Figure 1

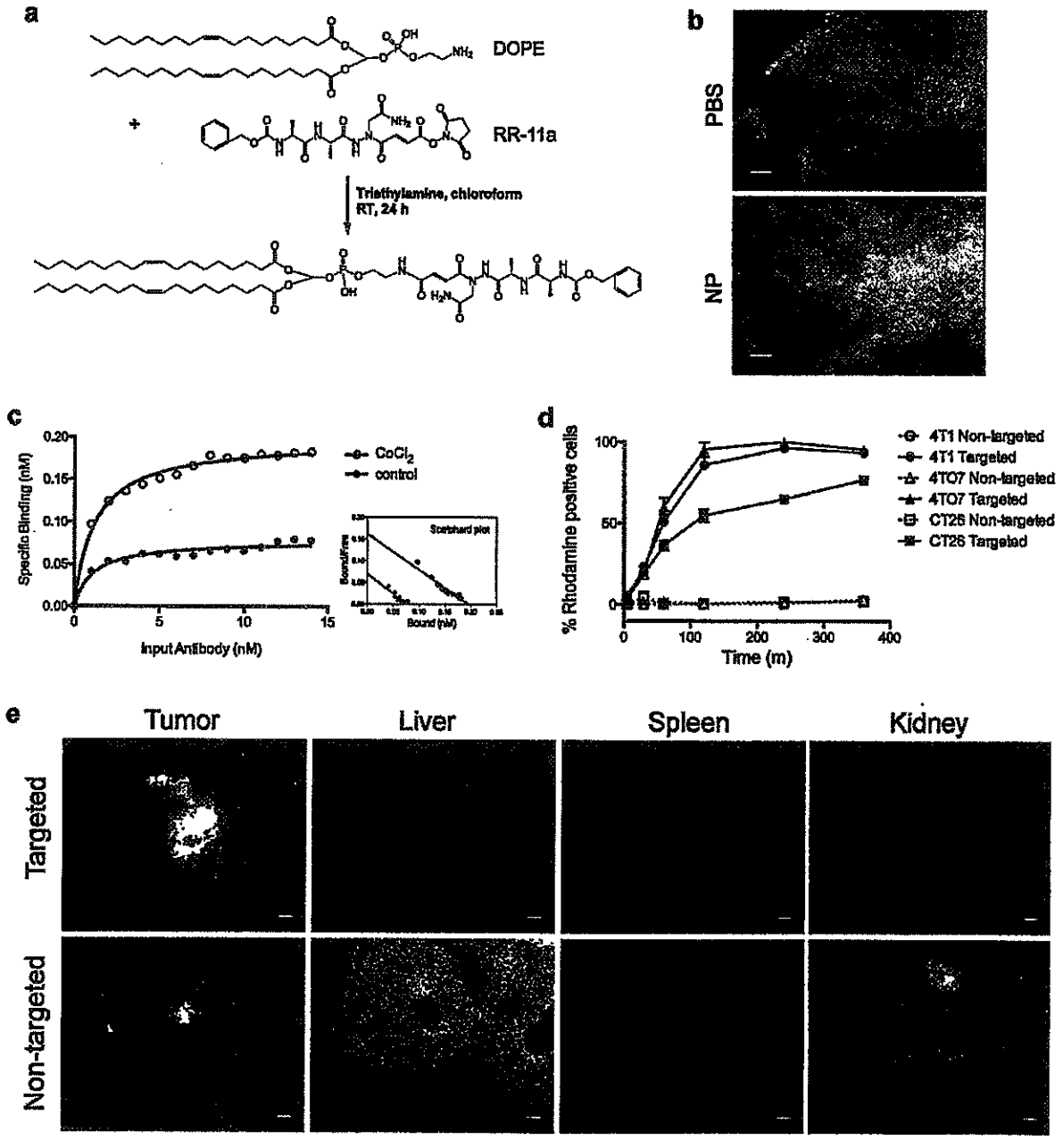

a
DOPE
RR-11a
Triethylamine, chloroform
RT, 24 h
b
PBS
NP
c
Specific Binding (nM)
Input Antibody (nM)
CoCl2
control
Scatchard plot
Bound/Free
Bound (nM)
d
% Rhodamine positive cells
Time (m)
4T1 Non-targeted
4T1 Targeted
4TO7 Non-targeted
4TO7 Targeted
CT26 Non-targeted
CT26 Targeted
e
Tumor
Liver
Spleen
Kidney
Targeted
Non-targeted

