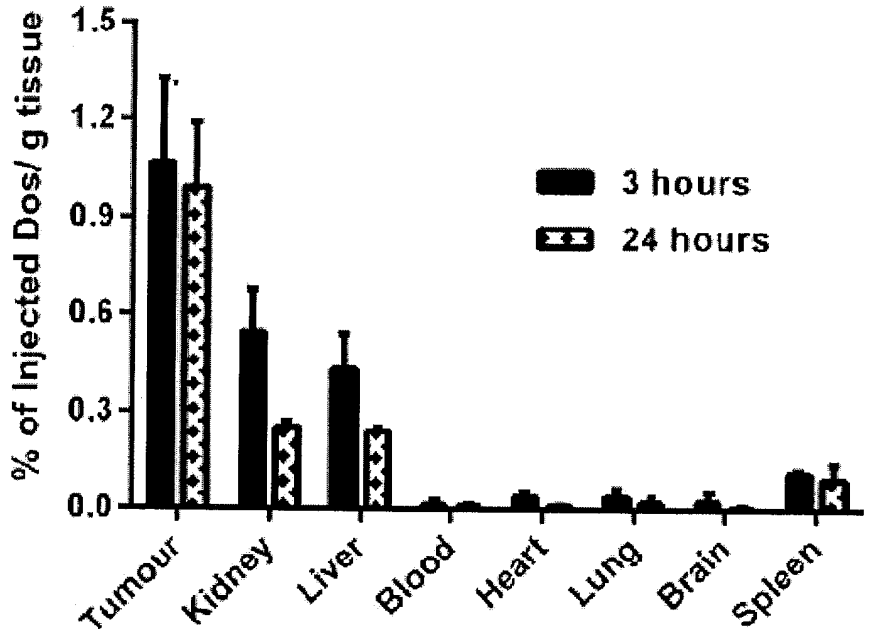

% of Injected Dos/ g tissue
1.5
1.2
0.9
0.6
0.3
0.0
3 hours
24 hours
Tumour
Kidney
Liver
Blood
Heart
Lung
Brain
Spleen

FIGURE 15

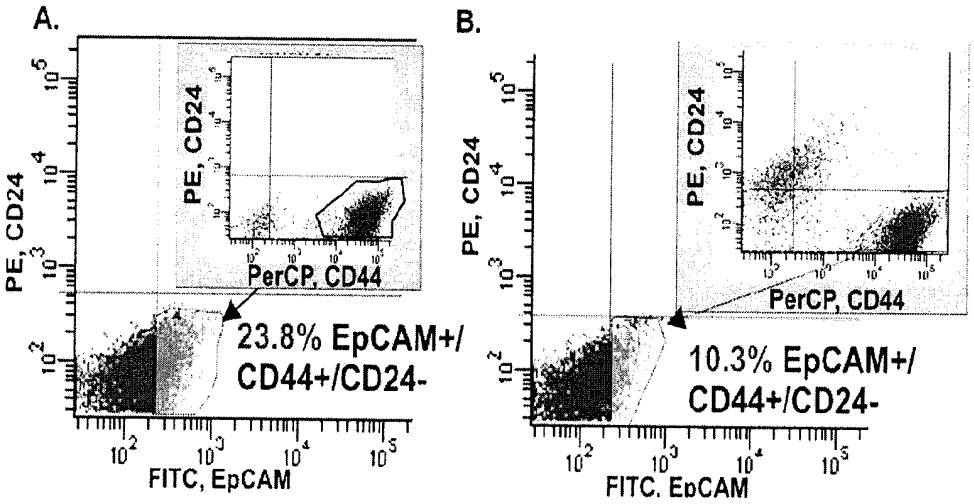

A.
PE, CD24
PerCP, CD44
23.8% EpCAM+/
CD44+/CD24-
FITC, EpCAM
B.
PE, CD24
PerCP, CD44
10.3% EpCAM+/
CD44+/CD24-
FITC, EpCAM

