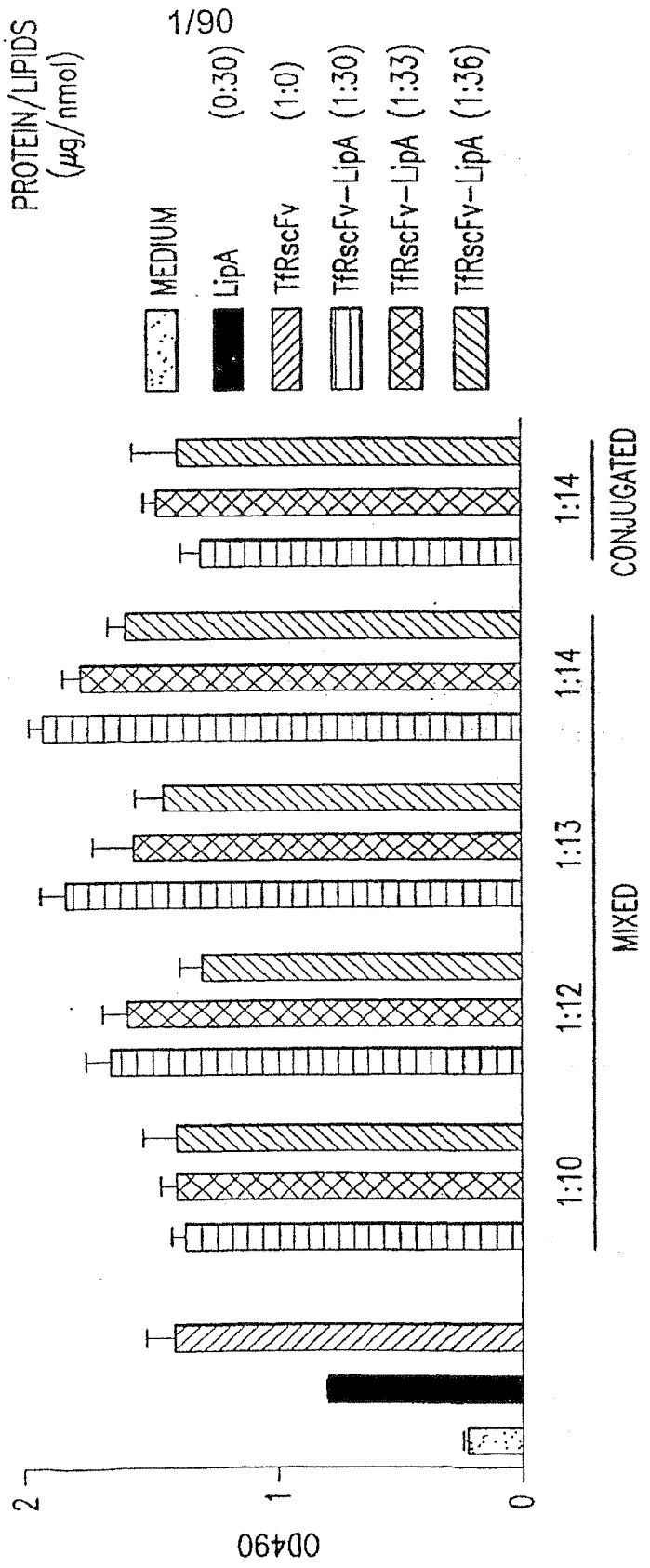

PROTEIN/LIPIDS
(μg/nmol)
1/90
MEDIUM
LipA (0:30)
TfRscFv (1:0)
TfRscFv–LipA (1:30)
TfRscFv–LipA (1:33)
TfRscFv–LipA (1:36)
OD490
2
1
0
1:10
1:12
1:13
1:14
MIXED
1:14
CONJUGATED
DNA/LIPID RATIO (μg/nmol)

FIG. 1

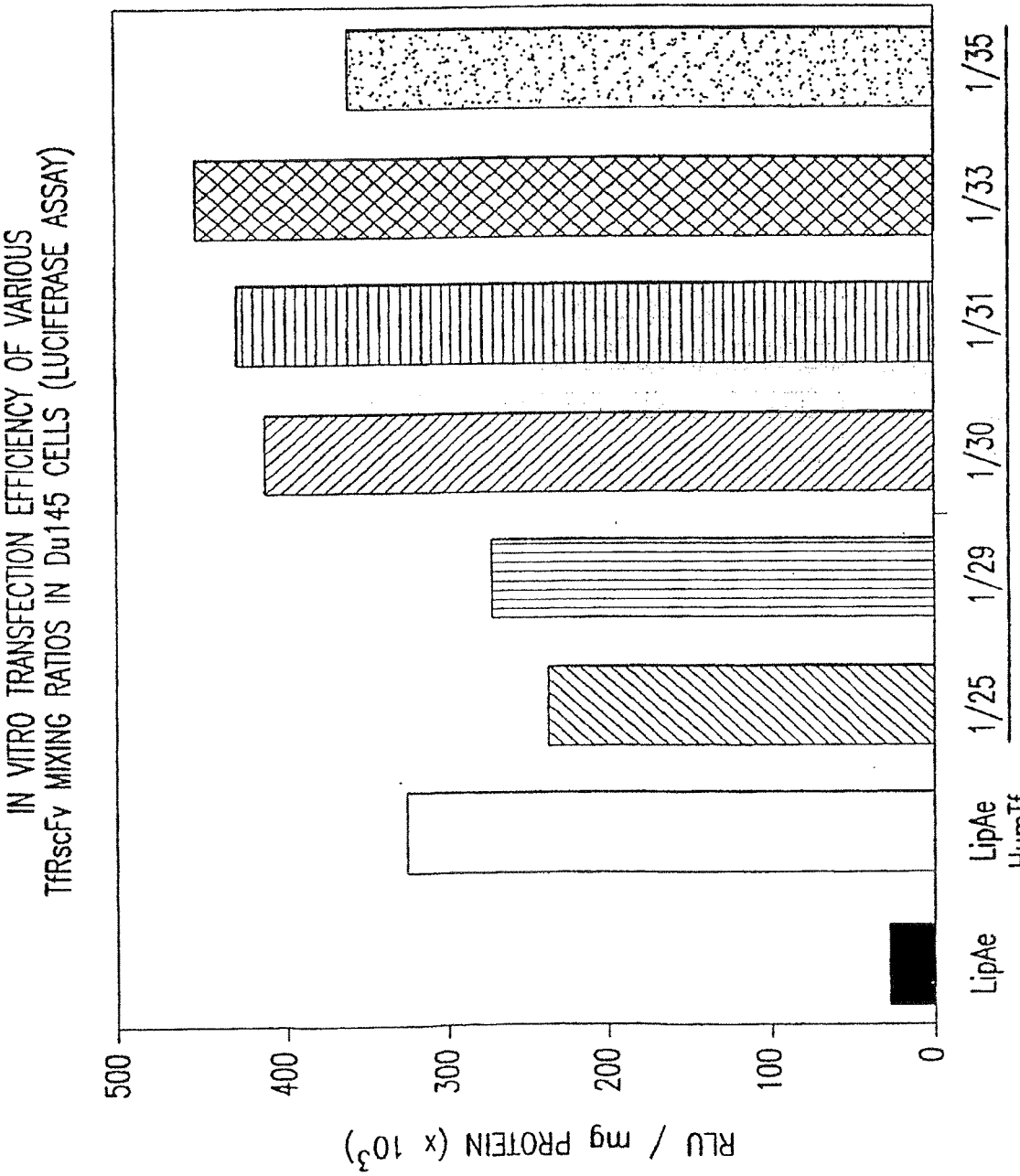

IN VITRO TRANSFECTION EFFICIENCY OF VARIOUS
TfRscFv MIXING RATIOS IN Du145 CELLS (LUCIFERASE ASSAY)
RLU / mg PROTEIN (x 10³)
500
400
300
200
100
0
LipAe
LipAe
HumTf
1/25
1/29
1/30
1/31
1/33
1/35
TfRscFv:Lipid

FIG.2

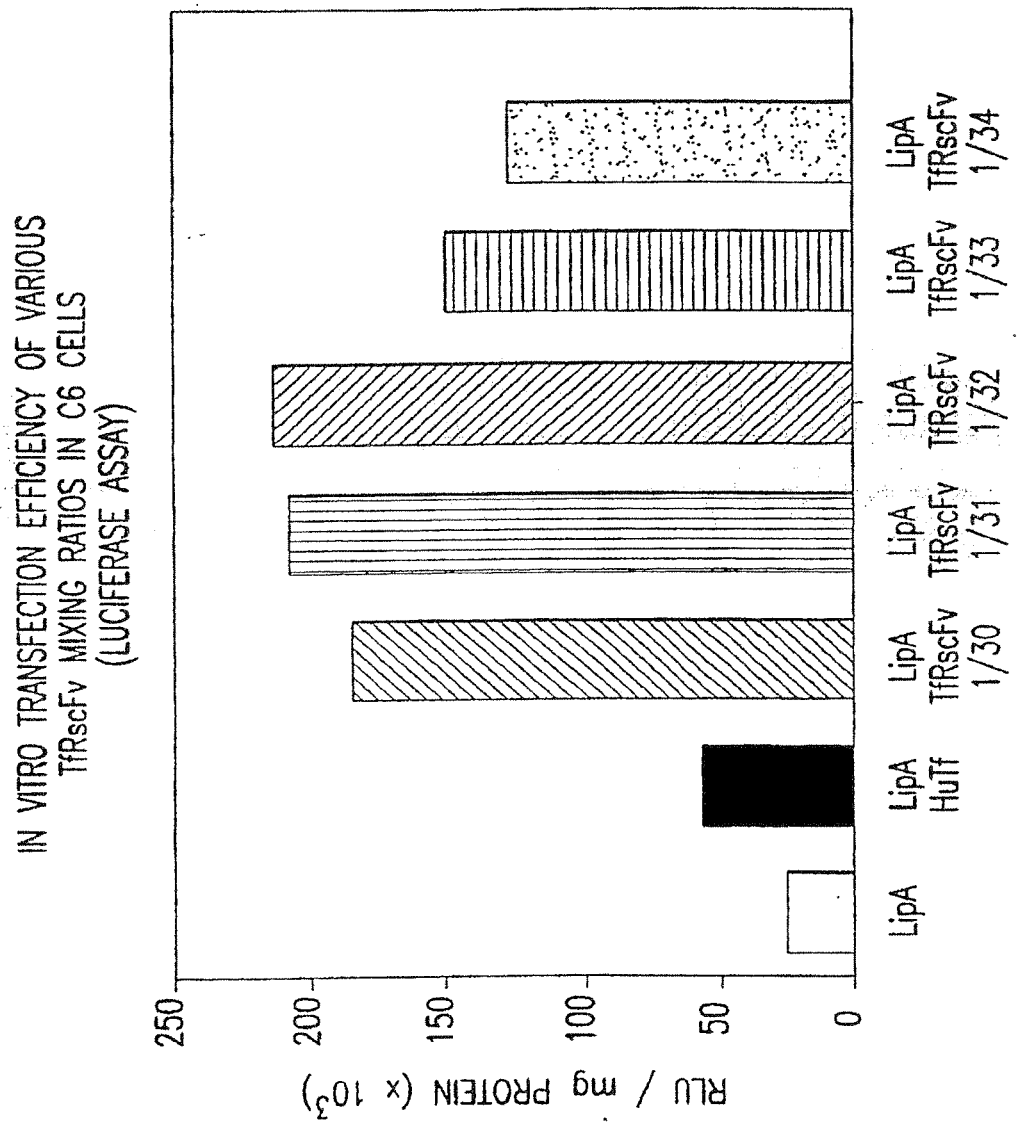

IN VITRO TRANSFECTION EFFICIENCY OF VARIOUS TfRscFv MIXING RATIOS IN C6 CELLS (LUCIFERASE ASSAY)
RLU / mg PROTEIN (x 10³)
250
200
150
100
50
0
LipA
LipA HuTf
LipA TfRscFv 1/30
LipA TfRscFv 1/31
LipA TfRscFv 1/32
LipA TfRscFv 1/33
LipA TfRscFv 1/34