Figure 2

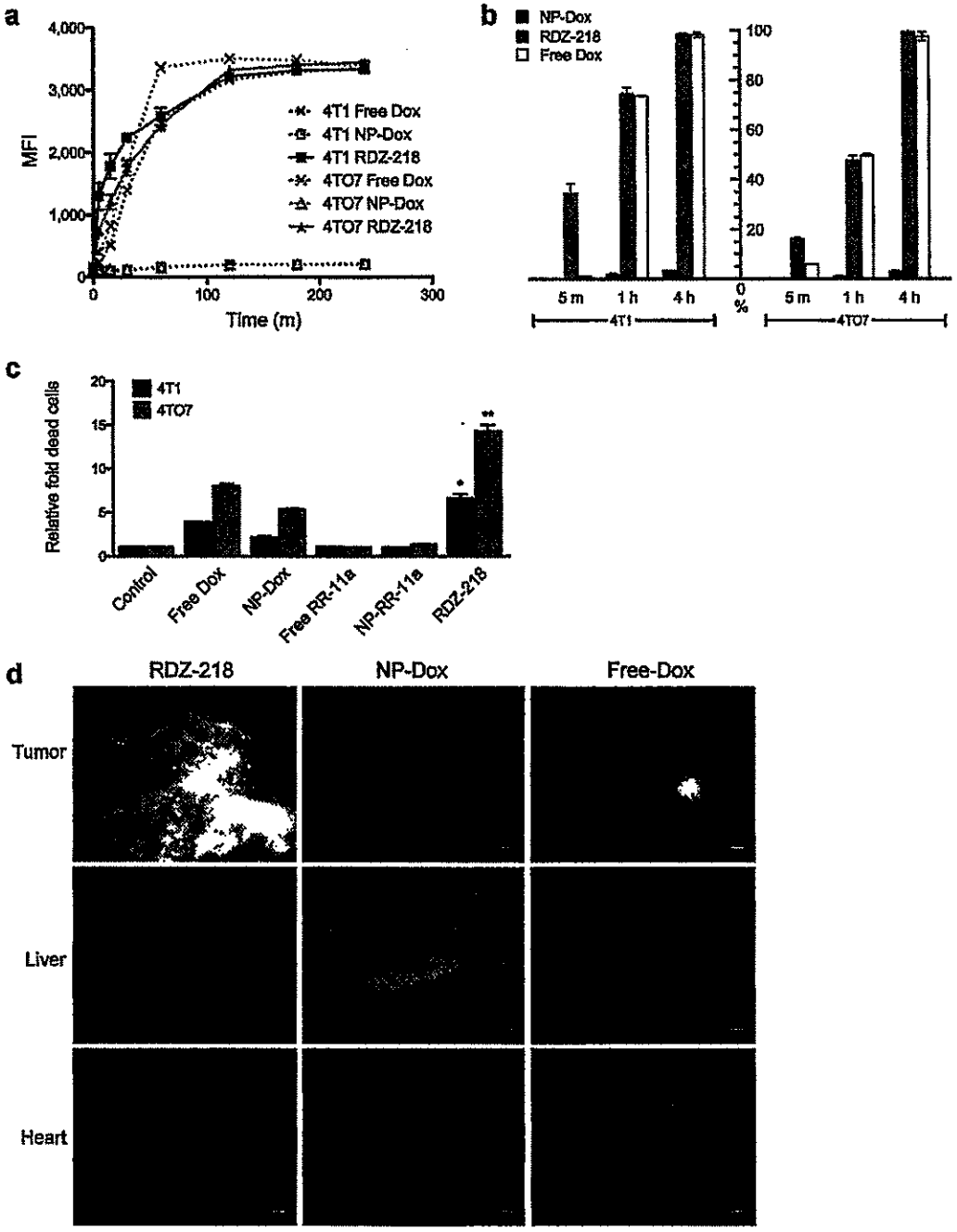
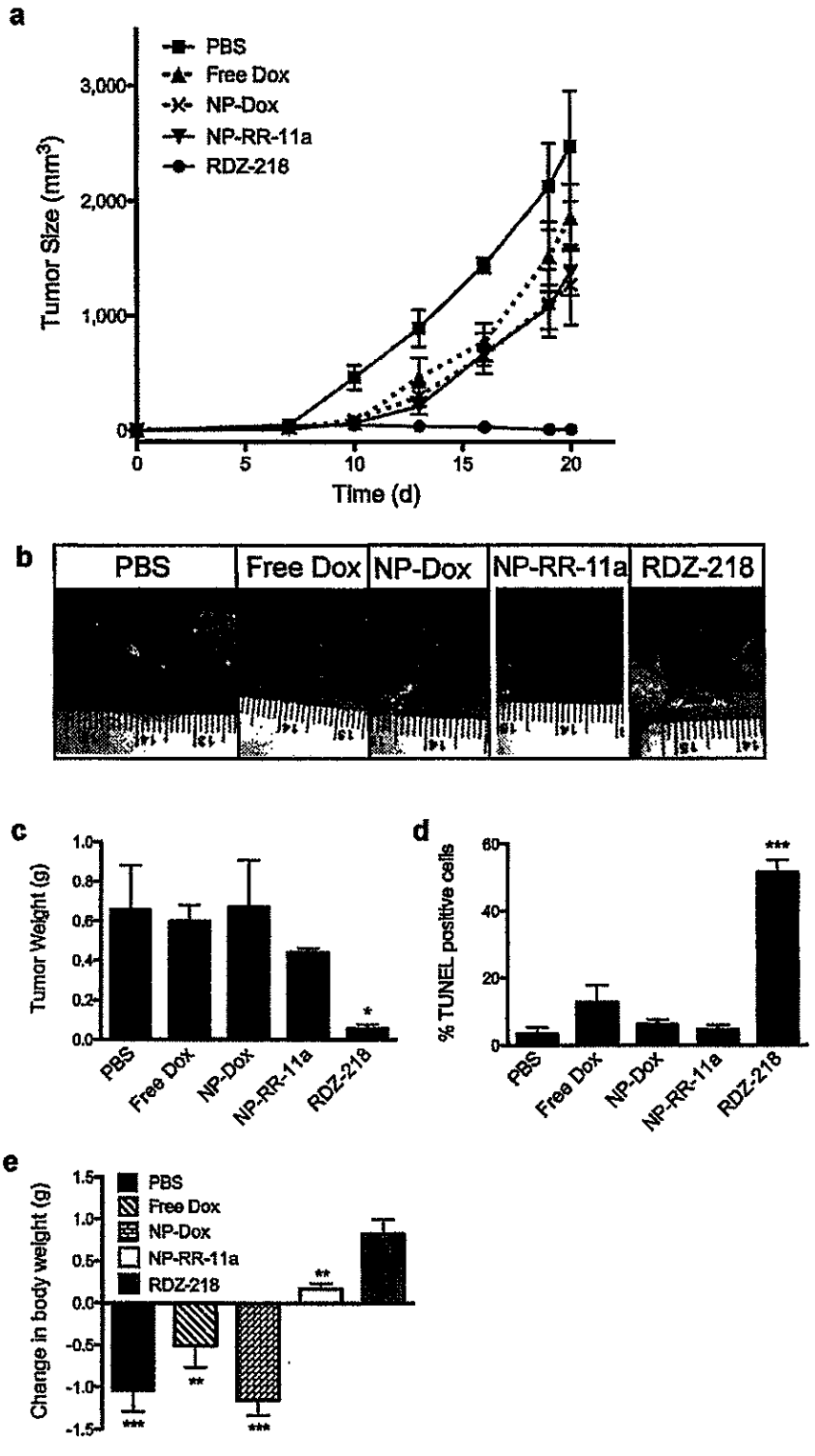
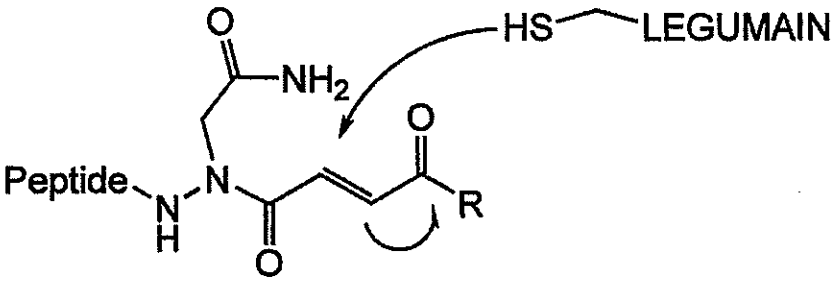

