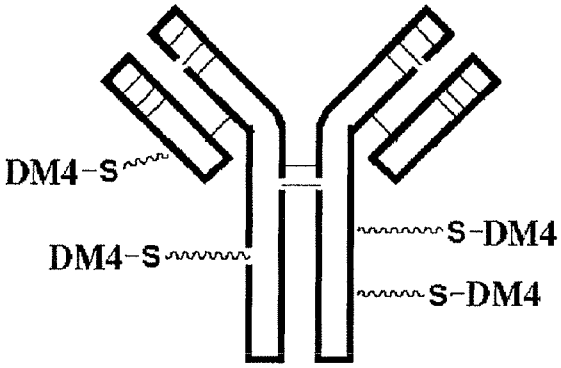
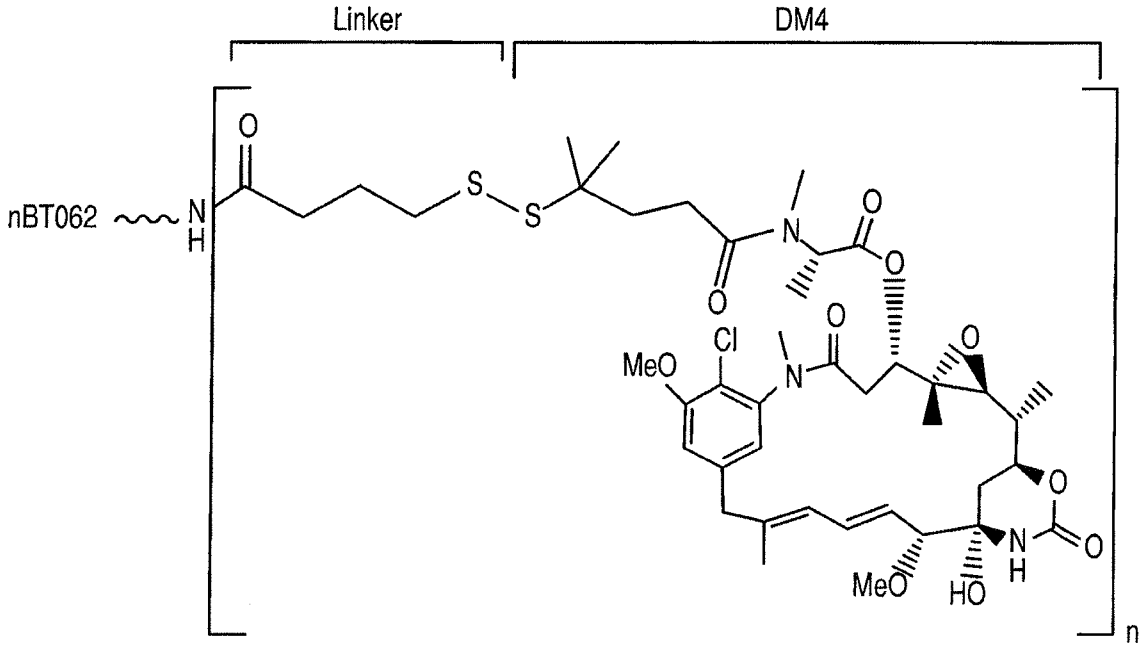
FIG. 1





*n is approximately 3.5 drug linked per antibody molecule

FIG. 2

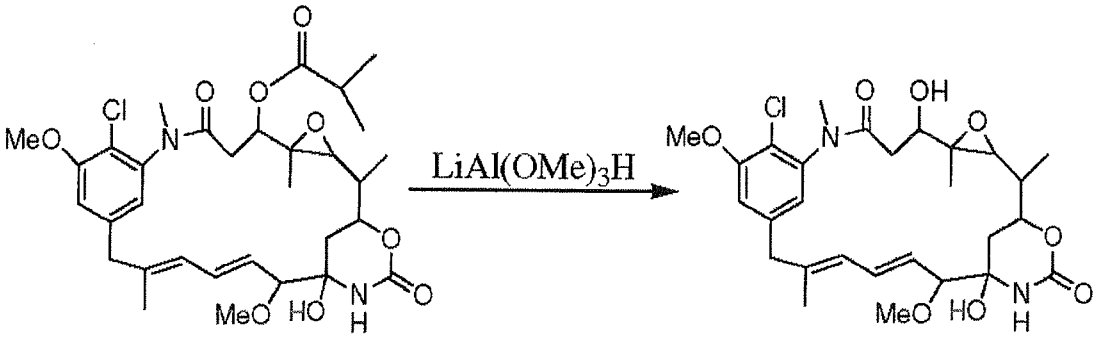
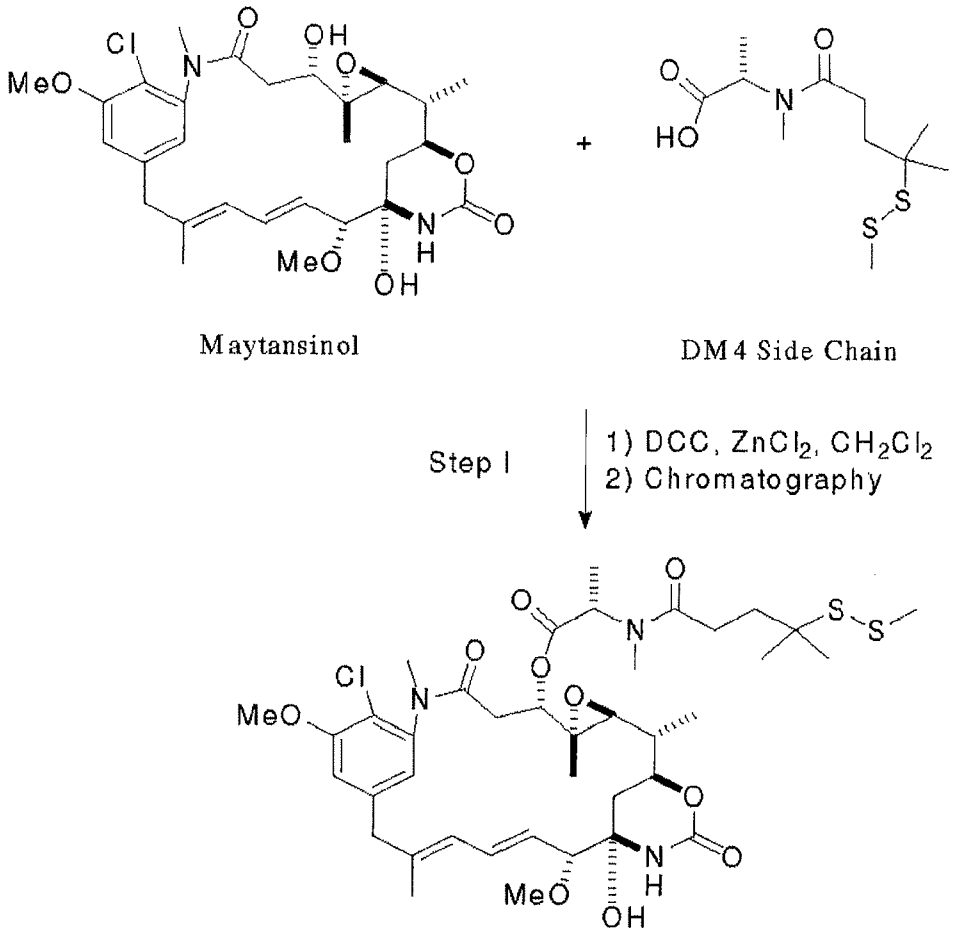