FIG.3

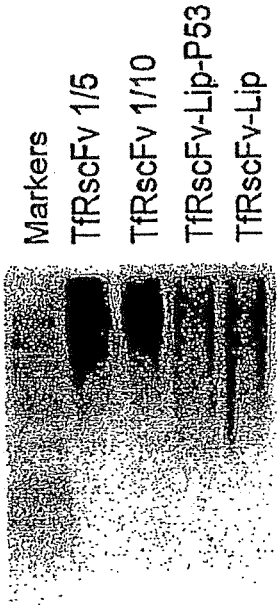


FIG.4

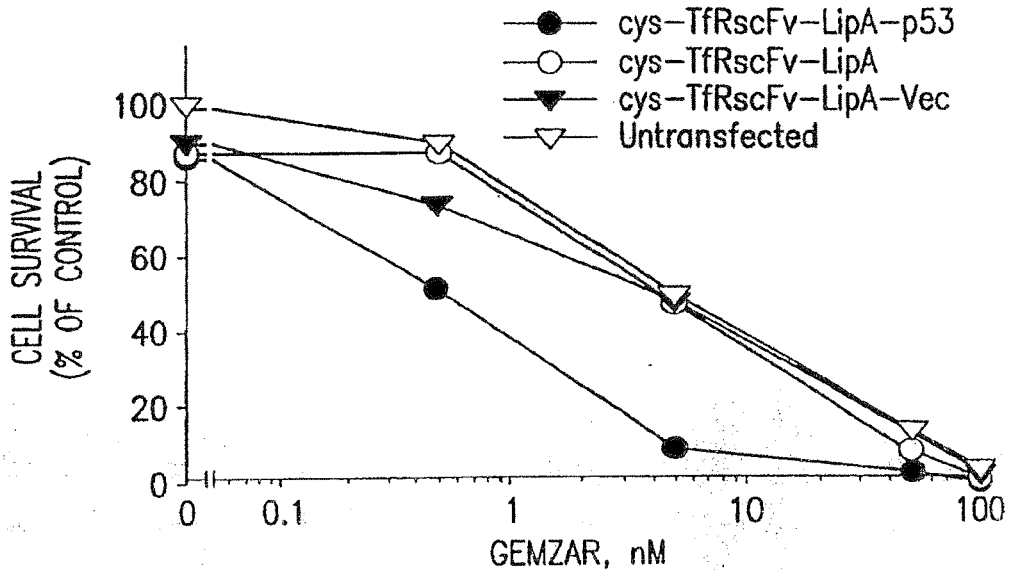

cys–TfRscFv–LipA–p53
cys–TfRscFv–LipA
cys–TfRscFv–LipA–Vec
Untransfected
CELL SURVIVAL (% OF CONTROL)
100
80
60
40
20
0
0
0.1
1
10
100
GEMZAR, nM

FIG.5A

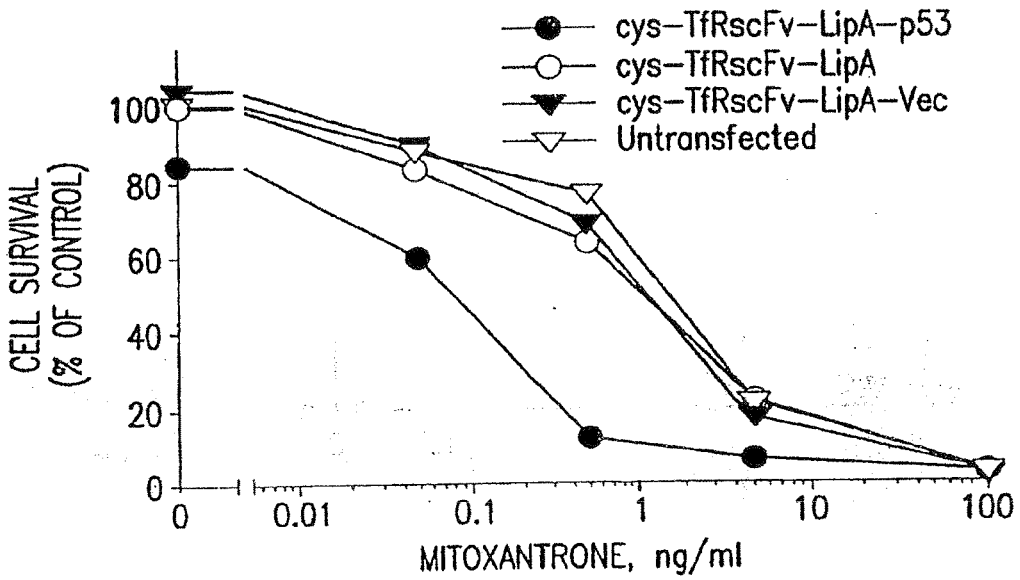

cys–TfRscFv–LipA–p53
cys–TfRscFv–LipA
cys–TfRscFv–LipA–Vec
Untransfected
CELL SURVIVAL (% OF CONTROL)
100
80
60
40
20
0
0
0.01
0.1
1
10
100
MITOXANTRONE, ng/ml

FIG.5B

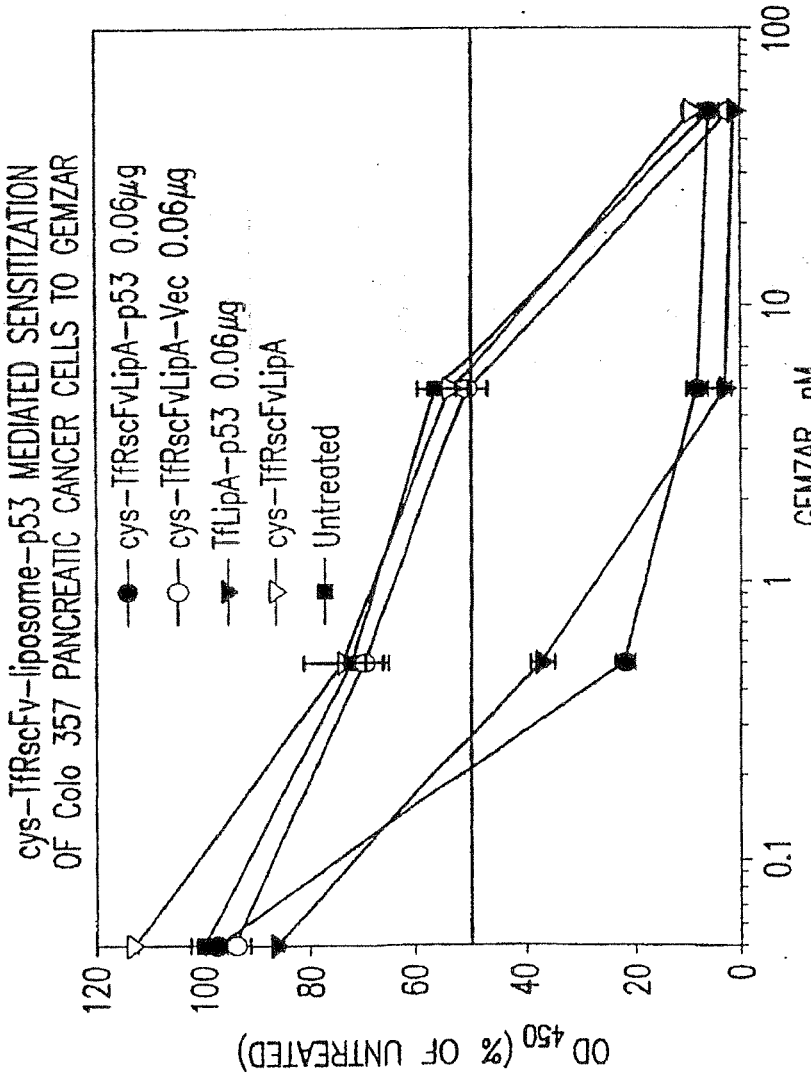

cys-TfRscFv-liposome-p53 MEDIATED SENSITIZATION
OF Colo 357 PANCREATIC CANCER CELLS TO GEMZAR
cys-TfRscFvLipA-p53 0.06μg
cys-TfRscFvLipA-Vec 0.06μg
TfLipA-p53 0.06μg
cys-TfRscFvLipA
Untreated
OD 450 (% OF UNTREATED)
GEMZAR, nM
0
20
40
60
80
100
120
0.1
1
10
100