a
MFI
Time (m)
4T1 Free Dox
4T1 NP-Dox
4T1 RDZ-218
4TO7 Free Dox
4TO7 NP-Dox
4TO7 RDZ-218
b
NP-Dox
RDZ-218
Free Dox
%
5 m
1 h
4 h
4T1
4TO7
c
Relative fold dead cells
4T1
4TO7
Control
Free Dox
NP-Dox
Free RR-11a
NP-RR-11a
RDZ-218
d
RDZ-218
NP-Dox
Free-Dox
Tumor
Liver
Heart

Figure 3

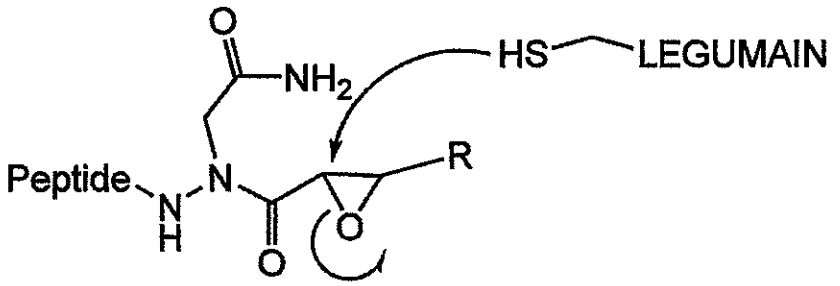

a
PBS
Free Dox
NP-Dox
NP-RR-11a
RDZ-218
Tumor Size (mm3)
3,000
2,000
1,000
0
0
5
10
15
20
Time (d)
b
PBS
Free Dox
NP-Dox
NP-RR-11a
RDZ-218
c
Tumor Weight (g)
1.0
0.8
0.6
0.4
0.2
0.0
*
PBS
Free Dox
NP-Dox
NP-RR-11a
RDZ-218
d
% TUNEL positive cells
60
40
20
0
***
PBS
Free Dox
NP-Dox
NP-RR-11a
RDZ-218
e
Change in body weight (g)
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
PBS
Free Dox
NP-Dox
NP-RR-11a
RDZ-218
**
**
***
***

(a)



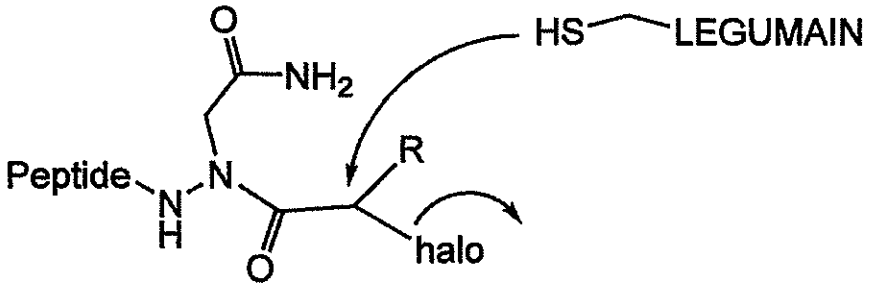
Aza-Asn Michael acceptor inhibitor

(b)



Aza-Asn-epoxide inhibitor

(c)