FIG. 3



Maytansinol

DM4 Side Chain

L-DM4-SMe

L-DM4

FIG. 4

DCC: 1,3-dicyclohexylcarbodiimide
DTT: Dithiothreitol
DME: 1,2-Dimethoxyethane

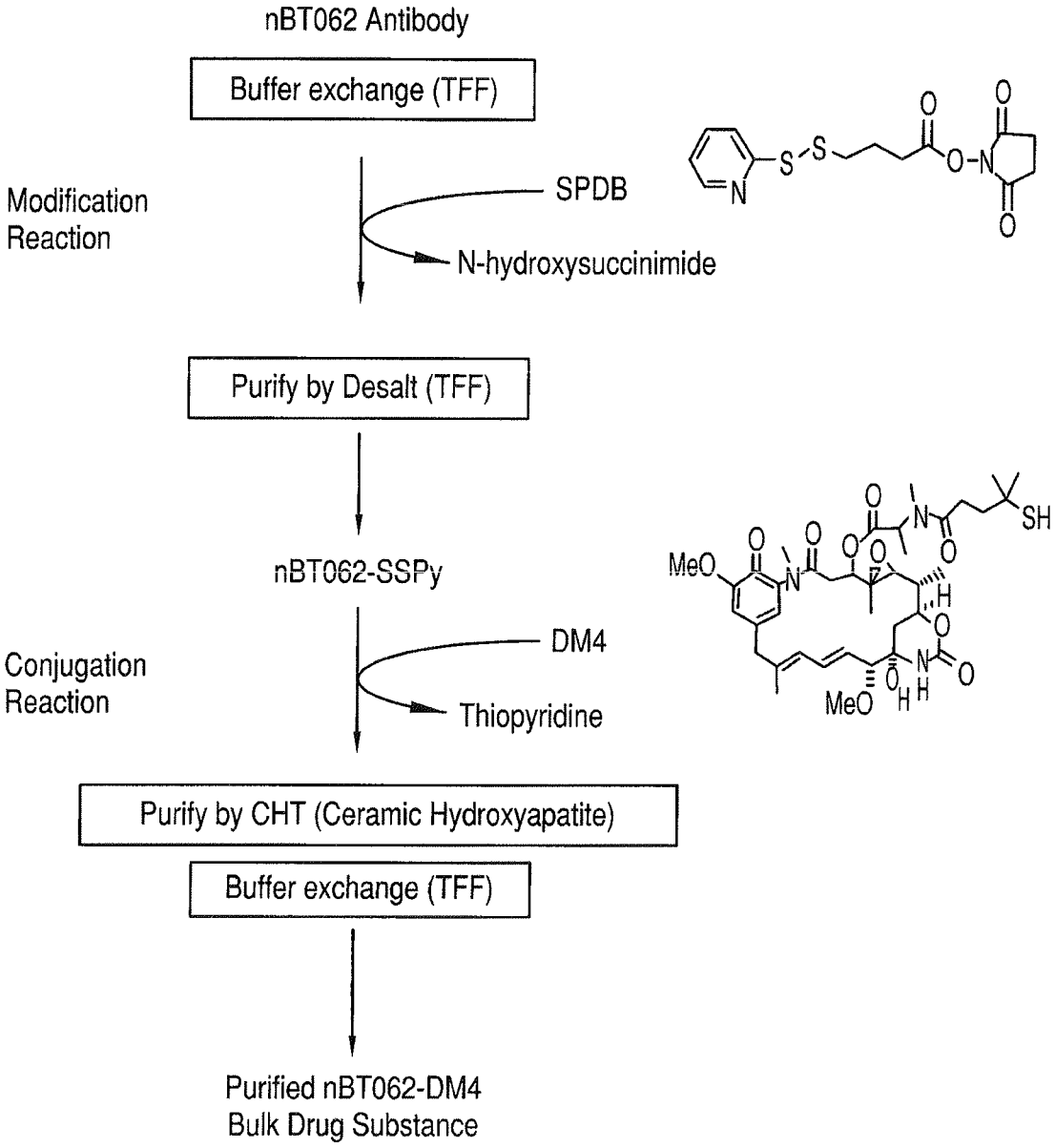

nBT062 Antibody
Buffer exchange (TFF)
Modification Reaction
SPDB
N-hydroxysuccinimide
Purify by Desalt (TFF)
nBT062-SSPy
Conjugation Reaction
DM4
Thiopyridine
Purify by CHT (Ceramic Hydroxyapatite)
Buffer exchange (TFF)
Purified nBT062-DM4
Bulk Drug Substance

FIG. 5

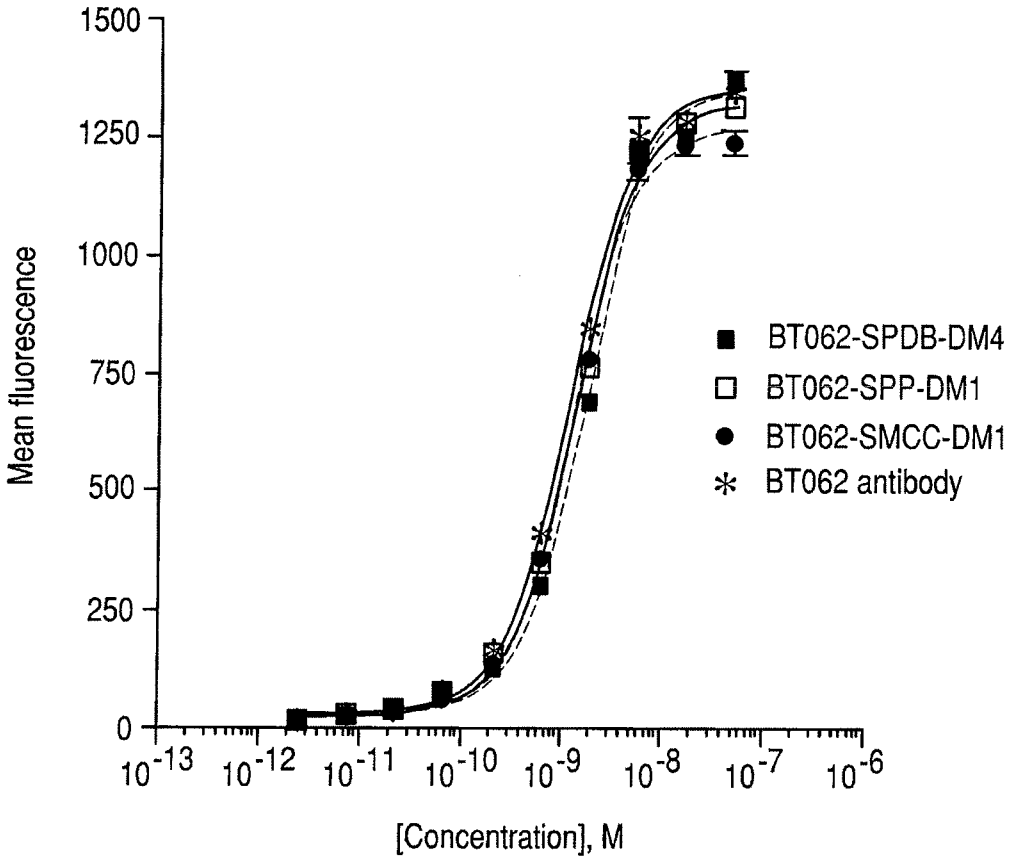

1500
1250
1000
750
500
250
0
Mean fluorescence
10-13
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[Concentration], M
BT062-SPDB-DM4
BT062-SPP-DM1
BT062-SMCC-DM1
BT062 antibody