FIG.6A

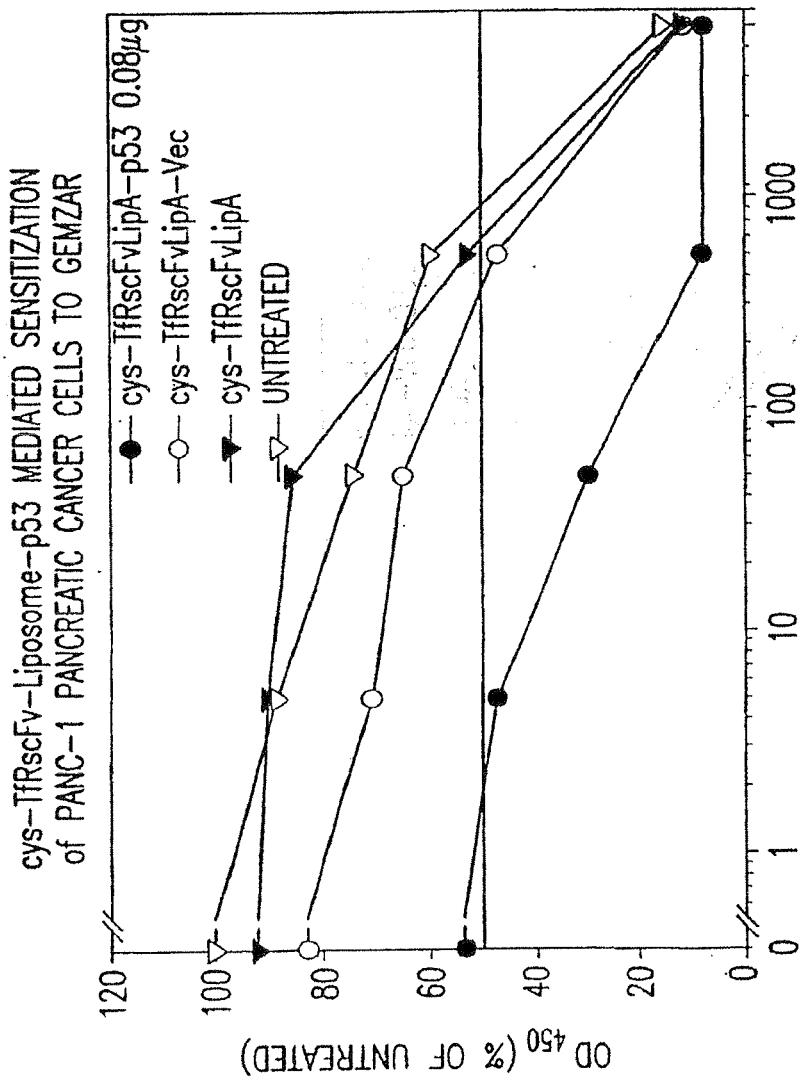

cys-TfRscFv-Liposome-p53 MEDIATED SENSITIZATION
of PANC-1 PANCREATIC CANCER CELLS TO GEMZAR
cys-TfRscFvLipA-p53 0.08μg
cys-TfRscFvLipA-Vec
cys-TfRscFvLipA
UNTREATED
OD 450 (% OF UNTREATED)
GEMZAR, nM
0
20
40
60
80
100
120
0
1
10
100
1000

FIG.6B

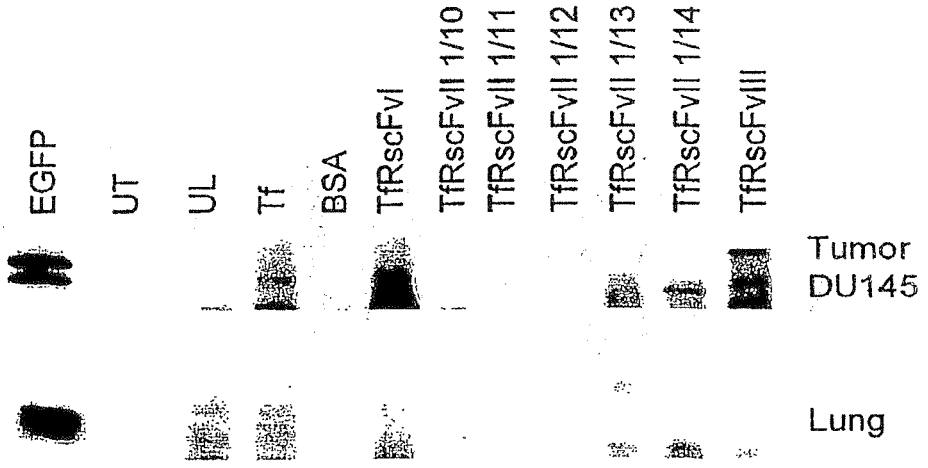

EGFP
UT
UL
Tf
BSA
TfRscFvI
TfRscFvII 1/10
TfRscFvII 1/11
TfRscFvII 1/12
TfRscFvII 1/13
TfRscFvII 1/14
TfRscFvIII
Tumor
DU145
Lung

FIG.7A

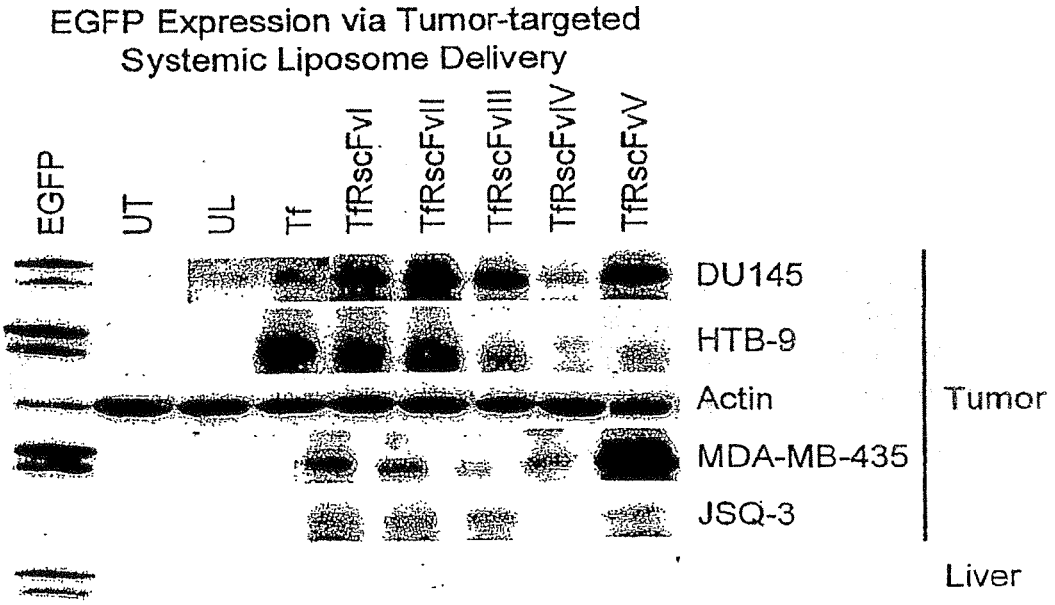

EGFP Expression via Tumor-targeted
Systemic Liposome Delivery
EGFP
UT
UL
Tf
TfRscFvI
TfRscFvII
TfRscFvIII
TfRscFvIV
TfRscFvV
DU145
HTB-9
Actin
MDA-MB-435
JSQ-3
Tumor
Liver

FIG.7B

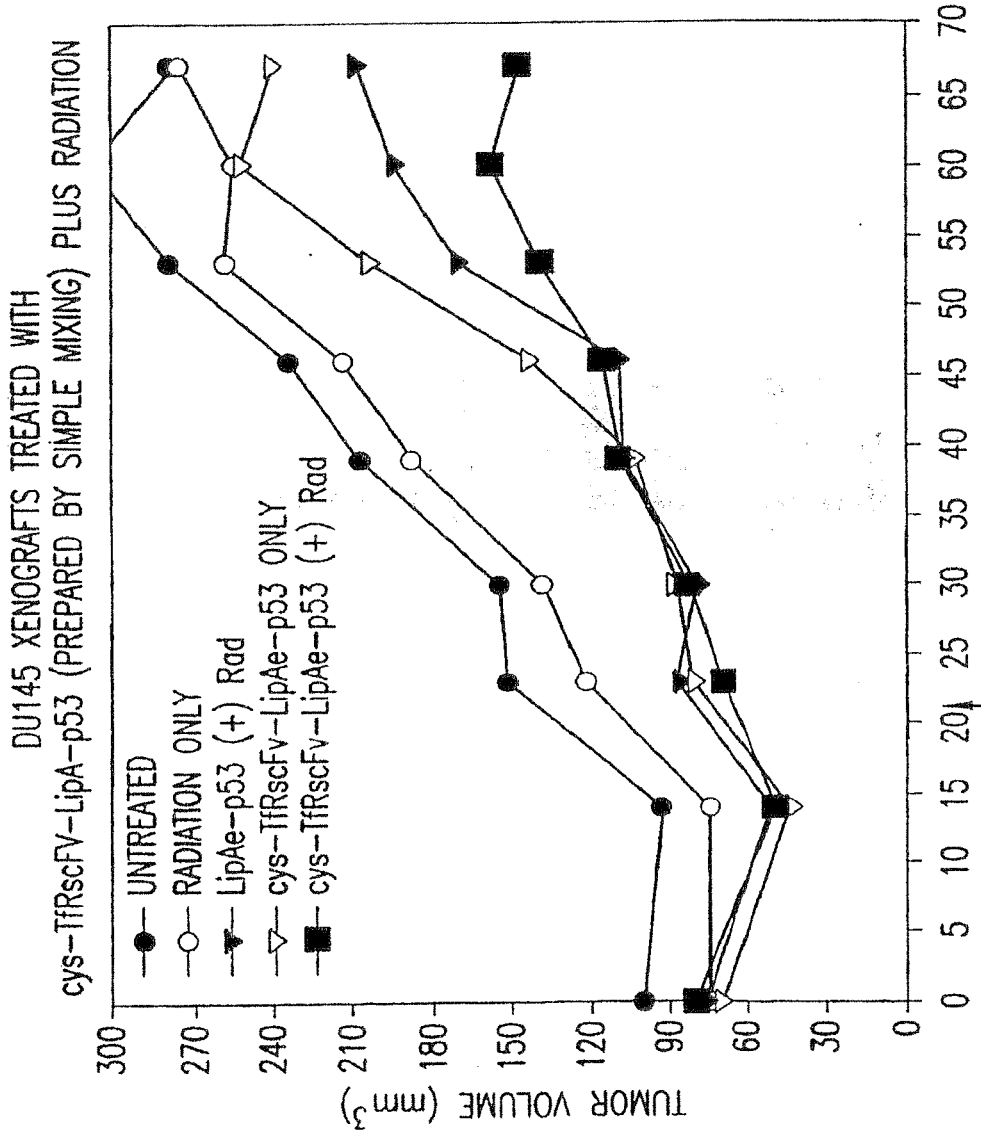

DU145 XENOGRAFTS TREATED WITH
cys-TfRscFv-LipA-p53 (PREPARED BY SIMPLE MIXING) PLUS RADIATION
UNTREATED
RADIATION ONLY
LipAe-p53 (+) Rad
cys-TfRscFv-LipAe-p53 ONLY
cys-TfRscFv-LipAe-p53 (+) Rad
TUMOR VOLUME (mm3)
300
270
240
210
180
150
120
90
60
30
0
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70
DAYS
DAY 21
END TREATMENT
10 IV
32 Gy