FIGURE 16

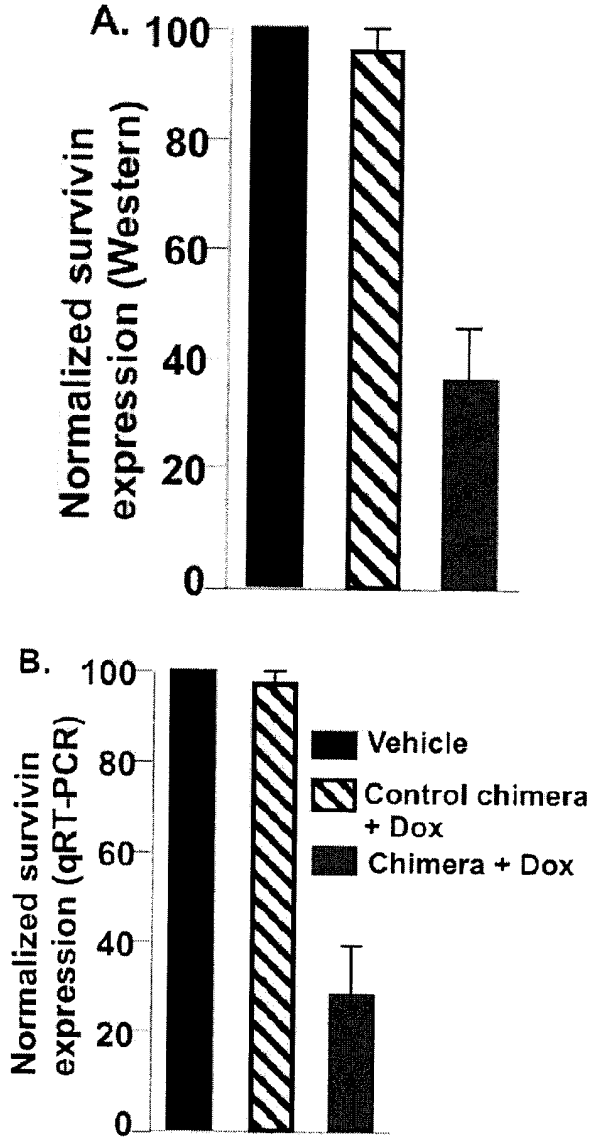

A.
Normalized survivin expression (Western)
100
80
60
40
20
0
B.
Normalized survivin expression (qRT-PCR)
100
80
60
40
20
0
Vehicle
Control chimera + Dox
Chimera + Dox

FIGURE 17

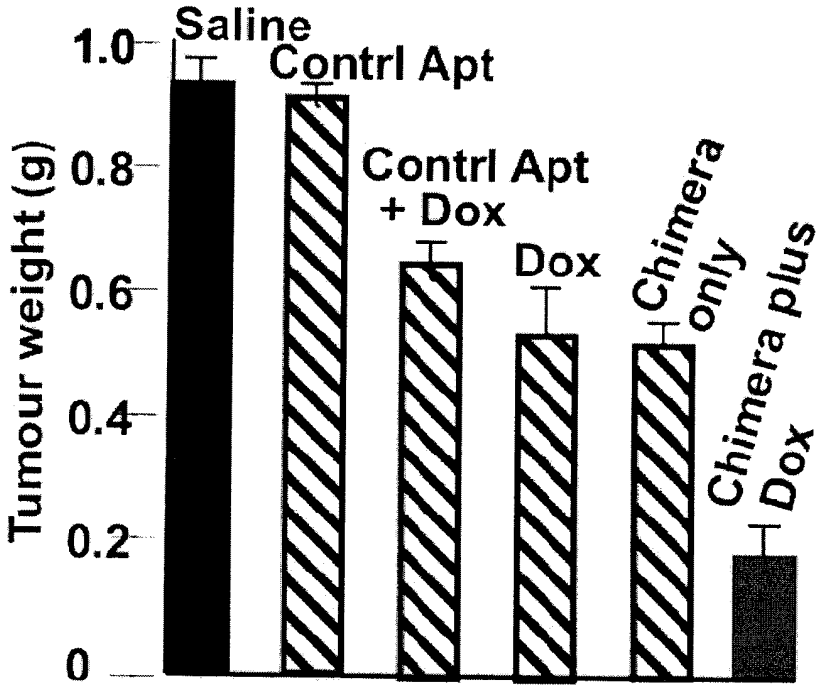

Tumour weight (g)
1.0
0.8
0.6
0.4
0.2
0
Saline
Contrl Apt
Contrl Apt + Dox
Dox
Chimera only
Chimera plus Dox

FIGURE 18