FIG. 6

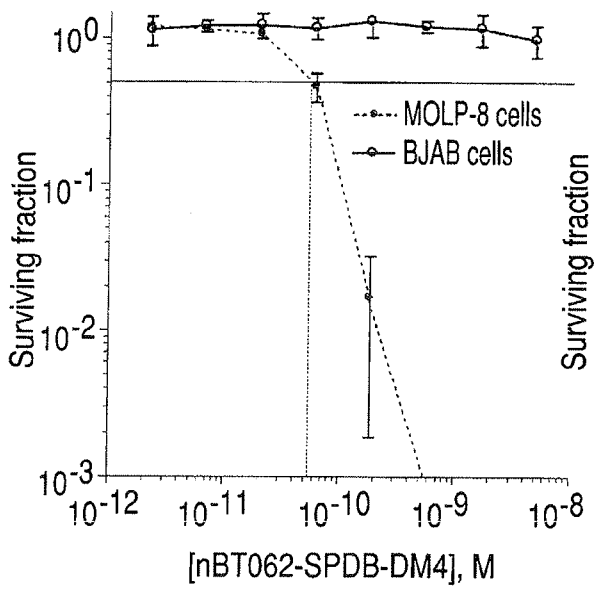


FIG. 7A

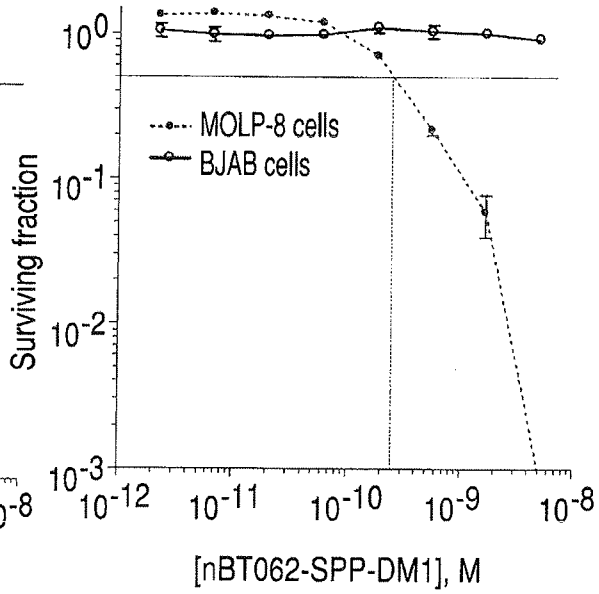


FIG. 7B

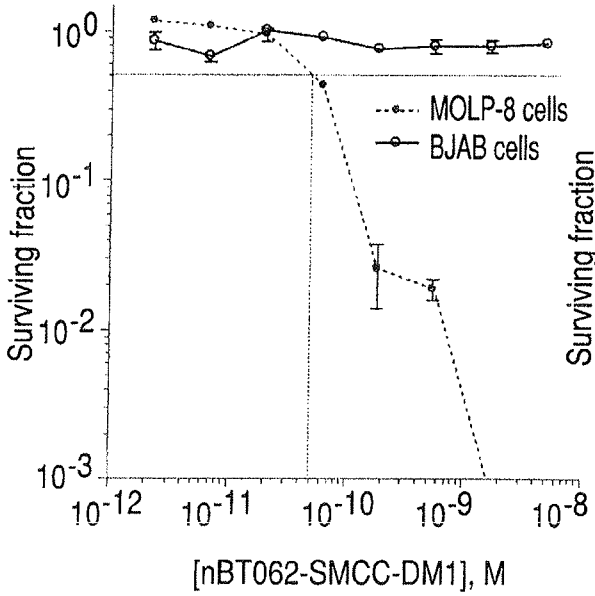


FIG. 7C

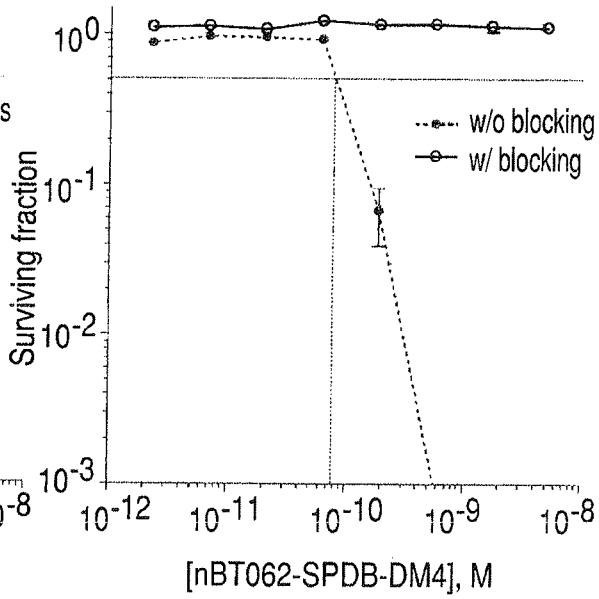


FIG. 7D

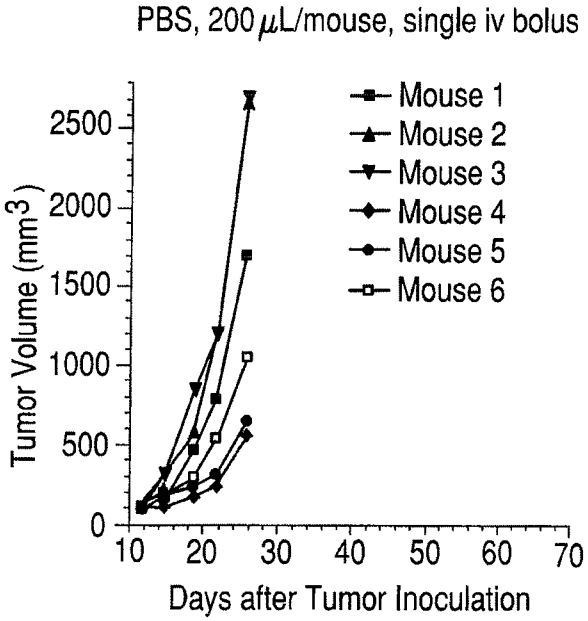


FIG. 8A

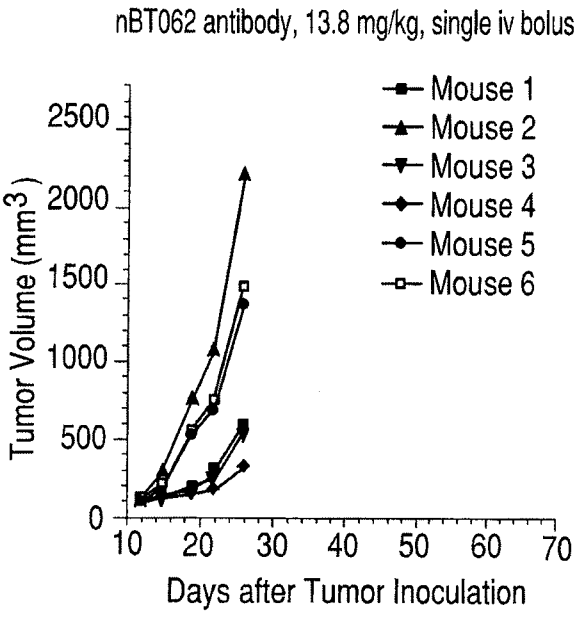


FIG. 8B

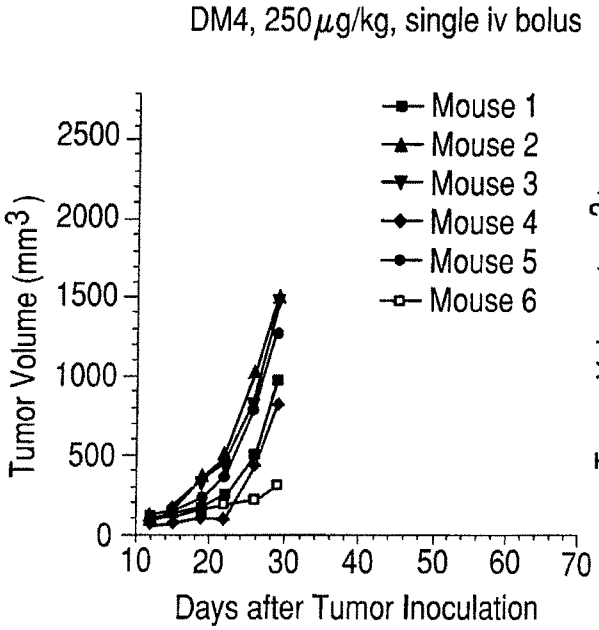


FIG. 8C

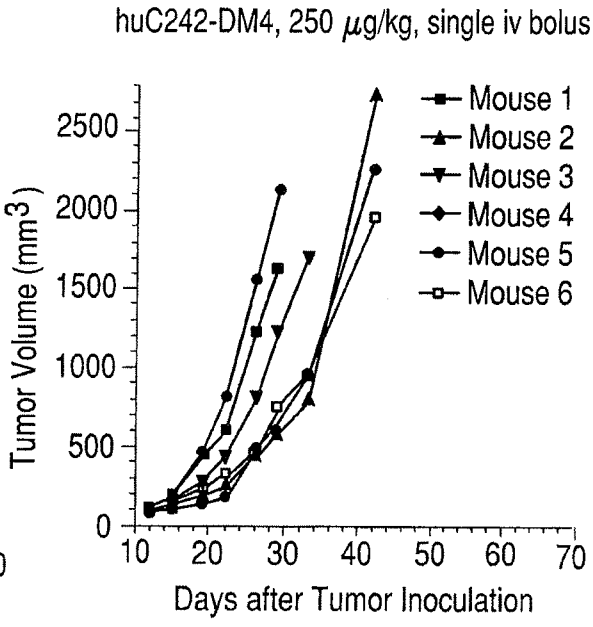


FIG. 8D

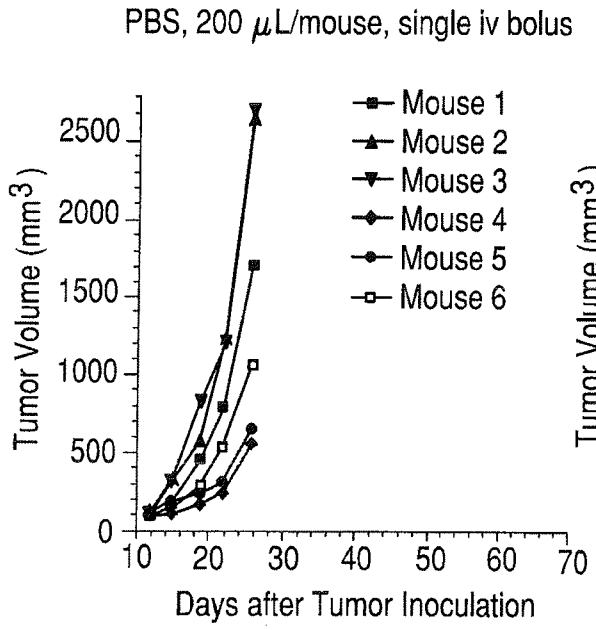


FIG. 9A

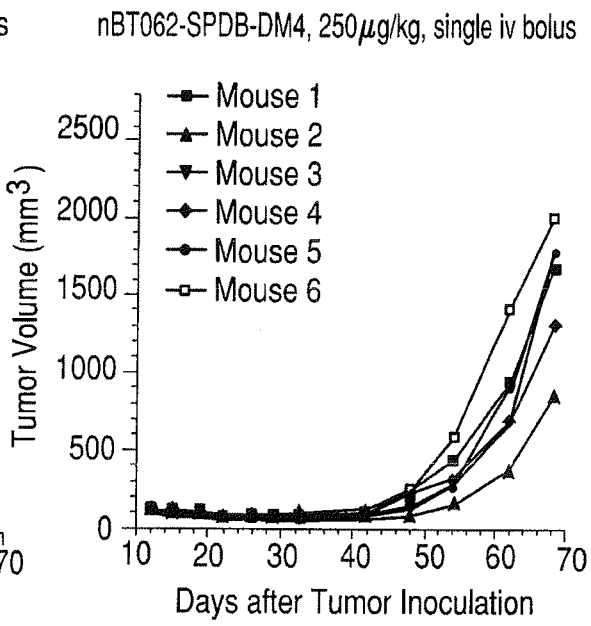


FIG. 9B

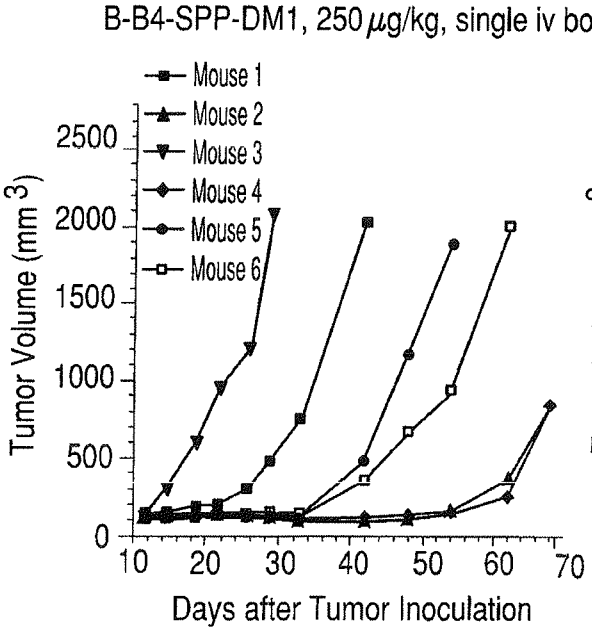


FIG. 9C

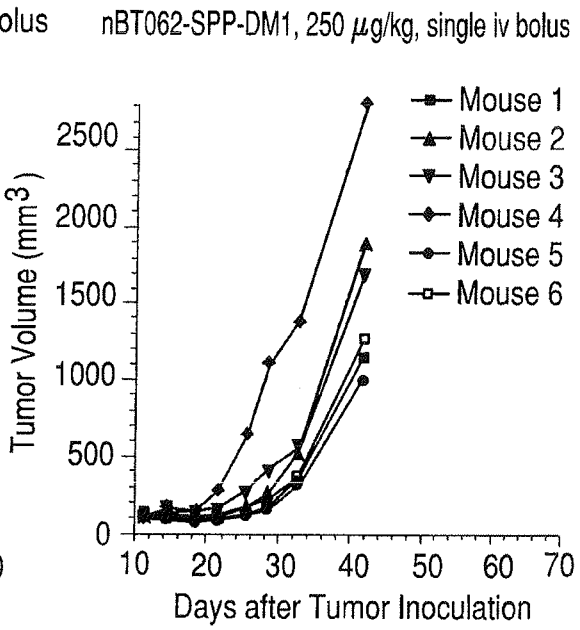