FIG.8

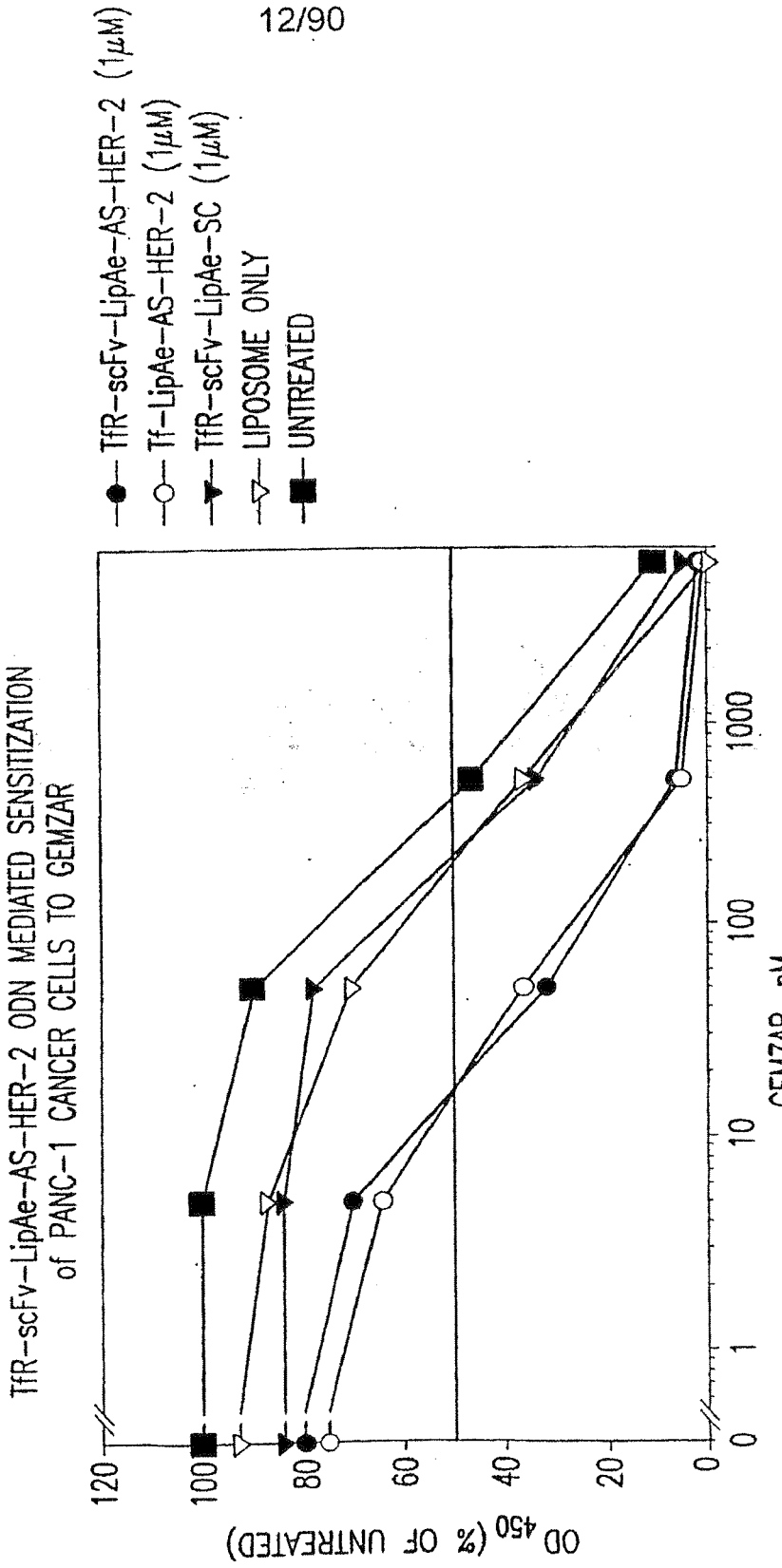

TfR-scFv-LipAe-AS-HER-2 ODN MEDIATED SENSITIZATION
of PANC-1 CANCER CELLS TO GEMZAR
TfR-scFv-LipAe-AS-HER-2 (1μM)
Tf-LipAe-AS-HER-2 (1μM)
TfR-scFv-LipAe-SC (1μM)
LIPOSOME ONLY
UNTREATED
OD 450 (% OF UNTREATED)
120
100
80
60
40
20
0
0
1
10
100
1000
GEMZAR, nM

FIG.9

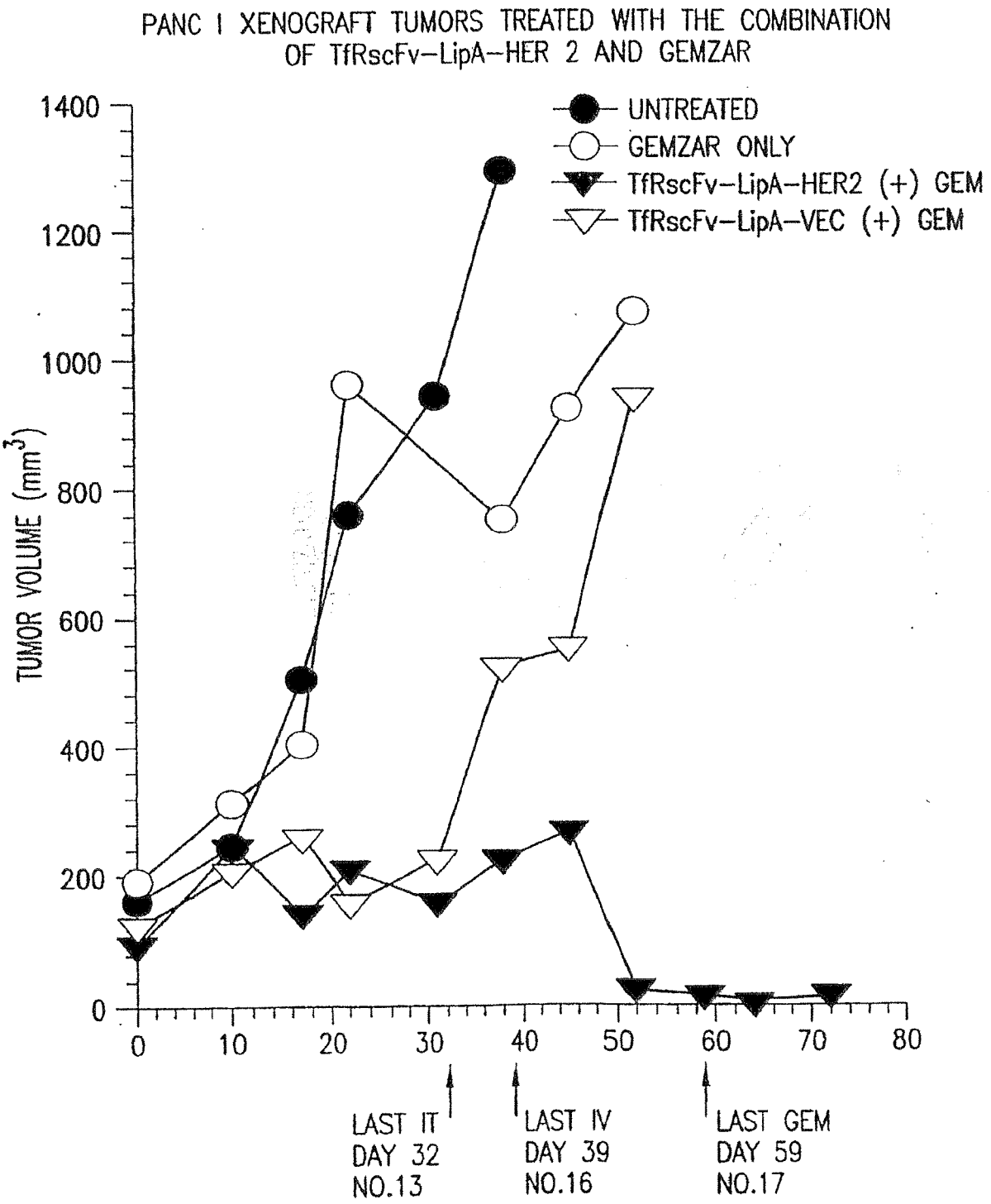

PANC I XENOGRAFT TUMORS TREATED WITH THE COMBINATION OF TfRscFv–LipA–HER 2 AND GEMZAR
UNTREATED
GEMZAR ONLY
TfRscFv–LipA–HER2 (+) GEM
TfRscFv–LipA–VEC (+) GEM
TUMOR VOLUME (mm3)
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50
60
70
80
LAST IT
DAY 32
NO.13
LAST IV
DAY 39
NO.16
LAST GEM
DAY 59
NO.17