Aza-Asn halomethylketone inhibitor

Figure 4

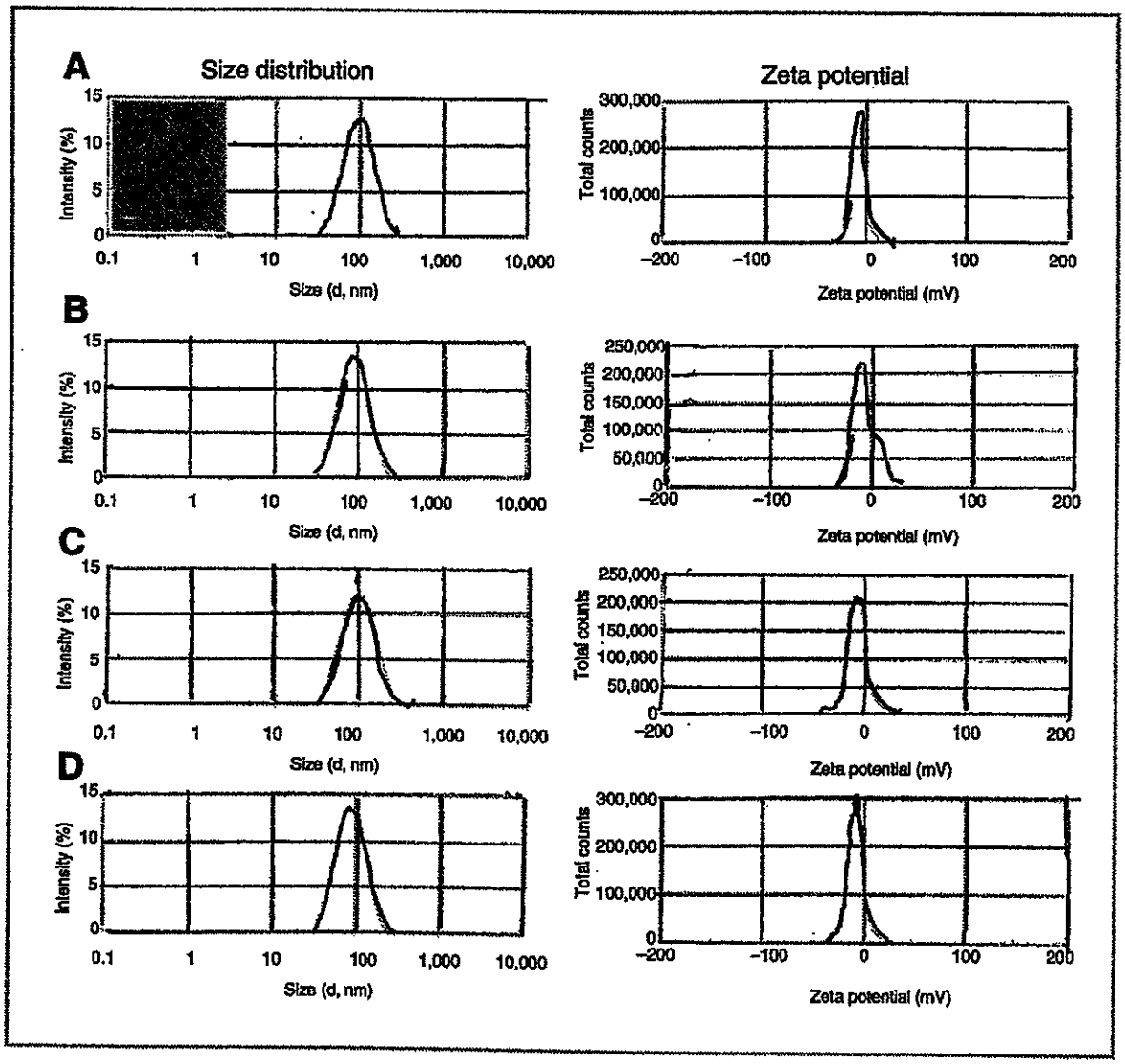

A
Size distribution
Zeta potential
B
C
D
Intensity (%)
Size (d, nm)
Total counts
Zeta potential (mV)