FIG. 9D

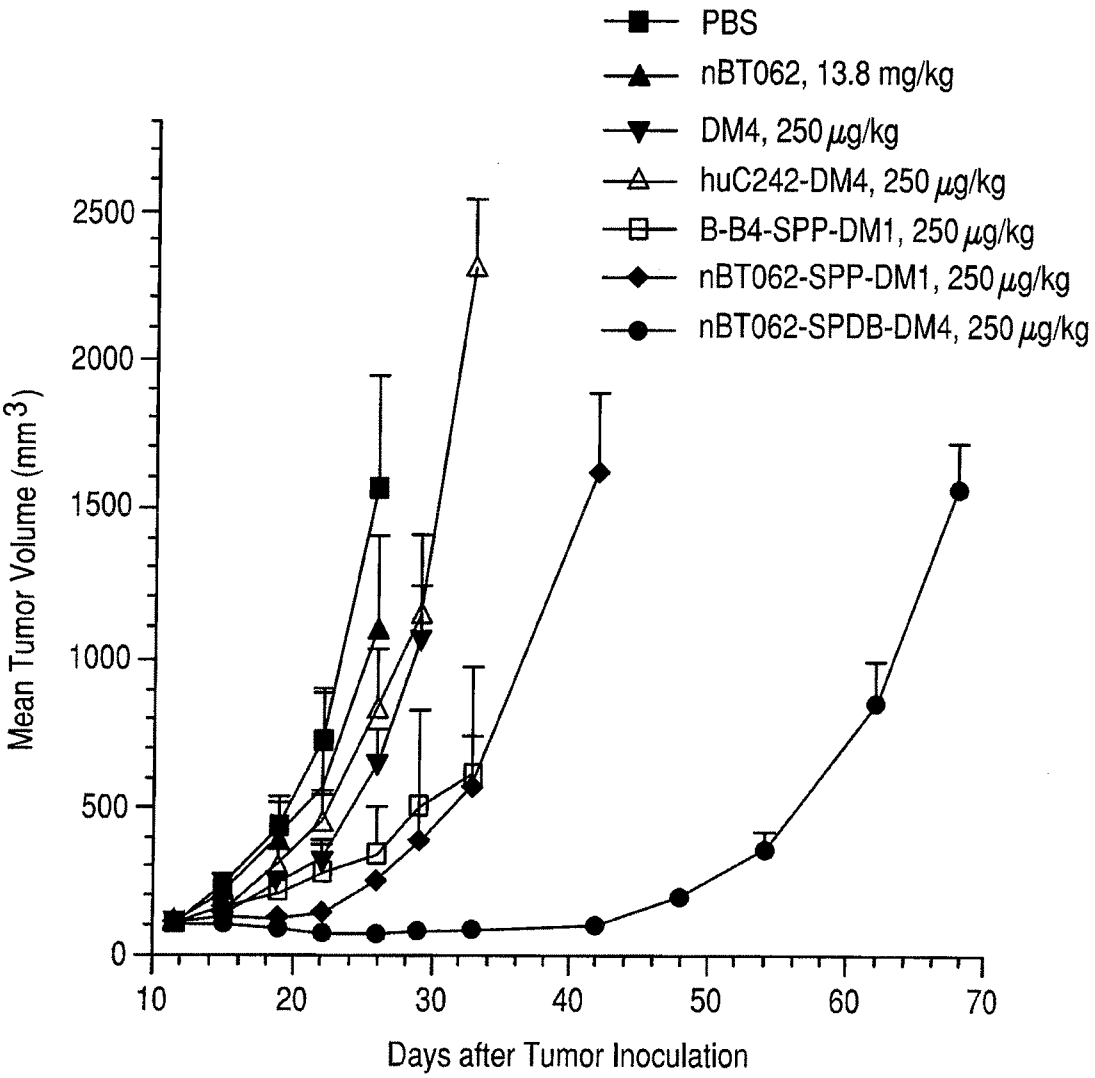

PBS
nBT062, 13.8 mg/kg
DM4, 250 μg/kg
huC242-DM4, 250 μg/kg
B-B4-SPP-DM1, 250 μg/kg
nBT062-SPP-DM1, 250 μg/kg
nBT062-SPDB-DM4, 250 μg/kg
Mean Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
20
30
40
50
60
70
Days after Tumor Inoculation

FIG. 10

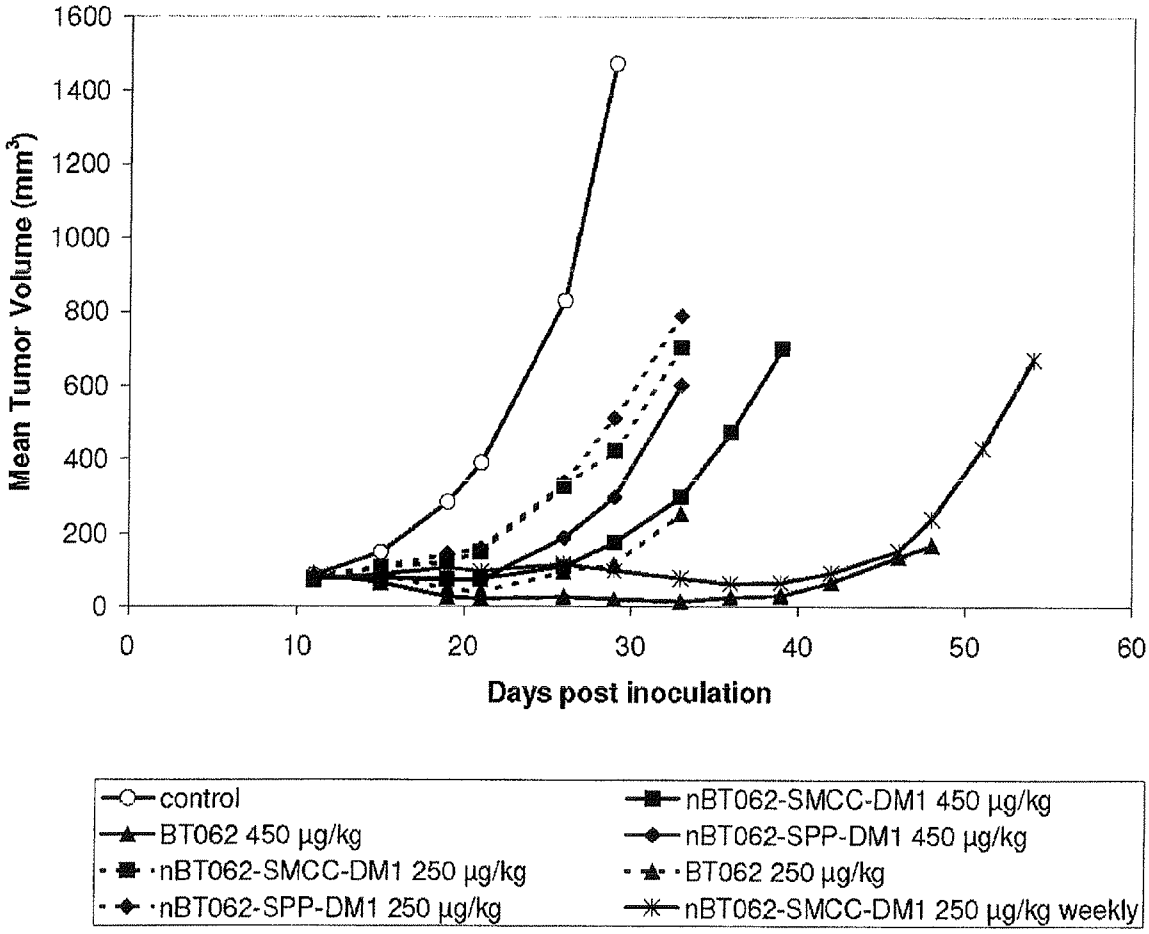

1600
1400
1200
1000
800
600
400
200
0
Mean Tumor Volume (mm3)
0
10
20
30
40
50
60
Days post inoculation
control
BT062 450 µg/kg
nBT062-SMCC-DM1 250 µg/kg
nBT062-SPP-DM1 250 µg/kg
nBT062-SMCC-DM1 450 µg/kg
nBT062-SPP-DM1 450 µg/kg
BT062 250 µg/kg
nBT062-SMCC-DM1 250 µg/kg weekly