FIG.10A

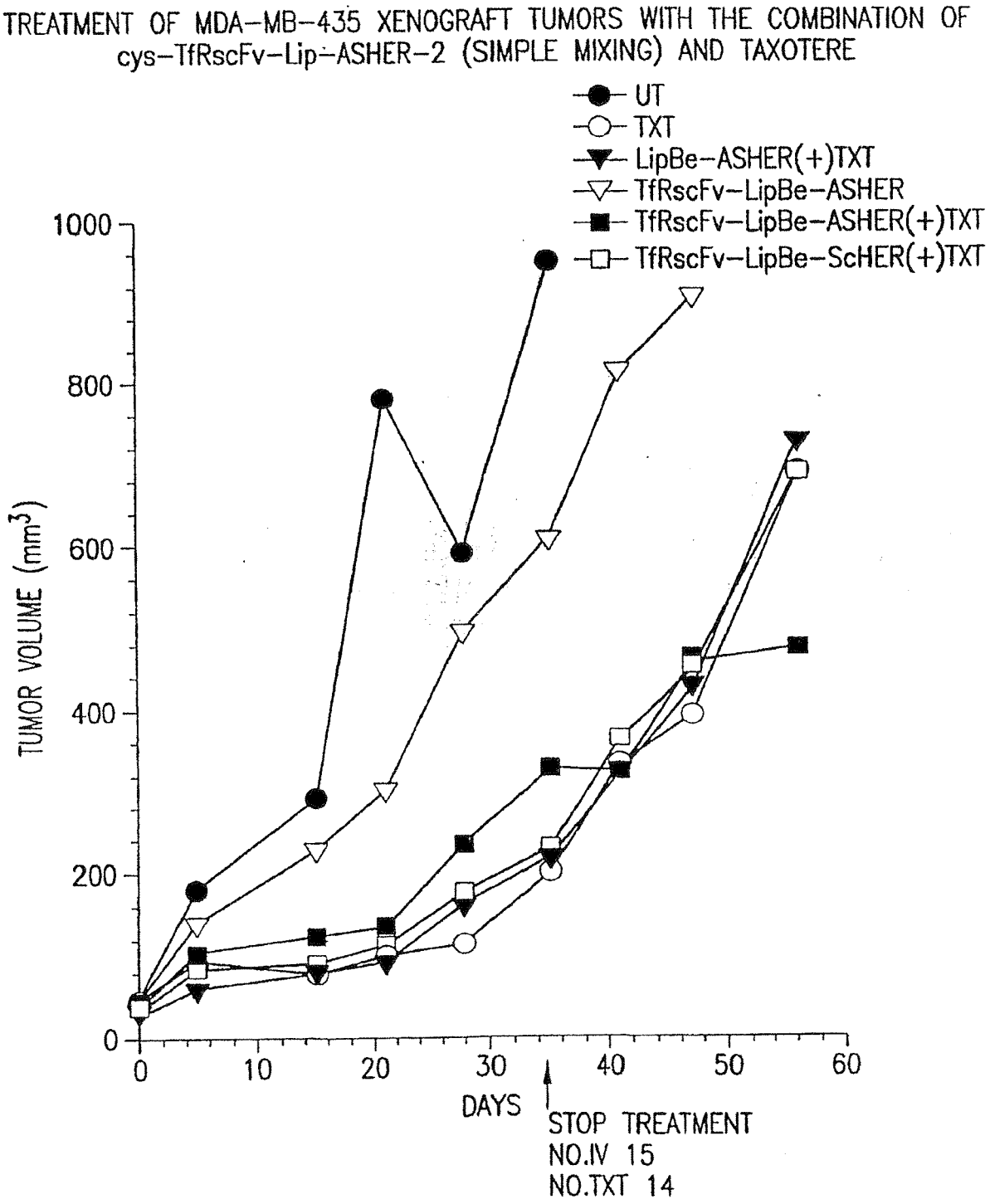

TREATMENT OF MDA-MB-435 XENOGRAFT TUMORS WITH THE COMBINATION OF cys-TfRscFv-Lip-ASHER-2 (SIMPLE MIXING) AND TAXOTERE
UT
TXT
LipBe-ASHER(+)TXT
TfRscFv-LipBe-ASHER
TfRscFv-LipBe-ASHER(+)TXT
TfRscFv-LipBe-ScHER(+)TXT
TUMOR VOLUME (mm3)
1000
800
600
400
200
0
0
10
20
30
40
50
60
DAYS
STOP TREATMENT
NO.IV 15
NO.TXT 14

FIG.10B

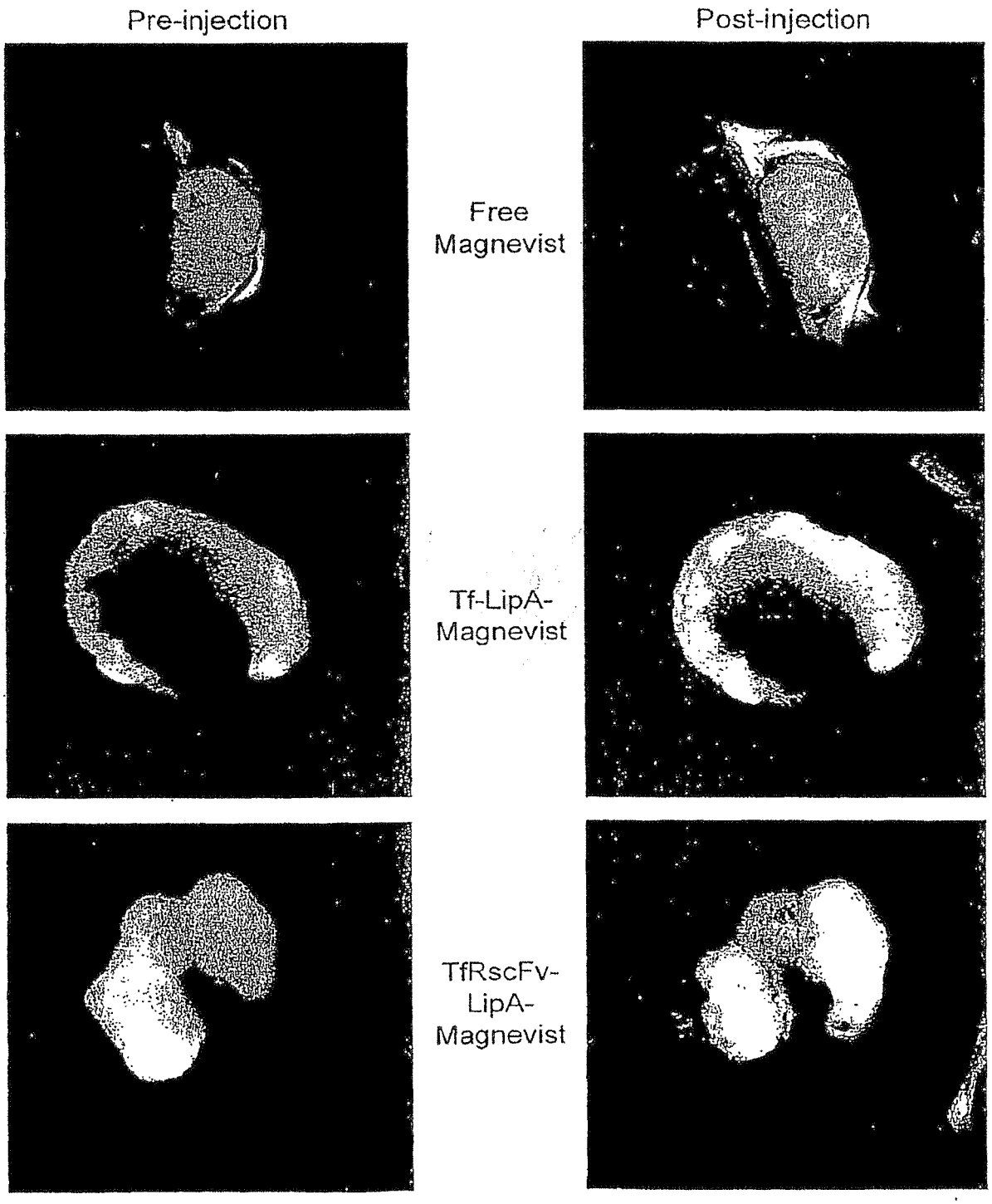

Pre-injection
Post-injection
Free Magnevist
Tf-LipA-Magnevist
TfRscFv-LipA-Magnevist

FIG.11

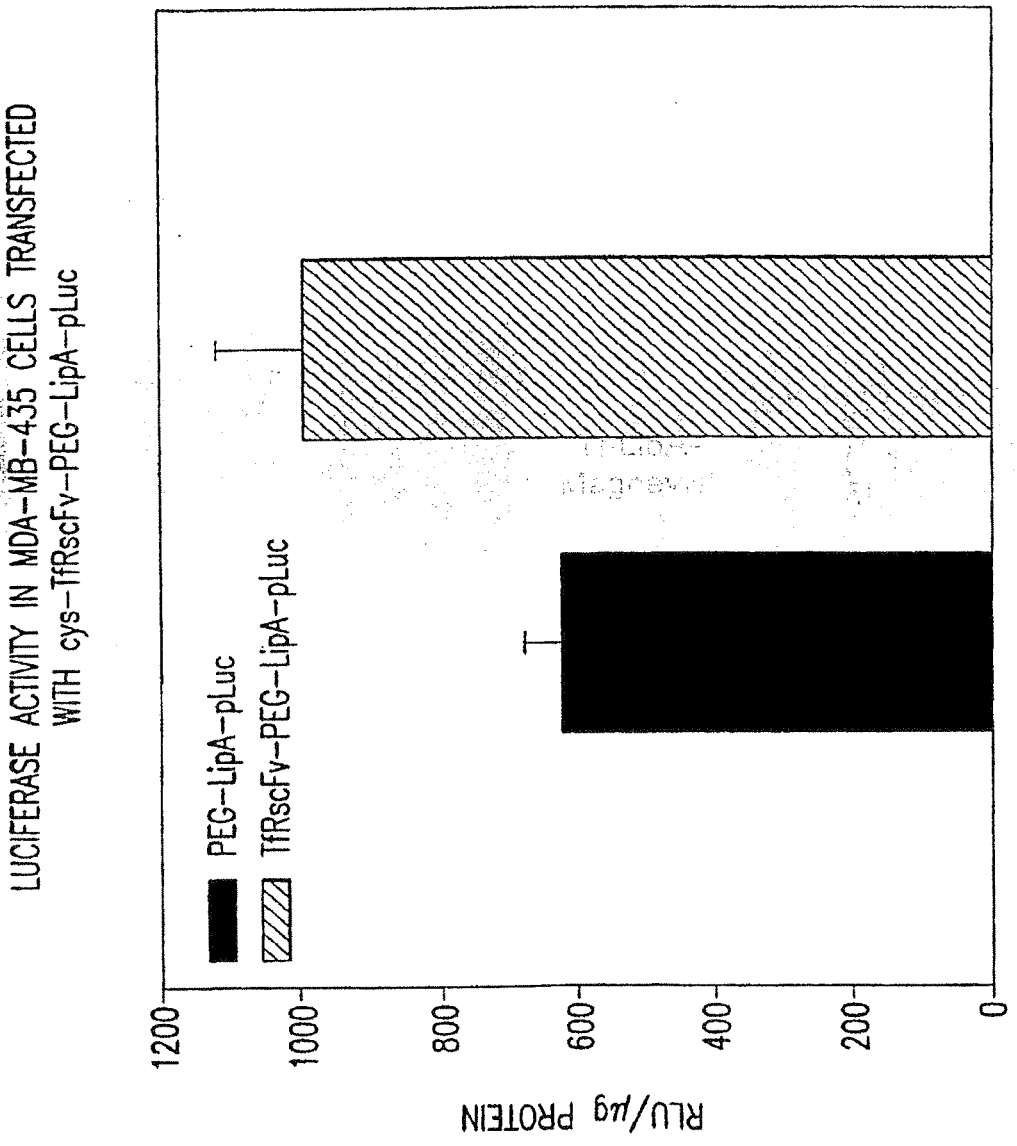
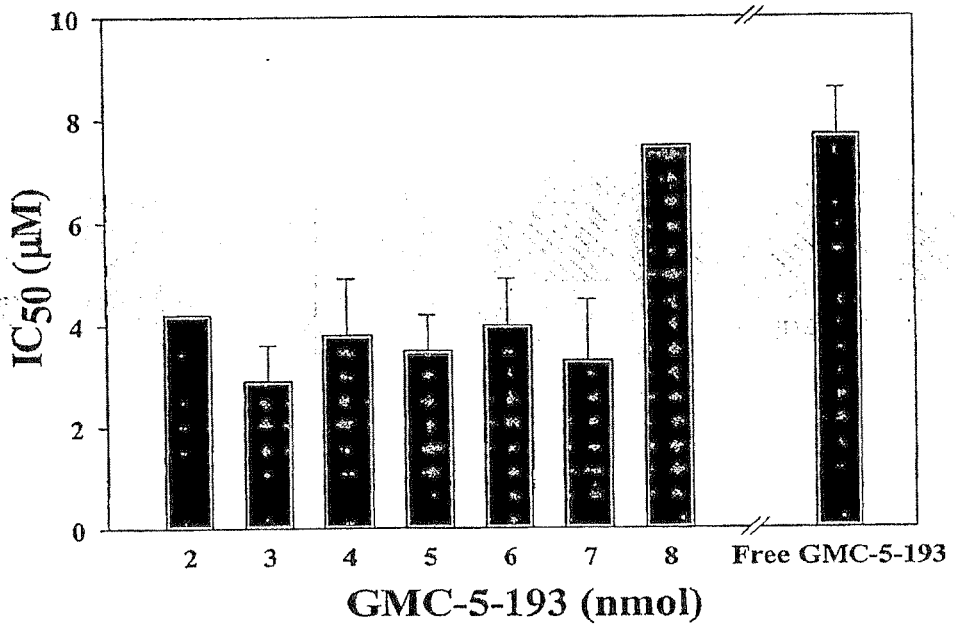