Figure 5

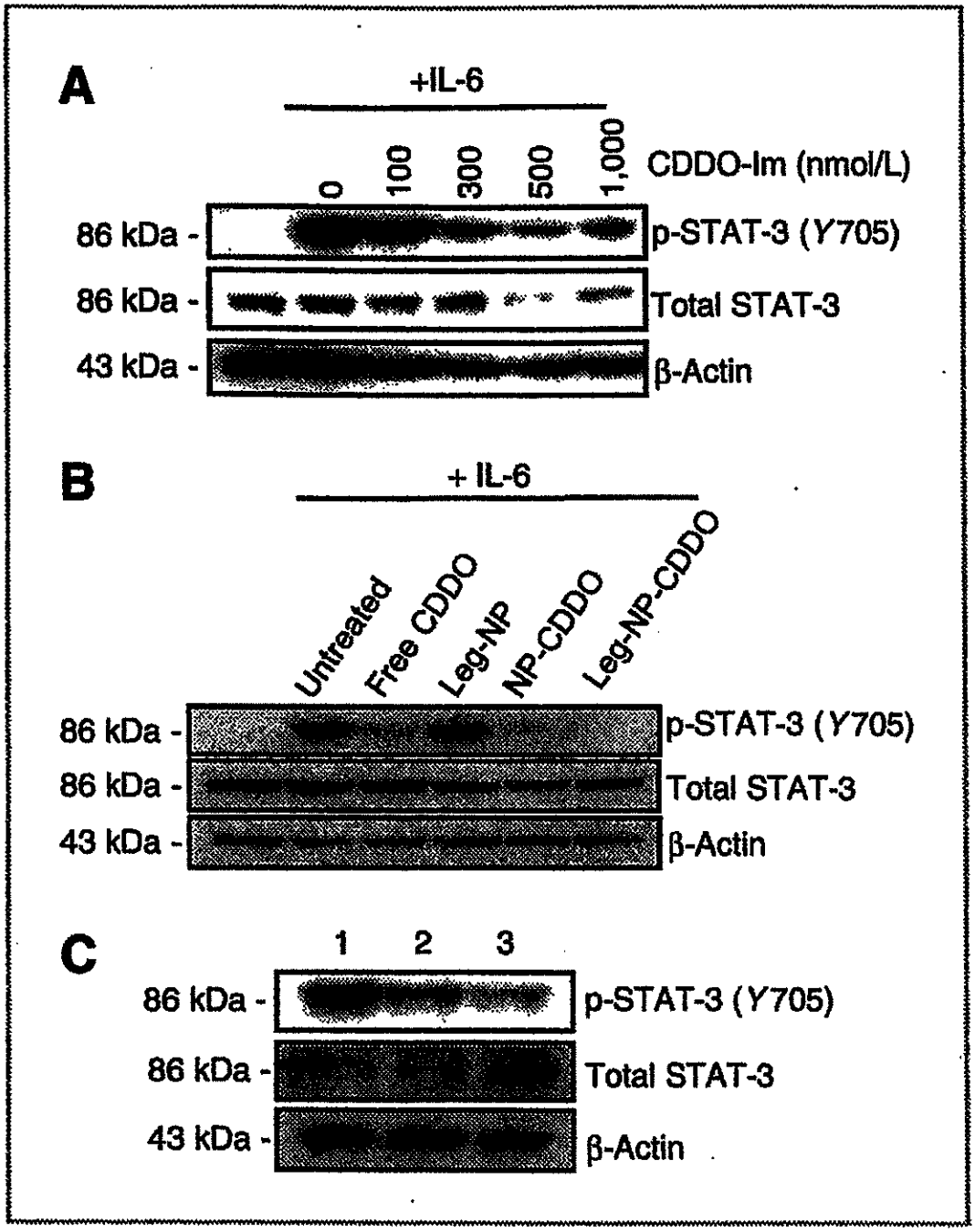

A
+IL-6
0
100
300
500
1,000
CDDO-Im (nmol/L)
86 kDa -
p-STAT-3 (Y705)
86 kDa -
Total STAT-3
43 kDa -
β-Actin
B
+ IL-6
Untreated
Free CDDO
Leg-NP
NP-CDDO
Leg-NP-CDDO
86 kDa -
p-STAT-3 (Y705)
86 kDa -
Total STAT-3
43 kDa -
β-Actin
C
1
2
3
86 kDa -
p-STAT-3 (Y705)
86 kDa -
Total STAT-3
43 kDa -
β-Actin