FIG. 11A

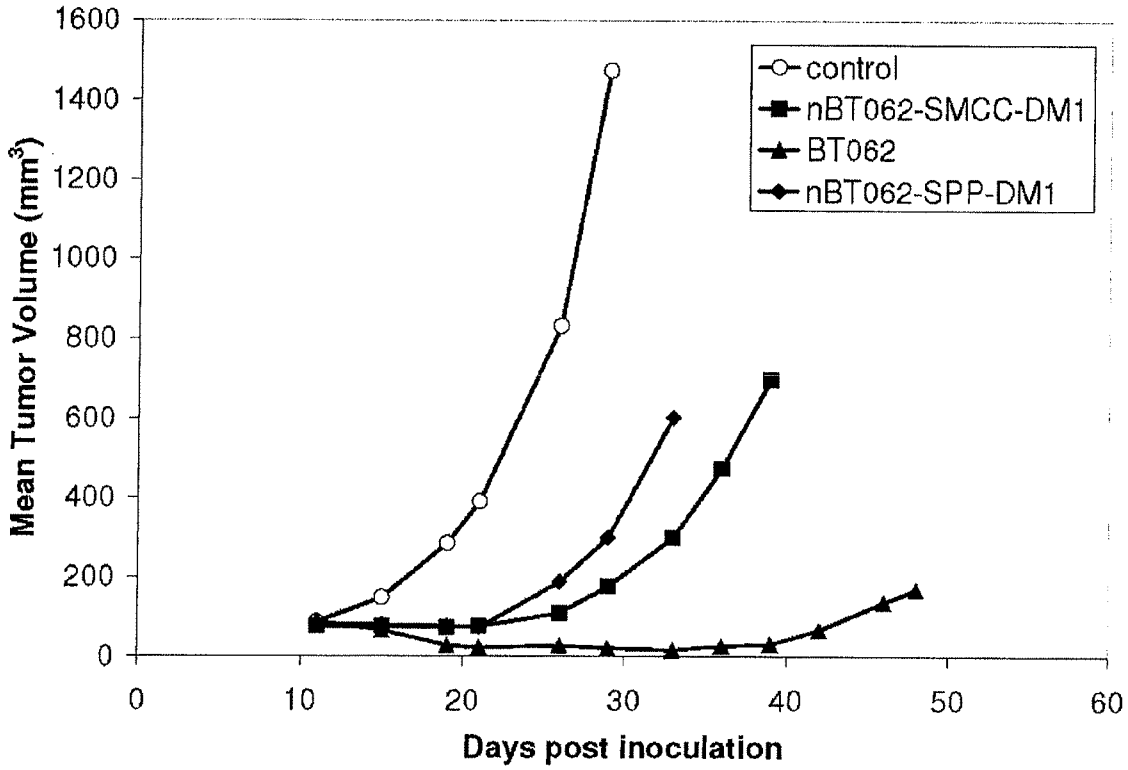

1600
1400
1200
1000
800
600
400
200
0
Mean Tumor Volume (mm3)
0
10
20
30
40
50
60
Days post inoculation
control
nBT062-SMCC-DM1
BT062
nBT062-SPP-DM1

FIG. 11B

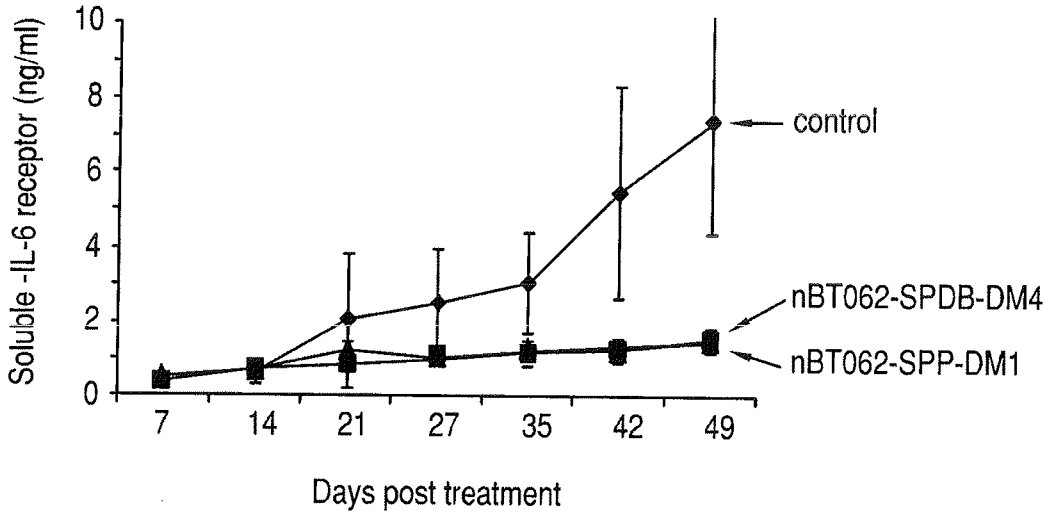

Soluble -IL-6 receptor (ng/ml)
10
8
6
4
2
0
7
14
21
27
35
42
49
Days post treatment
control
nBT062-SPDB-DM4
nBT062-SPP-DM1

FIG. 12

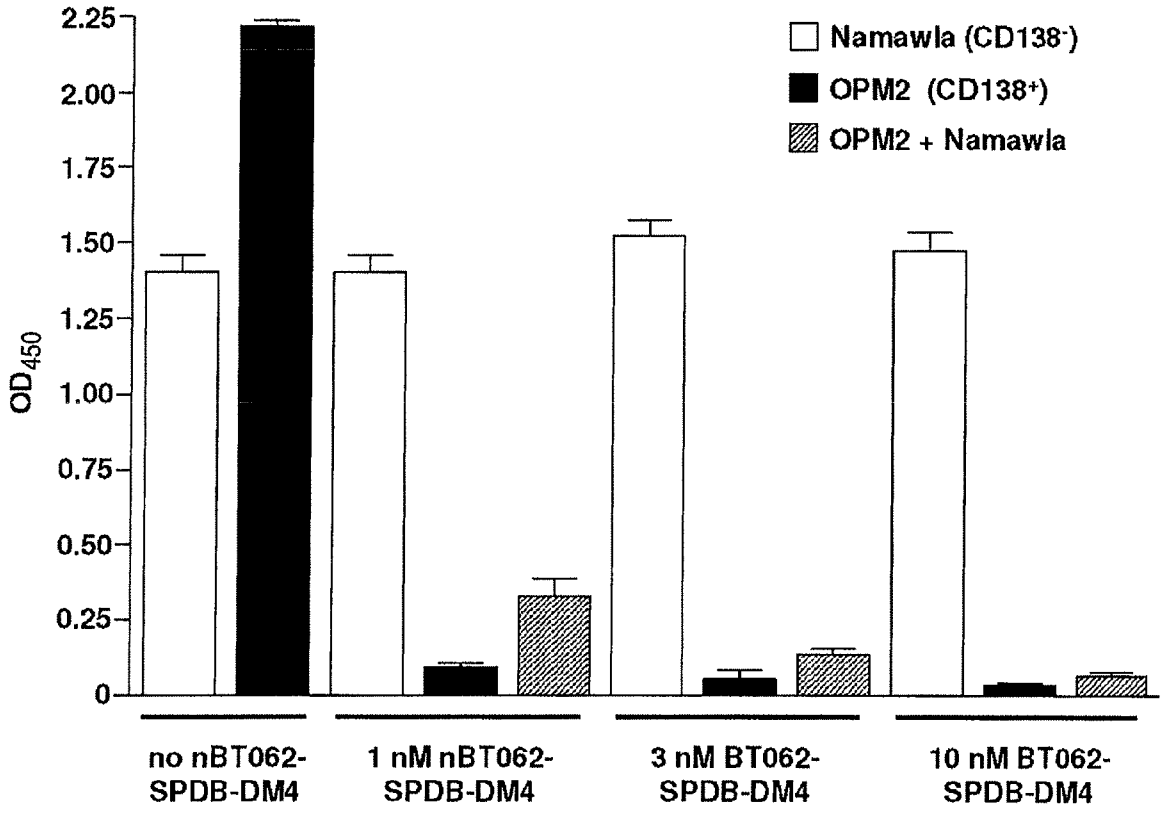

2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0
OD450
Namawla (CD138-)
OPM2 (CD138+)
OPM2 + Namawla
no nBT062-SPDB-DM4
1 nM nBT062-SPDB-DM4
3 nM BT062-SPDB-DM4
10 nM BT062-SPDB-DM4