LUCIFERASE ACTIVITY IN MDA-MB-435 CELLS TRANSFECTED WITH cys-TfRscFv-PEG-LipA-pLuc
PEG-LipA-pLuc
TfRscFv-PEG-LipA-pLuc
RLU/μg PROTEIN
0
200
400
600
800
1000
1200

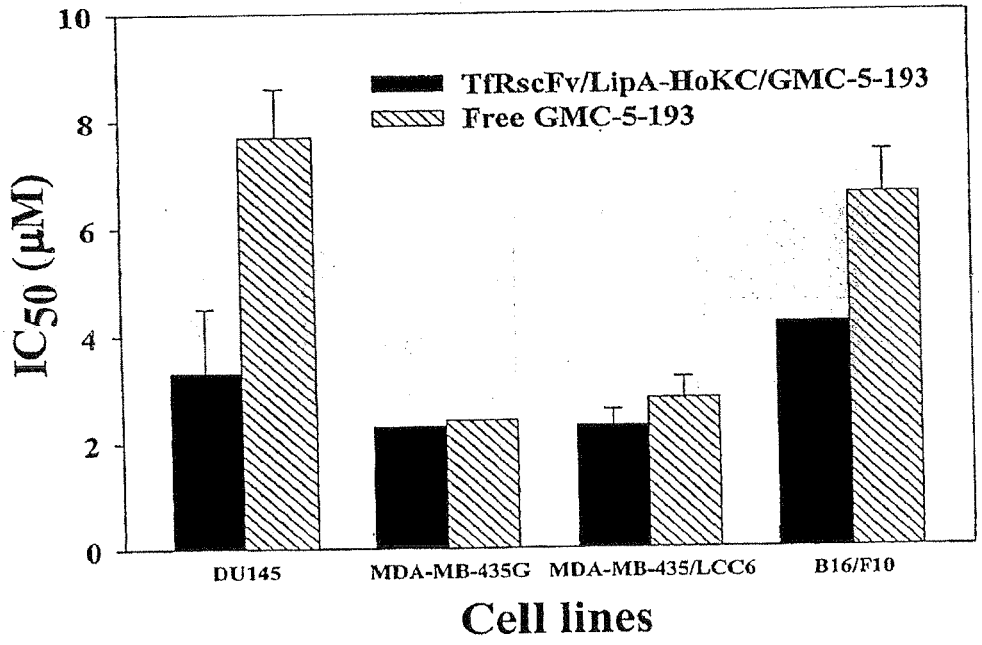
FIG.12

Fig. 13



Ratio: TfRscFv/LipA-HoKC/GMC-5-193=0.17 ug/7 nmol/X nmol

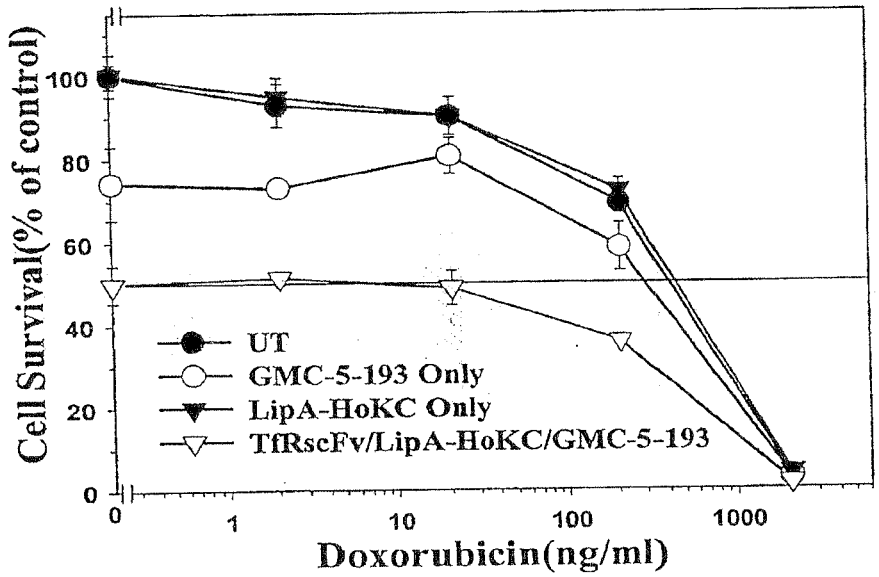
Fig. 14



Ratio: TfRscFv/LipA-HoKC/GMC-5-193=0.17 ug/7 nmol/7 nmol

Fig. 15A

Effect of Nanoimmunocomplex (scL-HK/GMC) on Sensitization of MDA-MB-435 Human Melanoma Cells to Doxorubicin

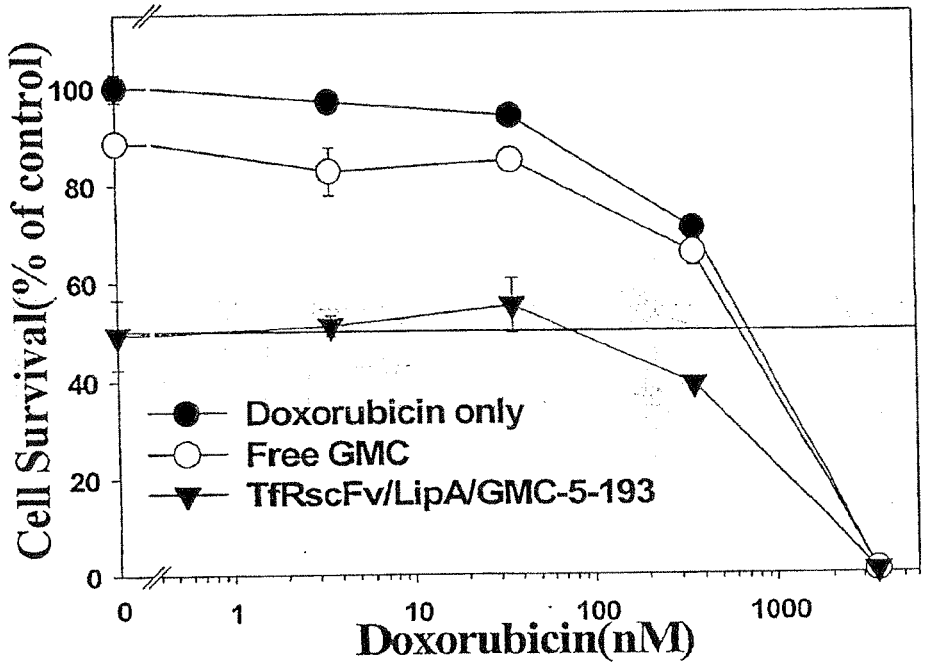


	IC_{50}:
UT	400 ng/mL
LipA-HoKC	420 ng/mL
GMC-5-193	300 ng/mL
TfRscFv/LipA-HoKC/GMC-5-193	8 ng/mL

	Fold Sensitization (compared to UT)
LipA-HoKC	1.0
GMC-5-193	1.3
TfRscFv/LipA-HoKC/GMC-5-193	50.0

Fig. 15B

Effect of TfRscFv/LipA/GMC-5-193 Nanoimmunocomplex On Sensitization of MDA-MB-435 Human Melanoma Cells to Doxorubicin

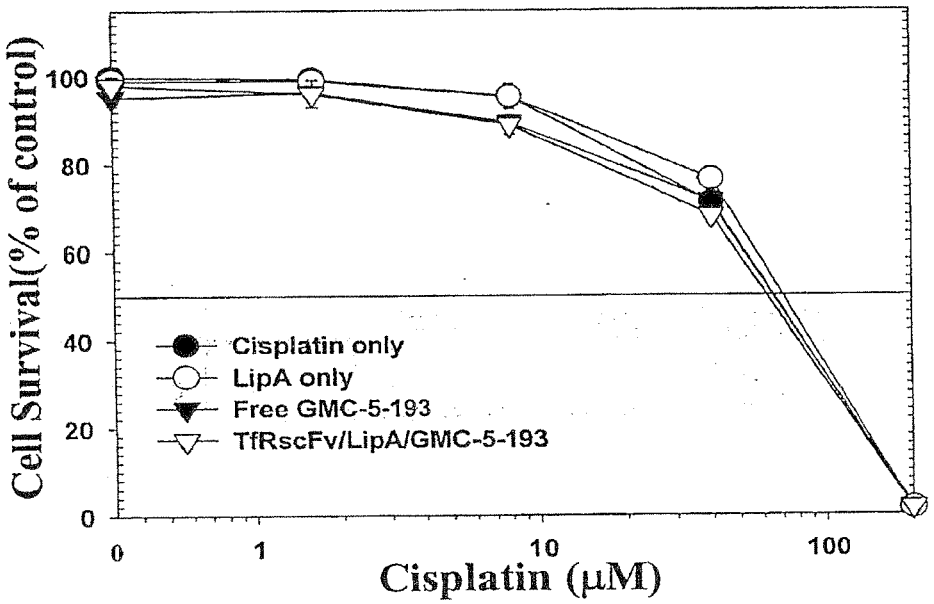


	IC_{50}:
Doxorubicin only	700 nM
Free GMC-5-193	620 nM
TfRscFv/LipA/GMC-5-193	73 nM

	Fold Sensitization (compared to Doxorubicin)
Free GMC-5-193	1.1
TfRscFv/LipA/GMC-5-193	9.6

Fig. 15C

Effect of tumor targeting liposomal delivery of GMC-5-193 on sensitization of B16/F10 mouse melanoma cells to Cisplatin



	IC_{50}:
Cisplatin only	64 μM
LipA only	70 μM
Free GMC-5-193	64 μM
TfRscFv/LipA/GMC-5-193	62 μM
	Fold Sensitization (compared to Cisplatin)
LipA only	0.9
Free GMC-5-193	1.0
TfRscFv/LipA/GMC-5-193	1.0