Figure 6

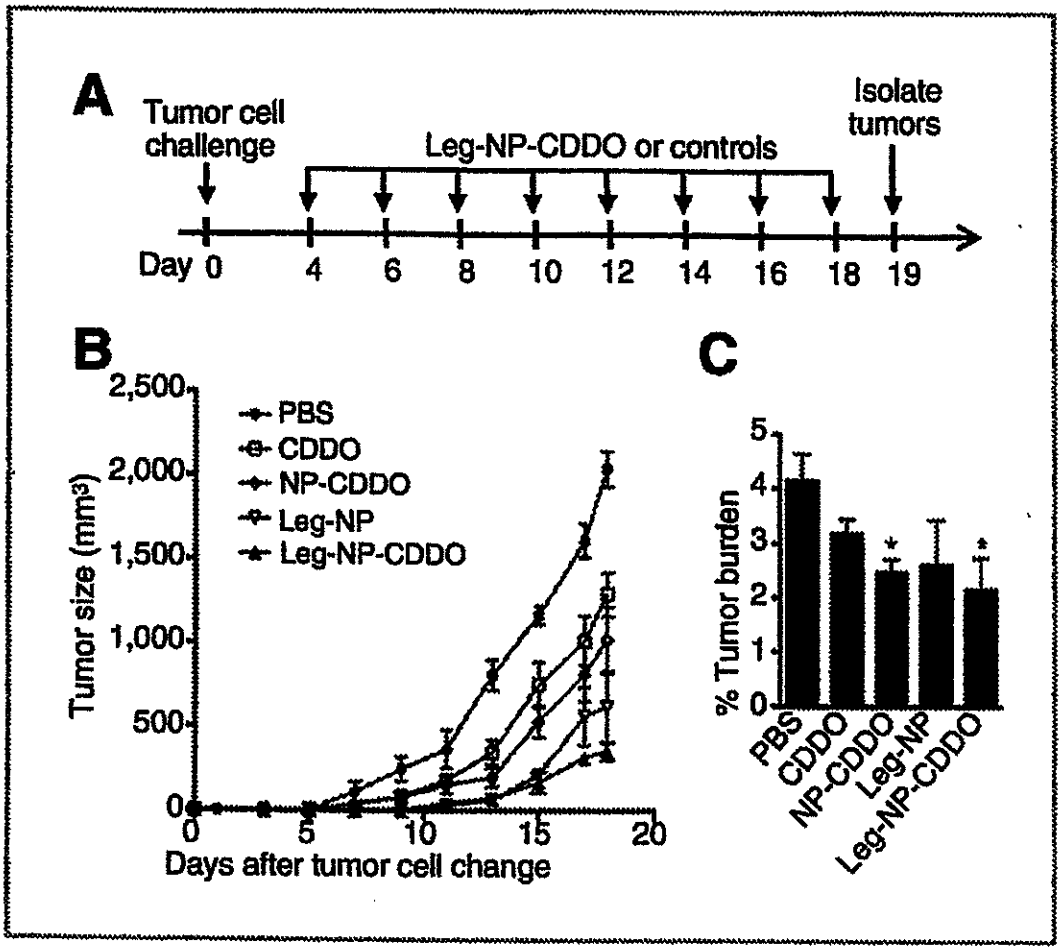

A
Tumor cell challenge
Leg-NP-CDDO or controls
Isolate tumors
Day 0
4
6
8
10
12
14
16
18
19
B
Tumor size (mm³)
2,500
2,000
1,500
1,000
500
0
PBS
CDDO
NP-CDDO
Leg-NP
Leg-NP-CDDO
0
5
10
15
20
Days after tumor cell change
C
% Tumor burden
5
4
3
2
1
0
PBS
CDDO
NP-CDDO
Leg-NP
Leg-NP-CDDO

Figure 7

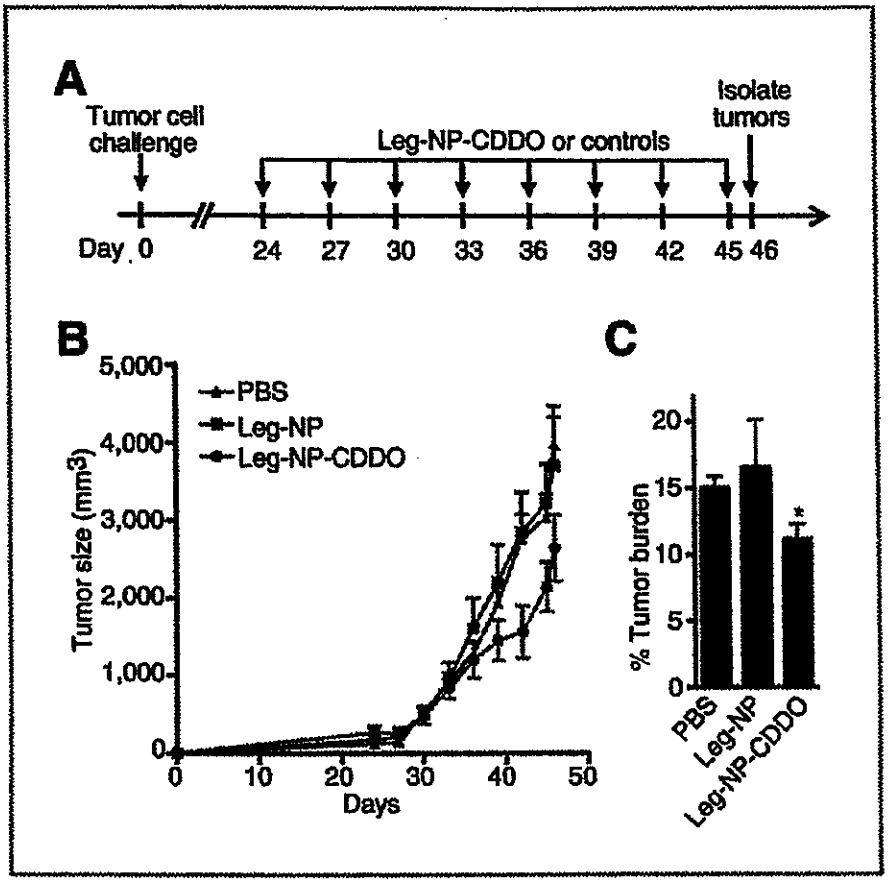

A
Tumor cell challenge
Leg-NP-CDDO or controls
Isolate tumors
Day 0
24
27
30
33
36
39
42
45
46
B
Tumor size (mm3)
5,000
4,000
3,000
2,000
1,000
0
PBS
Leg-NP
Leg-NP-CDDO
0
10
20
30
40
50
Days
C
% Tumor burden
20
15
10
5
0
*
PBS
Leg-NP
Leg-NP-CDDO