FIG. 13

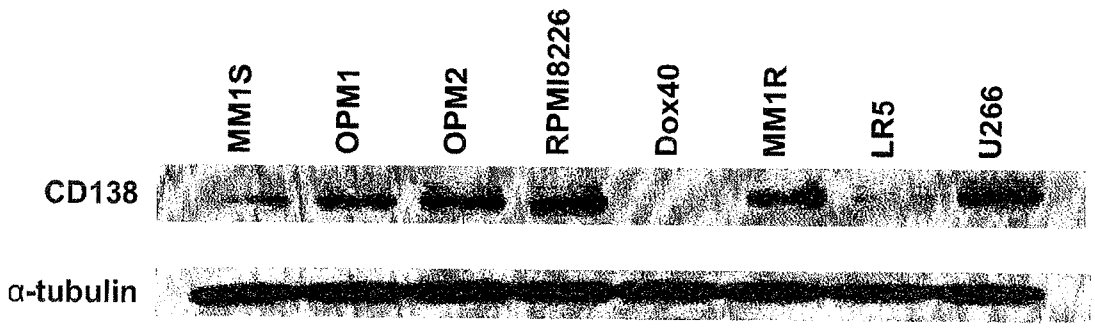


Fig. 14A

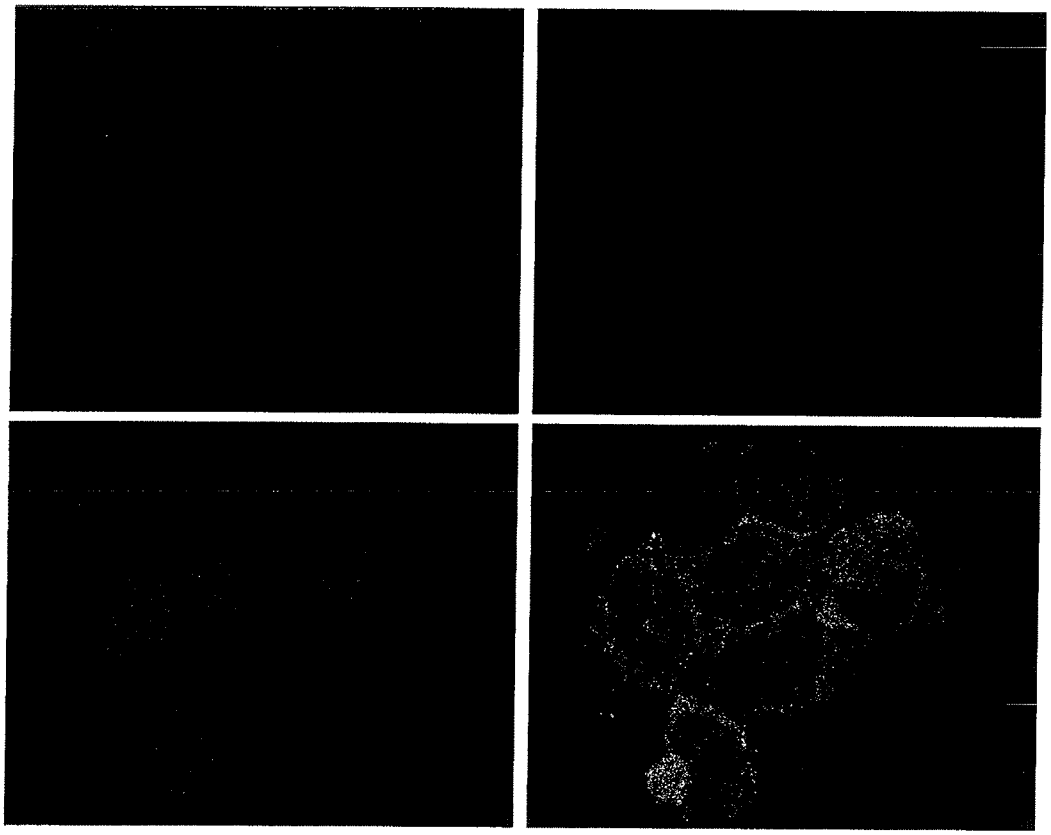


Fig. 14B

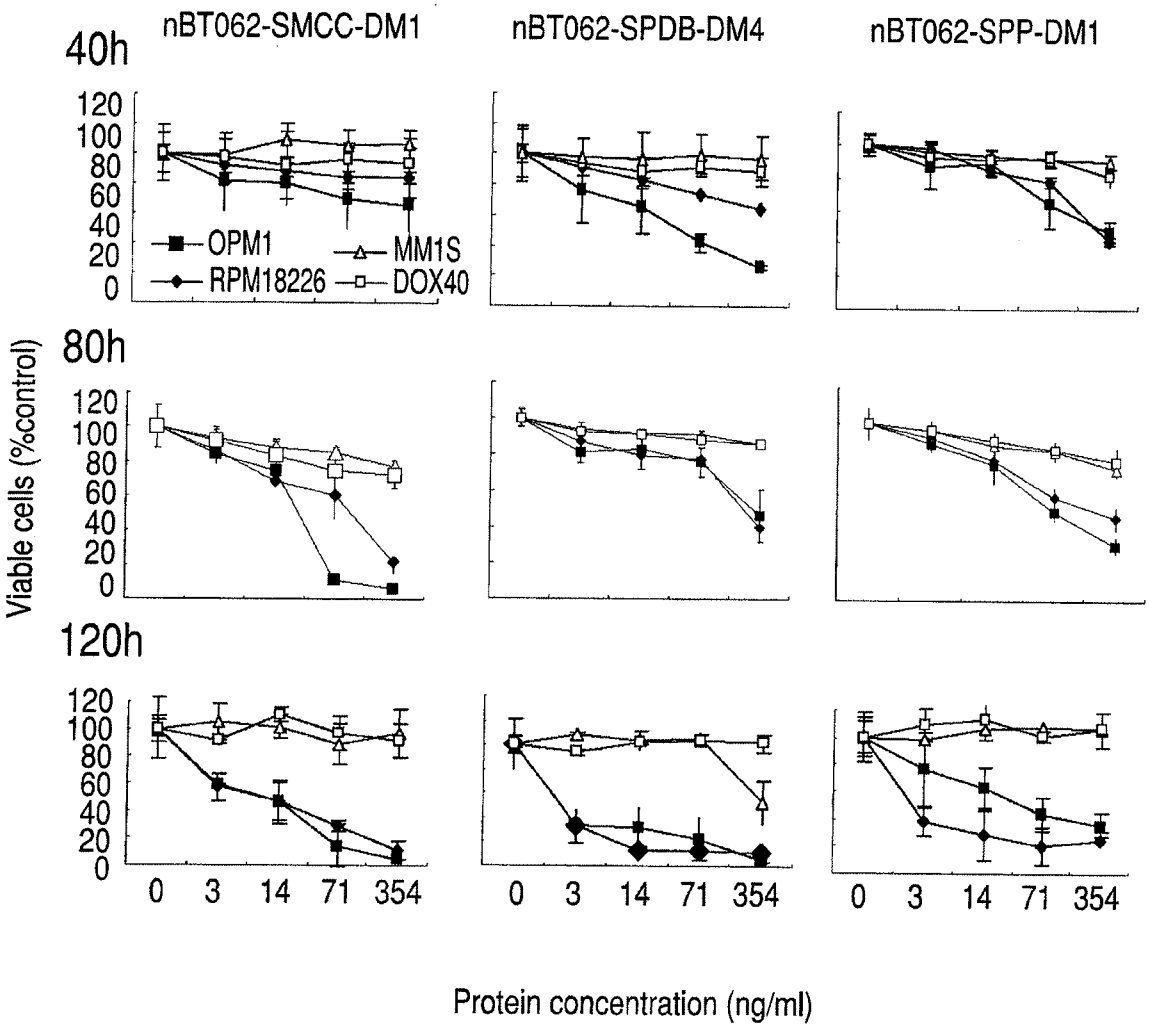

nBT062-SMCC-DM1
nBT062-SPDB-DM4
nBT062-SPP-DM1
40h
80h
120h
Viable cells (%control)
120
100
80
60
40
20
0
OPM1
MM1S
RPM18226
DOX40
0 3 14 71 354
Protein concentration (ng/ml)