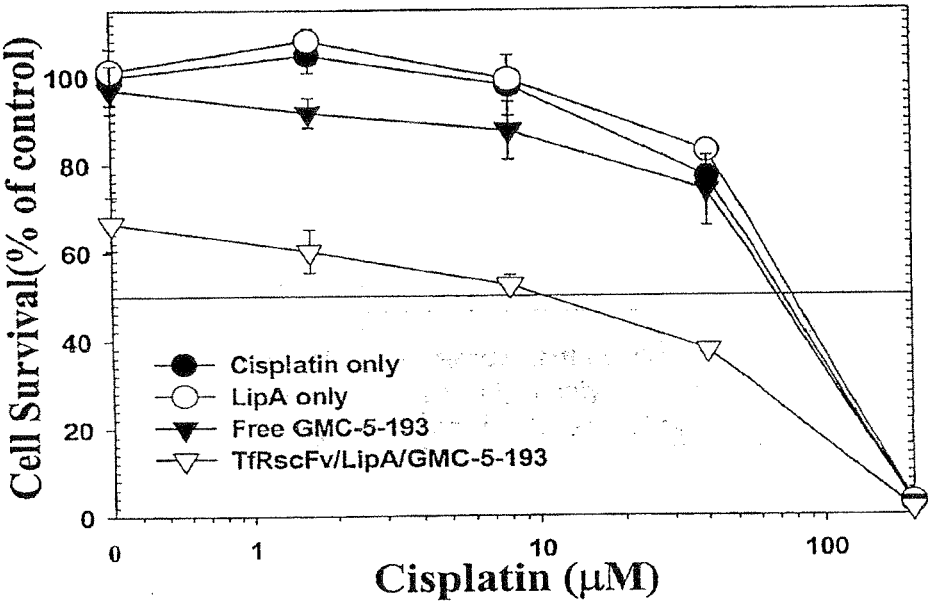
48 h incubation
9h XTT, 1.25 μM GMC-5-193

Plate5 B16 031706

1.25uM GMC-5-193

Fig. 15D

Effect of tumor targeting liposomal delivery of GMC-5-193 on sensitization of B16/F10 mouse melanoma cells to Cisplatin



	IC_{50}:
Cisplatin only	72 μM
LipA only	80 μM
Free GMC-5-193	70 μM
TfRscFv/LipA/GMC-5-193	11 μM

	Fold Sensitization (compared to Cisplatin)
LipA only	0.9
Free GMC-5-193	1.0
TfRscFv/LipA/GMC-5-193	6.5

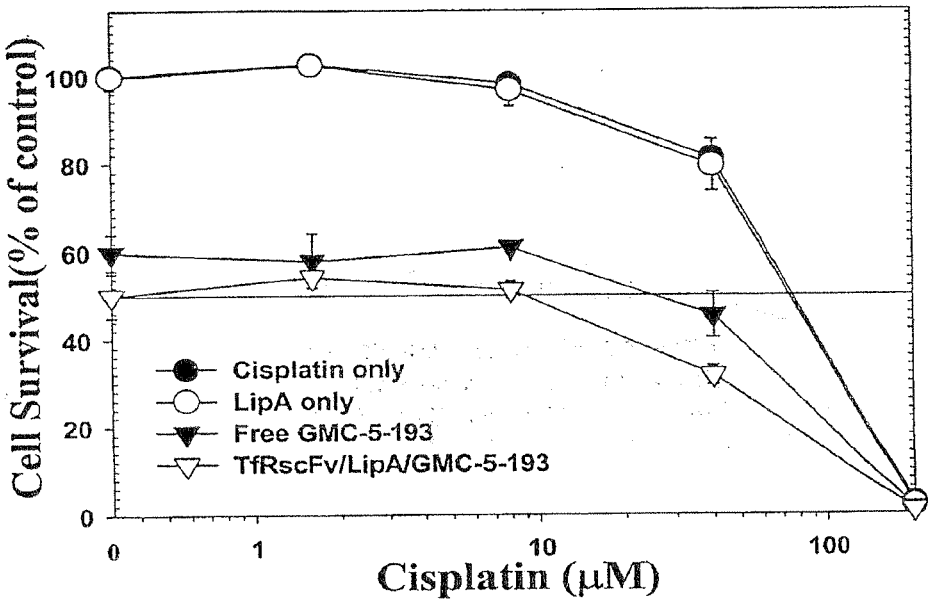
48 h incubation
7h XTT, 2 μM GMC-5-193

Plate3 B16 032406

2uM GMC-5-193

Fig. 15E

Effect of tumor targeting liposomal delivery of GMC-5-193 on sensitization of B16/F10 mouse melanoma cells to Cisplatin



	IC_{50}:
Cisplatin only	74 μM
LipA only	73 μM
Free GMC-5-193	24 μM
TfRscFv/LipA/GMC-5-193	9 μM

	Fold Sensitization (compared to Cisplatin)
LipA only	1.0
Free GMC-5-193	3.1
TfRscFv/LipA/GMC-5-193	8.2

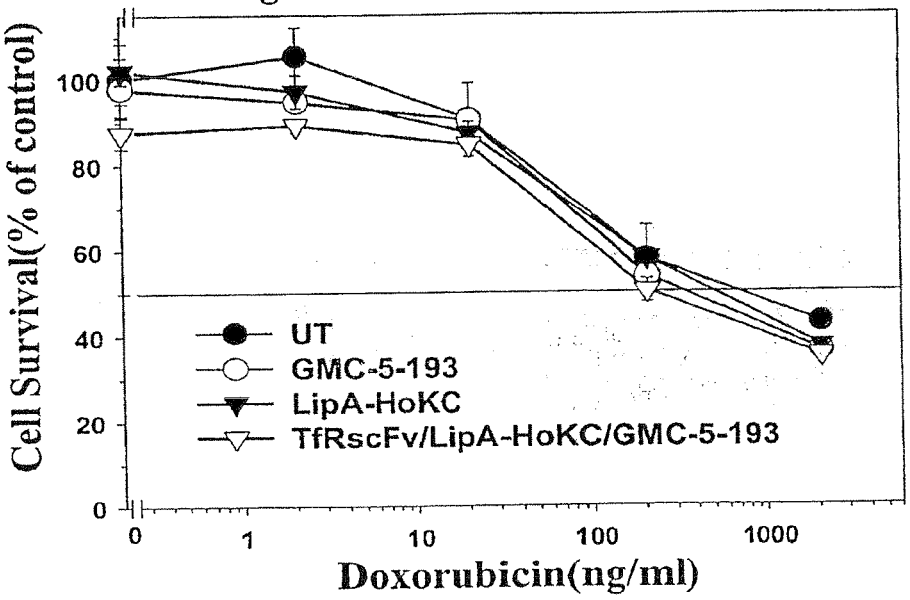
48 h incubation
9h XTT, 2.5 μM GMC-5-193

Plate7 B16 031706

2uM GMC-5-193

Fig 16 A

Effect of Tumor Targeting Liposomal Delivery of GMC-5-193 on Sensitization of Normal Human Lung Fibroblasts IMR-90 to Doxorubicin

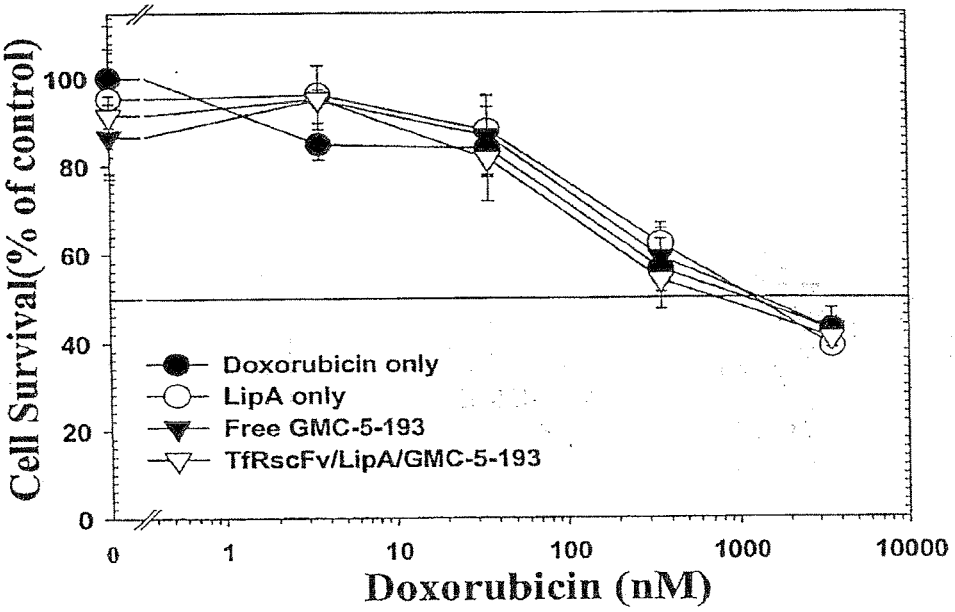


	IC_{50}:
UT	700 ng/mL
LipA-HoKC	500 ng/mL
GMC-5-193	320 ng/mL
TfRscFv/LipA-HoKC/GMC-5-193	200 ng/mL

	Fold Sensitization (compared to UT)
LipA-HoKC	1.4
GMC-5-193	2.2
TfRscFv/LipA-HoKC/GMC-5-193	3.5

Fig. 16B

Effect of tumor targeting liposomal delivery of GMC-5-193 on sensitization of IMR-90 human lung fibroblasts to Doxorubicin



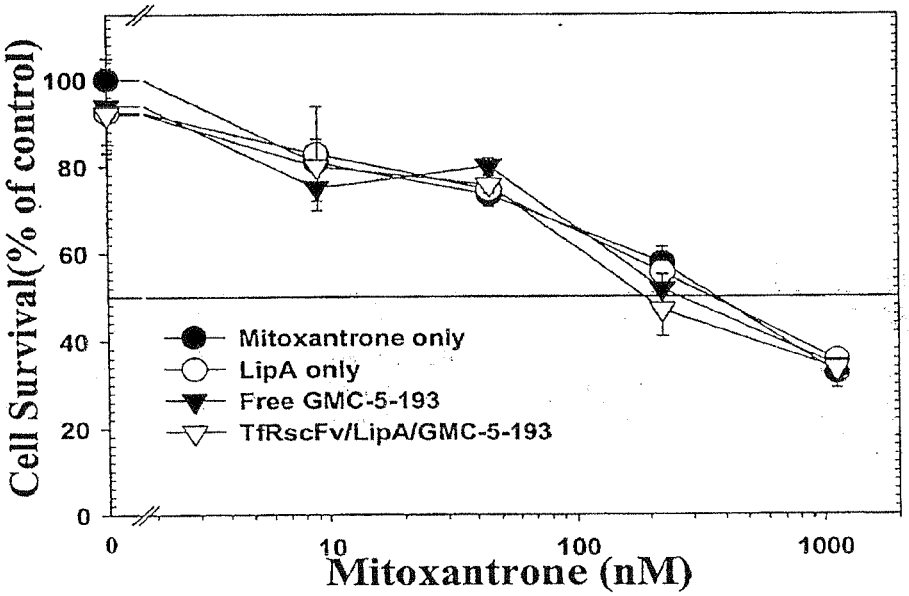
	IC_{50}:
Doxorubicin only	1100 nM
LipA only	1200 nM
Free GMC-5-193	1300 nM
TfRscFv/LipA/GMC-5-193	700 nM