Figure 8

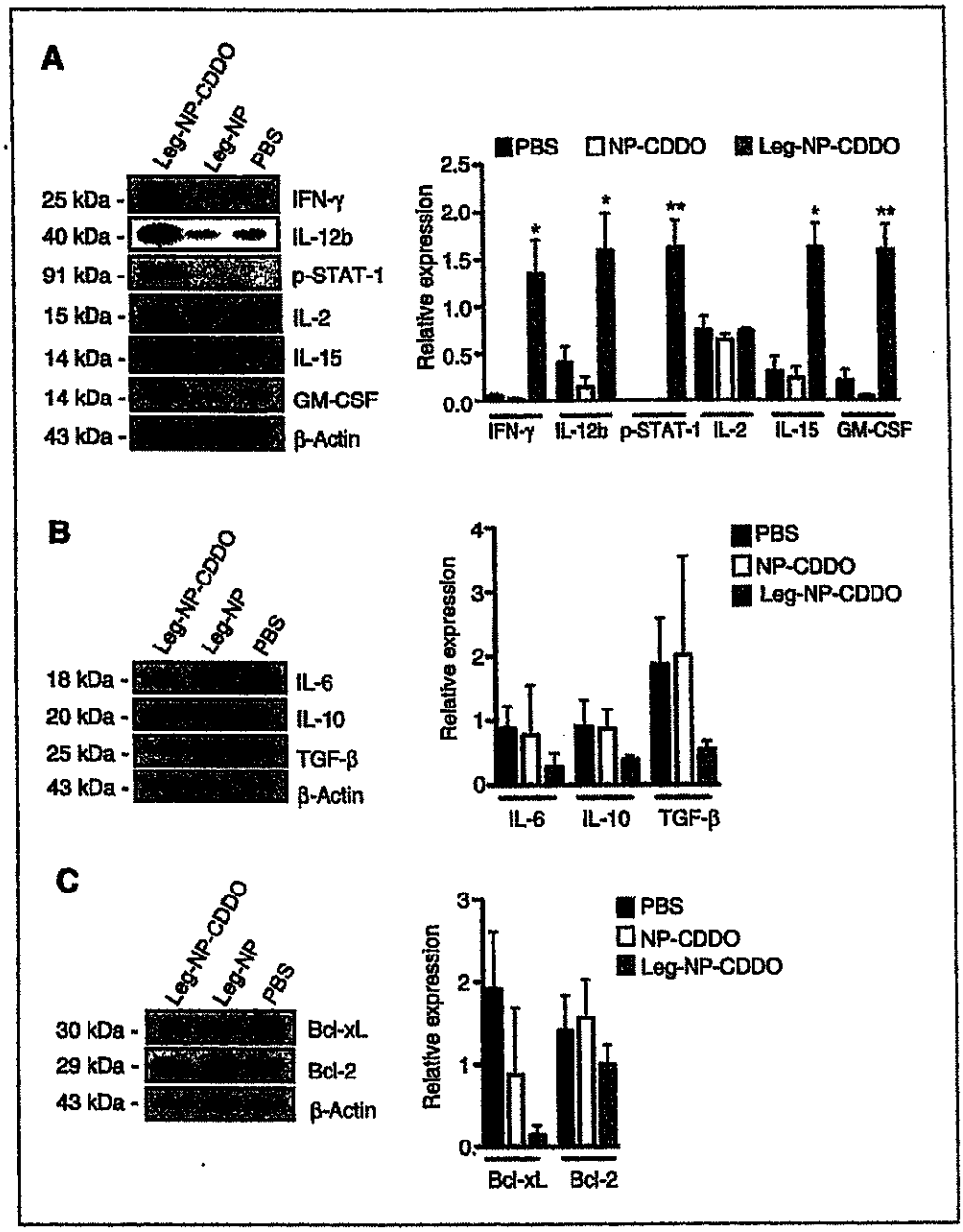

A
Leg-NP-CDDO
Leg-NP
PBS
25 kDa - IFN-γ
40 kDa - IL-12b
91 kDa - p-STAT-1
15 kDa - IL-2
14 kDa - IL-15
14 kDa - GM-CSF
43 kDa - β-Actin
PBS
NP-CDDO
Leg-NP-CDDO
Relative expression
2.5
2.0
1.5
1.0
0.5
0.0
IFN-γ
IL-12b
p-STAT-1
IL-2
IL-15
GM-CSF
B
Leg-NP-CDDO
Leg-NP
PBS
18 kDa - IL-6
20 kDa - IL-10
25 kDa - TGF-β
43 kDa - β-Actin
PBS
NP-CDDO
Leg-NP-CDDO
Relative expression
4
3
2
1
0
IL-6
IL-10
TGF-β
C
Leg-NP-CDDO
Leg-NP
PBS
30 kDa - Bcl-xL
29 kDa - Bcl-2
43 kDa - β-Actin
PBS
NP-CDDO
Leg-NP-CDDO
Relative expression
3
2
1
0
Bcl-xL
Bcl-2