Fig. 15A

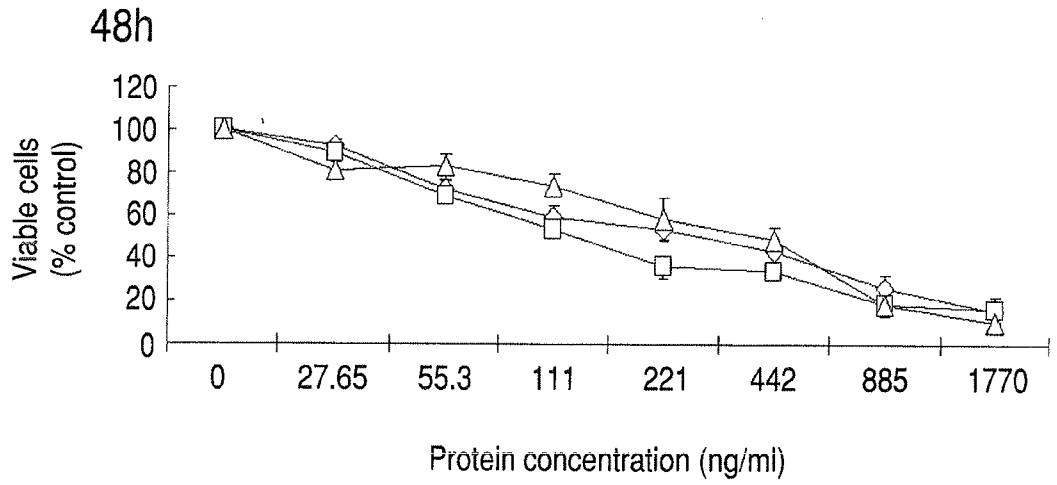


Fig. 15B

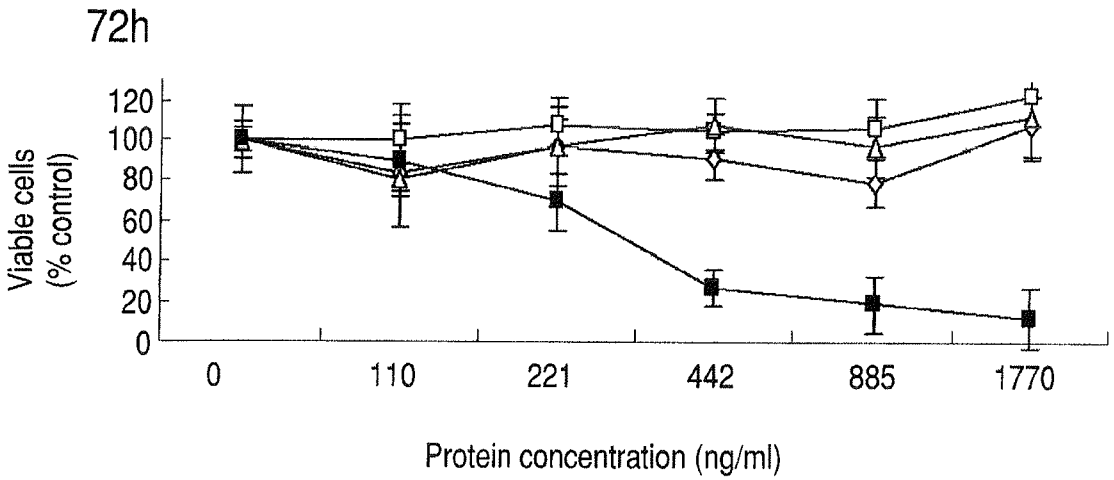
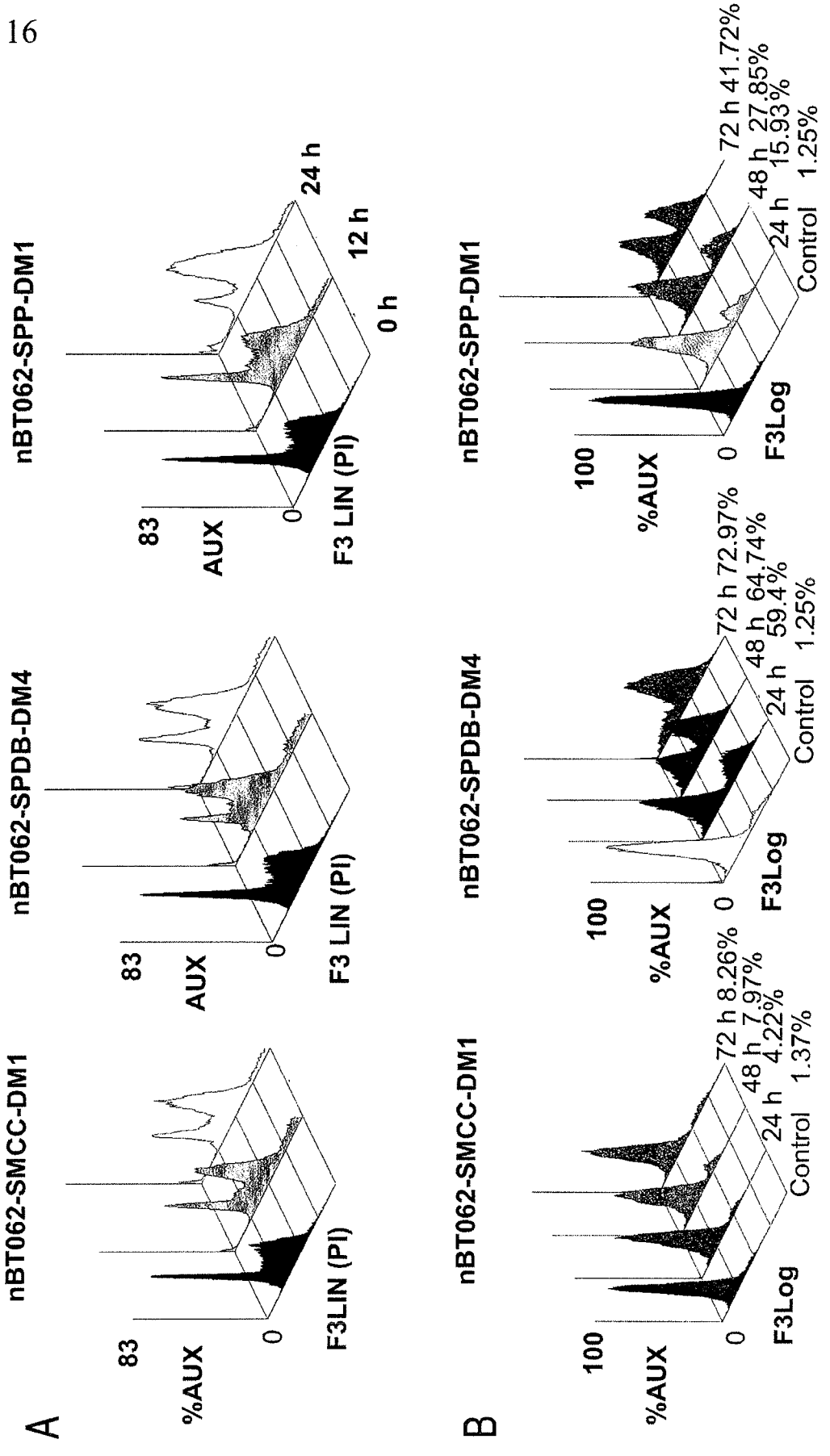


Fig. 15C

Fig. 16


A
nBT062-SMCC-DM1
%AUX
83
0
F3LIN (PI)
nBT062-SPDB-DM4
AUX
83
0
F3 LIN (PI)
nBT062-SPP-DM1
AUX
83
0
F3 LIN (PI)
0 h
12 h
24 h
B
nBT062-SMCC-DM1
%AUX
100
0
F3Log
Control 1.37%
24 h 4.22%
48 h 7.97%
72 h 8.26%
nBT062-SPDB-DM4
%AUX
100
0
F3Log
Control 1.25%
24 h 59.4%
48 h 64.74%
72 h 72.97%
nBT062-SPP-DM1
%AUX
100
0
F3Log
Control 1.25%
24 h 15.93%
48 h 27.85%
72 h 41.72%