Figure 9

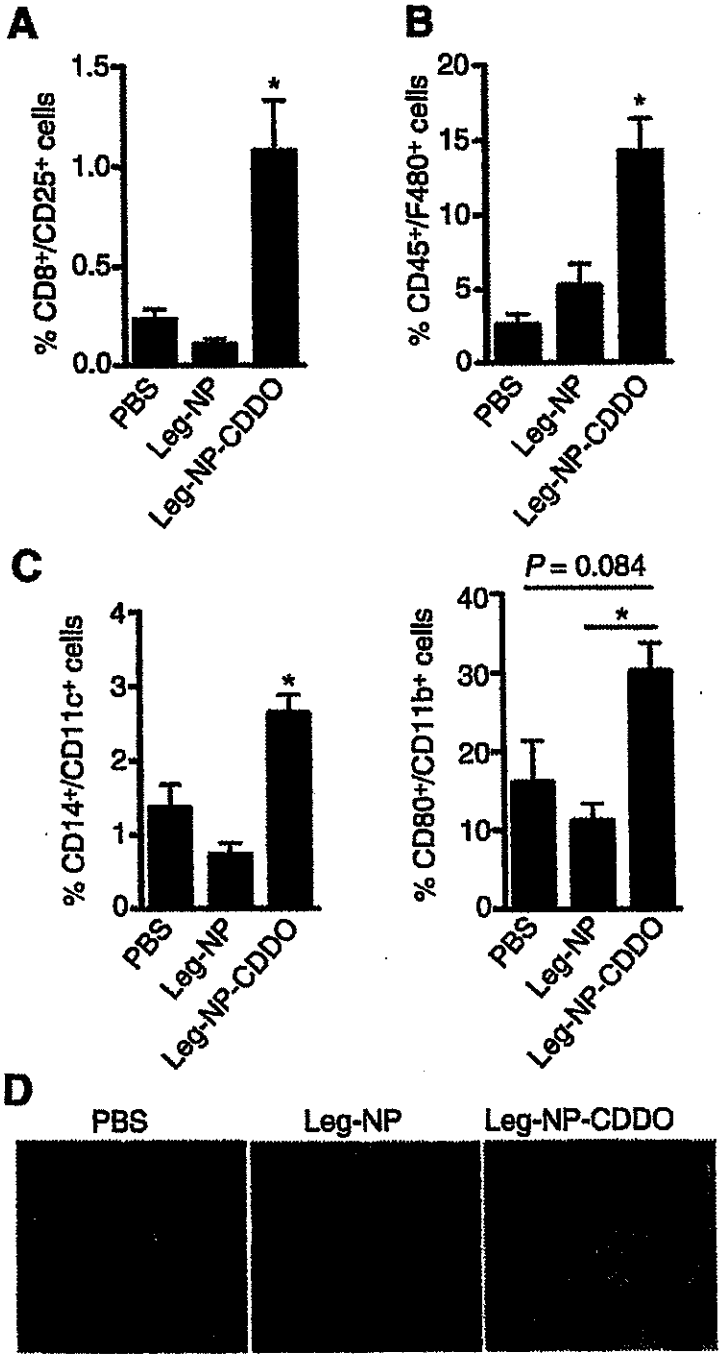

A
% CD8+/CD25+ cells
1.5
1.0
0.5
0.0
*
PBS
Leg-NP
Leg-NP-CDDO
B
% CD45+/F480+ cells
20
15
10
5
0
*
PBS
Leg-NP
Leg-NP-CDDO
C
% CD14+/CD11c+ cells
4
3
2
1
0
*
PBS
Leg-NP
Leg-NP-CDDO
% CD80+/CD11b+ cells
P = 0.084
*
40
30
20
10
0
PBS
Leg-NP
Leg-NP-CDDO
D
PBS
Leg-NP
Leg-NP-CDDO

Figure 10

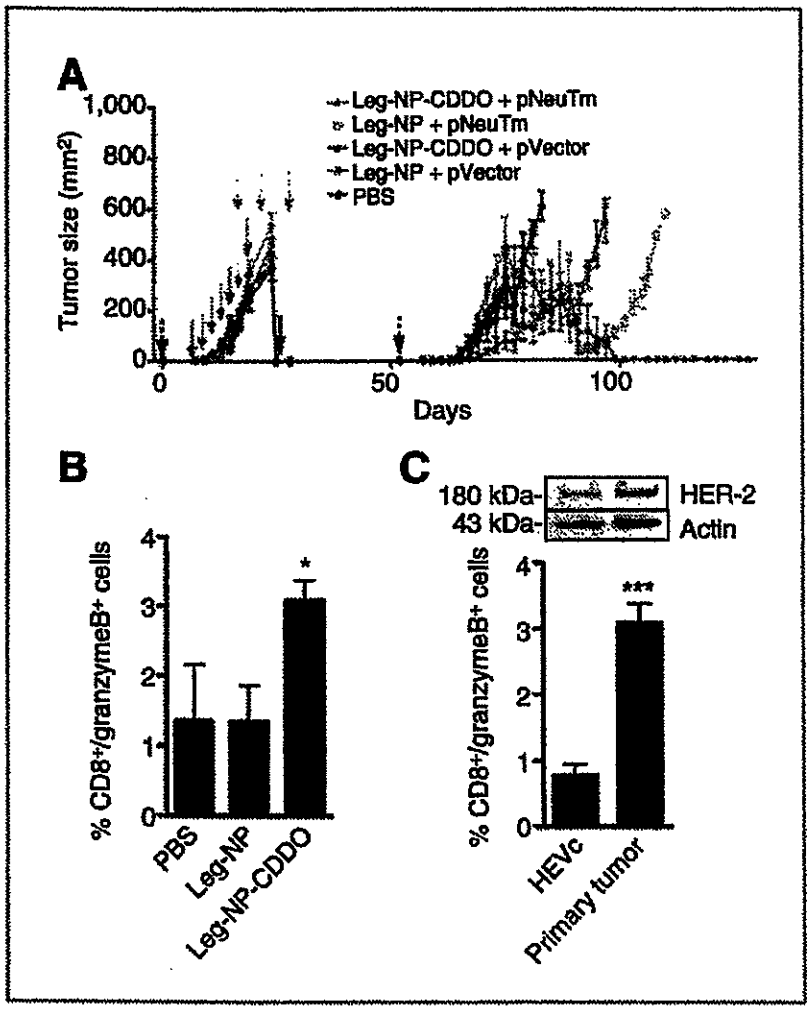

A
Tumor size (mm²)
1,000
800
600
400
200
0
0
50
100
Days
Leg-NP-CDDO + pNeuTm
Leg-NP + pNeuTm
Leg-NP-CDDO + pVector
Leg-NP + pVector
PBS
B
% CD8+/granzymeB+ cells
4
3
2
1
0
*
PBS
Leg-NP
Leg-NP-CDDO
C
180 kDa-
43 kDa-
HER-2
Actin
% CD8+/granzymeB+ cells
4
3
2
1
0
***
HEVc
Primary tumor

Figure. 11