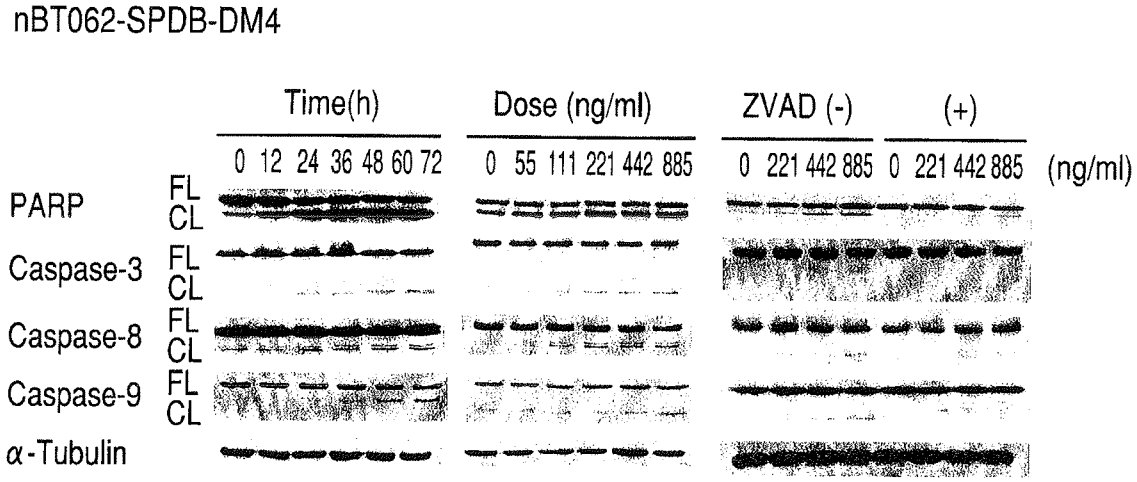
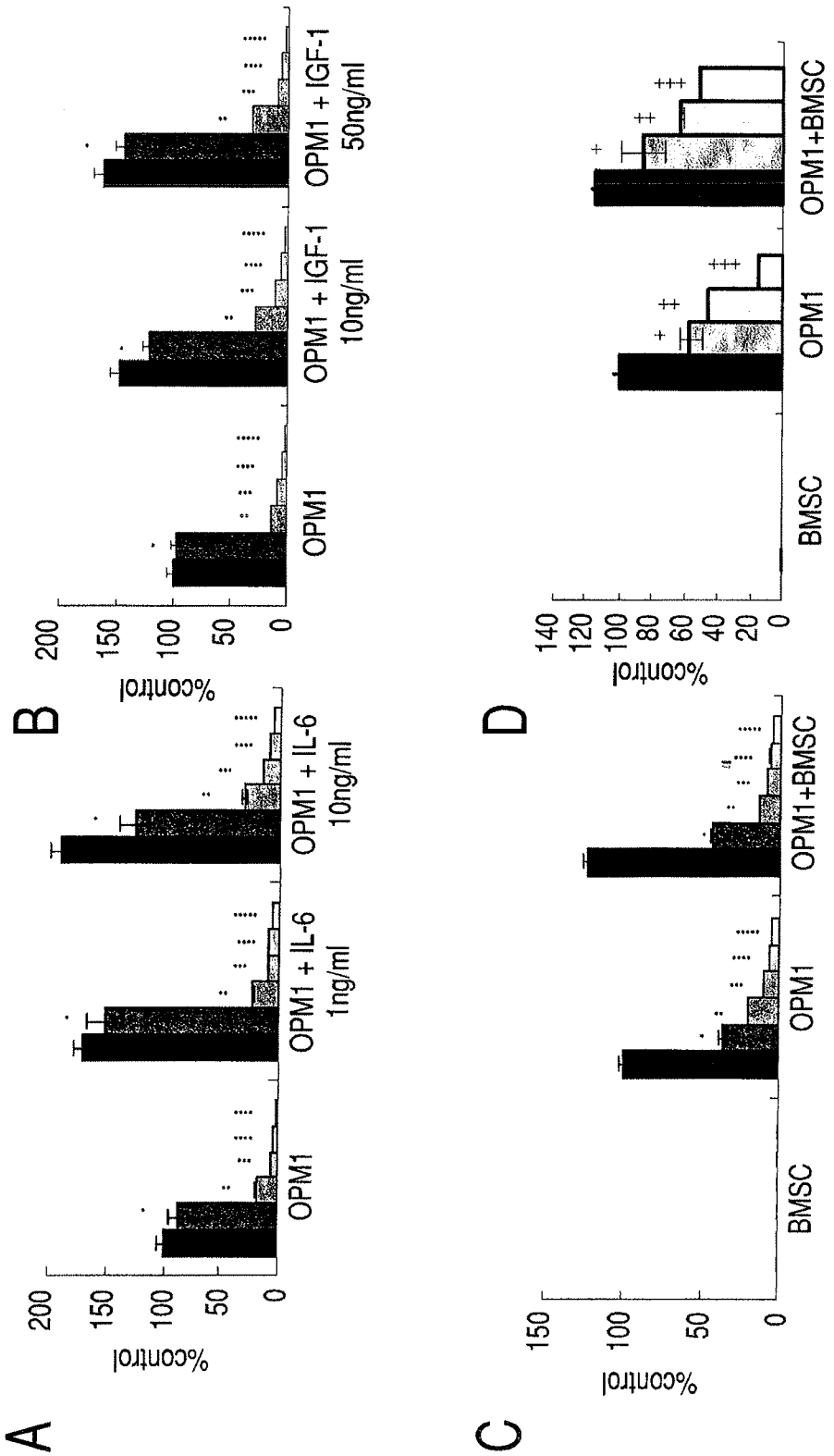

nBT062-SPDB-DM4
Time(h)
Dose (ng/ml)
ZVAD (-)
(+)
0 12 24 36 48 60 72
0 55 111 221 442 885
0 221 442 885
0 221 442 885
(ng/ml)
PARP
FL
CL
Caspase-3
FL
CL
Caspase-8
FL
CL
Caspase-9
FL
CL
α-Tubulin

Fig. 16C

FIG. 17


A
%control
200
150
100
50
0
OPM1
OPM1 + IL-6 1ng/ml
OPM1 + IL-6 10ng/ml
B
%control
200
150
100
50
0
OPM1
OPM1 + IGF-1 10ng/ml
OPM1 + IGF-1 50ng/ml
C
%control
150
100
50
0
BMSC
OPM1
OPM1+BMSC
D
%control
140
120
100
80
60
40
20
0
BMSC
OPM1
OPM1+BMSC
+
++
+++

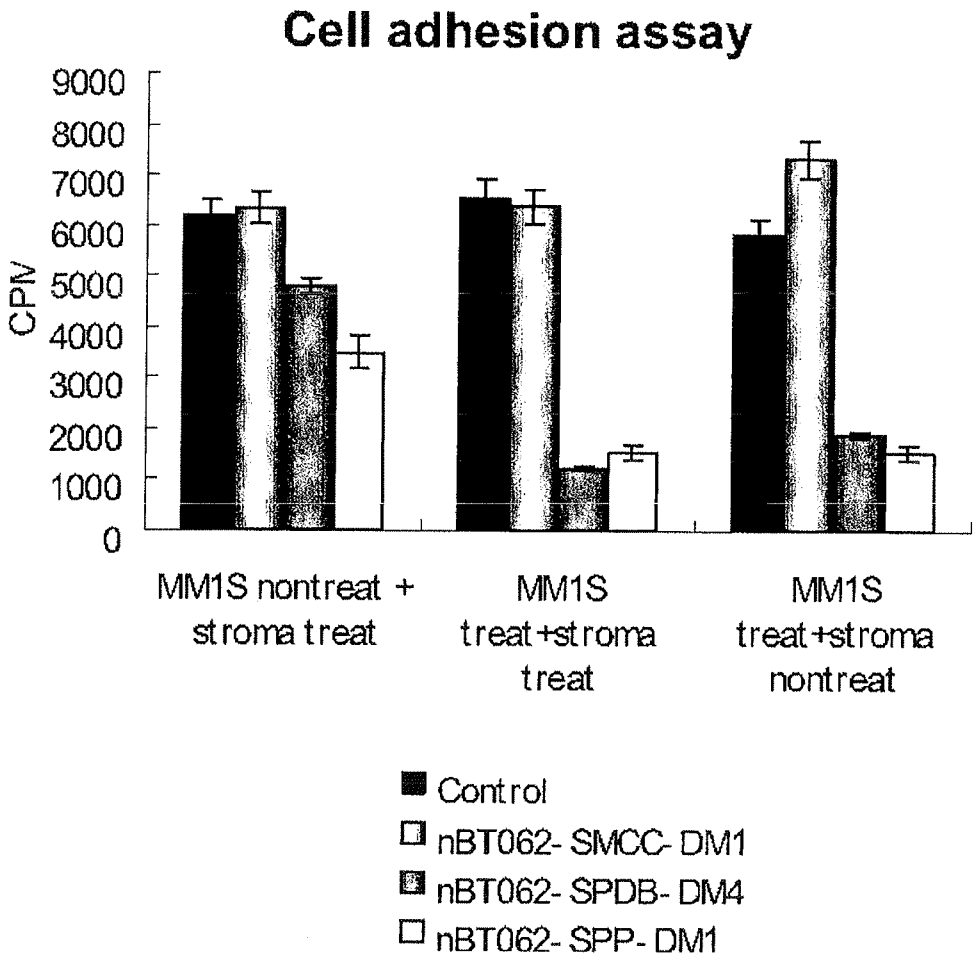

Cell adhesion assay
CPM
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
MM1S nontreat + stroma treat
MM1S treat+stroma treat
MM1S treat+stroma nontreat
Control
nBT062- SMCC- DM1
nBT062- SPDB- DM4
nBT062- SPP- DM1

Fig. 17E

Fig. 18A

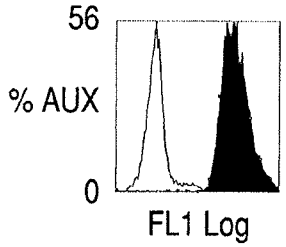


Fig. 18B

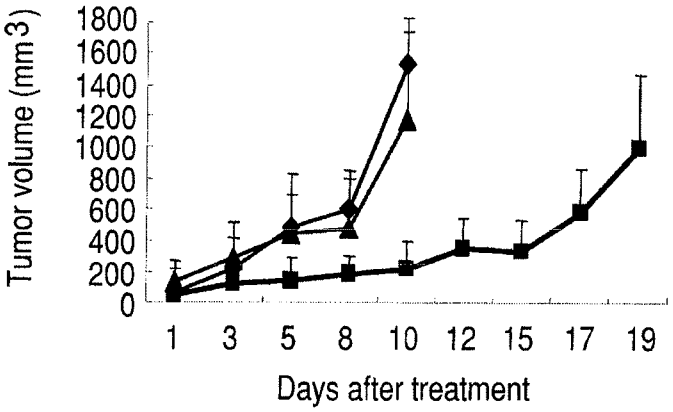


Fig. 18C

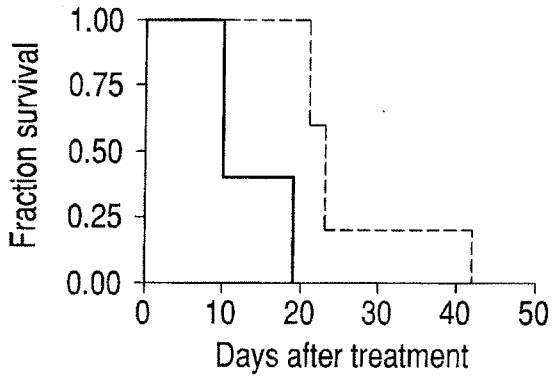


Fig. 18D