	Fold Sensitization (compared to Doxorubicin)
LipA only	0.9
Free GMC-5-193	0.8
TfRscFv/LipA/GMC-5-193	1.6

Plate3 IMR-90 010706

Fig. 16C

Effect of tumor targeting liposomal delivery of GMC-5-193 on sensitization of IMR-90 human lung fibroblasts to Mitoxantrone



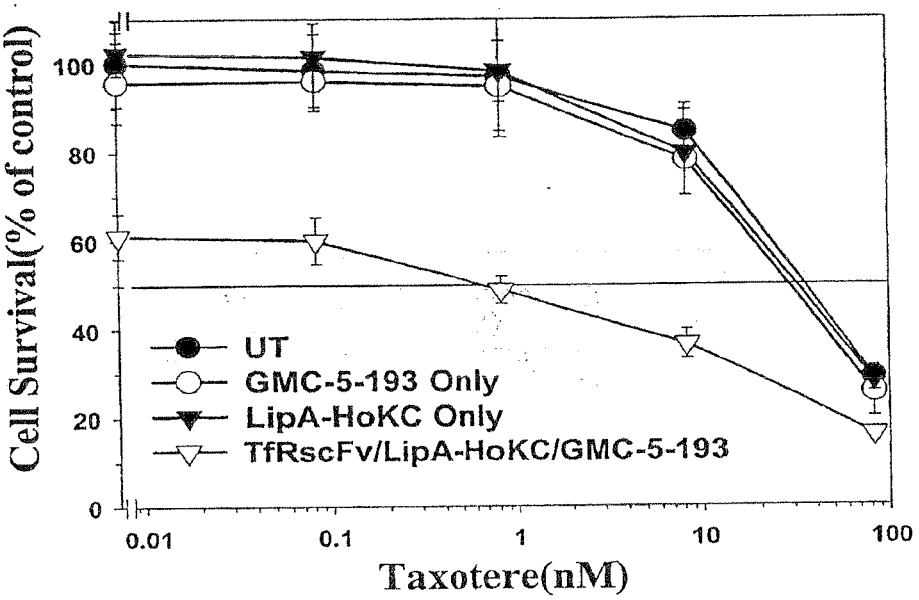
	IC_{50}:
Mitoxantrone only	350 nM
LipA only	340 nM
Free GMC-5-193	250 nM
TfRscFv/LipA/GMC-5-193	190 nM

	Fold Sensitization (compared to Mitoxantrone)
LipA only	1.0
Free GMC-5-193	1.4
TfRscFv/LipA /GMC-5-193	1.8

Plate1 IMR-90 010706

Fig. 17A

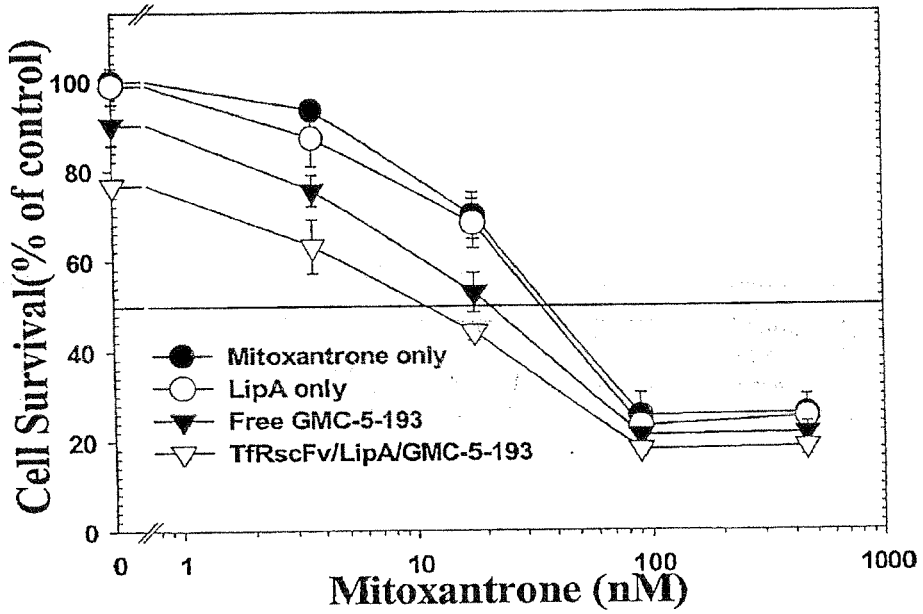
Effect of Tumor Targeting Liposomal Delivery of GMC-5-193 on Sensitization of DU145 Prostate Cancer Cells to Taxotere



	IC_{50}:
UT	33 nM
LipA-HoKC Only	30 nM
GMC-5-193 Only	28 nM
TfRscFv/LipA-HoKC/GMC-5-193	0.7 nM
Fold Sensitization	
(Compared to UT)	
LipA-HoKC Only	1.1
GMC-5-193 Only	1.2
TfRscFv/LipA-HoKC/GMC-5-193	47.1

Fig. 17B

Effect of tumor targeting liposomal delivery of GMC-5-193 on sensitization of DU145 human prostate cancer cells to Mitoxantrone



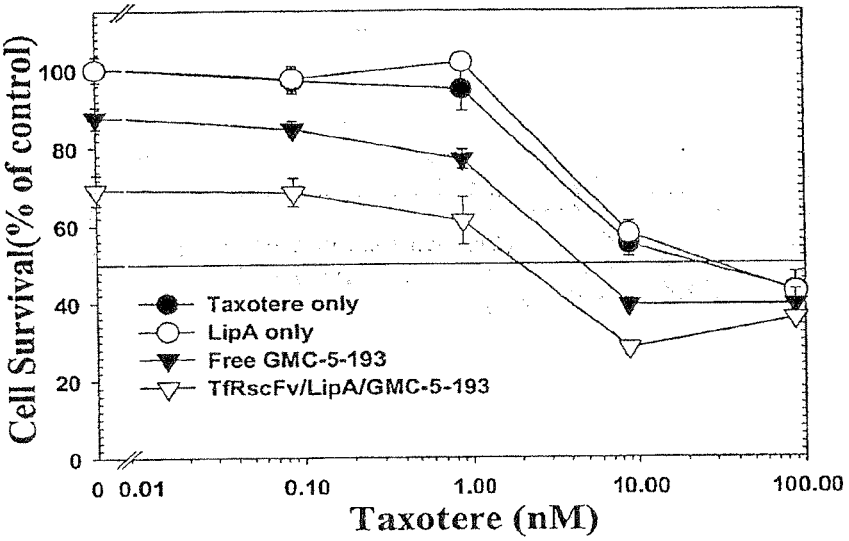
	IC_{50}:
Mitoxantrone only	35 nM
LipA only	33 nM
Free GMC-5-193	21 nM
TfRscFv/LipA/GMC-5-193	11 nM

	Fold Sensitization (compared to Mitoxantrone)
LipA only	1.1
Free GMC-5-193	1.7
TfRscFv/LipA/GMC-5-193	3.2

Plate3 DU145 012106

Fig. 17C

Effect of Tumor Targeting Liposomal Delivery of GMC-5-193 on Sensitization of MDA-MB 435 Human Melanoma Cells to Taxotere



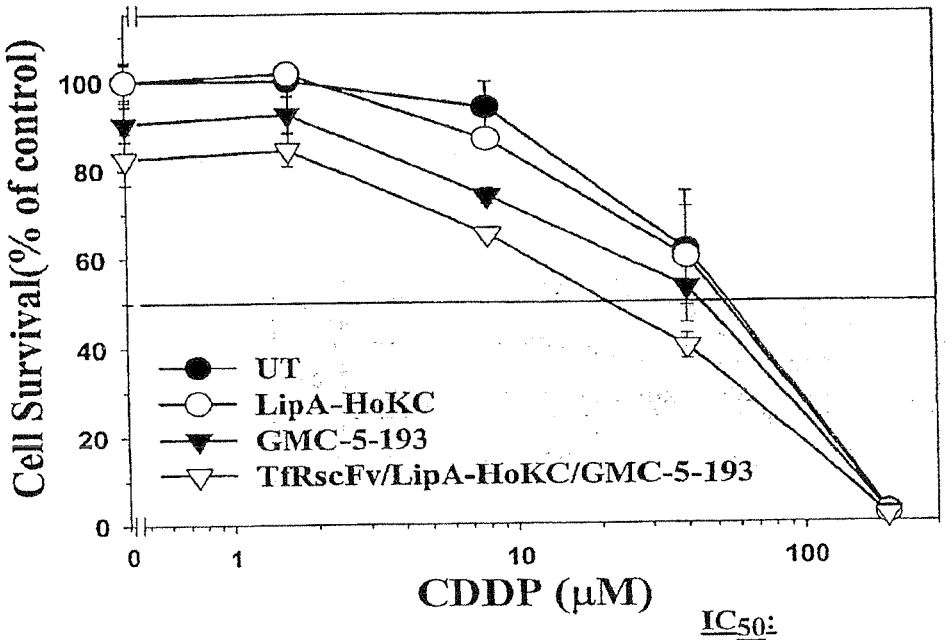
	IC_{50}:
Taxotere only	22 nM
LipA only	30 nM
Free GMC-5-193	4.5 nM
TfRscFv/LipA/GMC-5-193	1.9 nM

	Fold Sensitization (compared to Taxotere)
LipA only	0.7
Free GMC-5-193	4.9
TfRscFv/LipA/GMC-5-193	11.6

Plate8 435G 011306

Fig. 18

The Effect of Tumor Targeting Liposomal Delivery of GMC-5-193 on Sensitization of B16/F10 Mouse Melanoma Cells to CDDP



	IC_{50}:
UT	52 uM
LipA-HoKC	51 uM
GMC-5-193	42 uM
TfRscFv/LipA-HoKC/GMC-5-193	20 uM

	Fold Sensitization (compared to UT)
LipA-HoKC	1.0
GMC-5-193	1.2
TfRscFv/LipA-HoKC/GMC-5-193	2.6

Fig. 19A

***In Vitro* Comparison of Free GMC-5-193 or TfRscFv/LipA/GMC-5-193 Complex Uptake in MDA-MB-435 Cells**

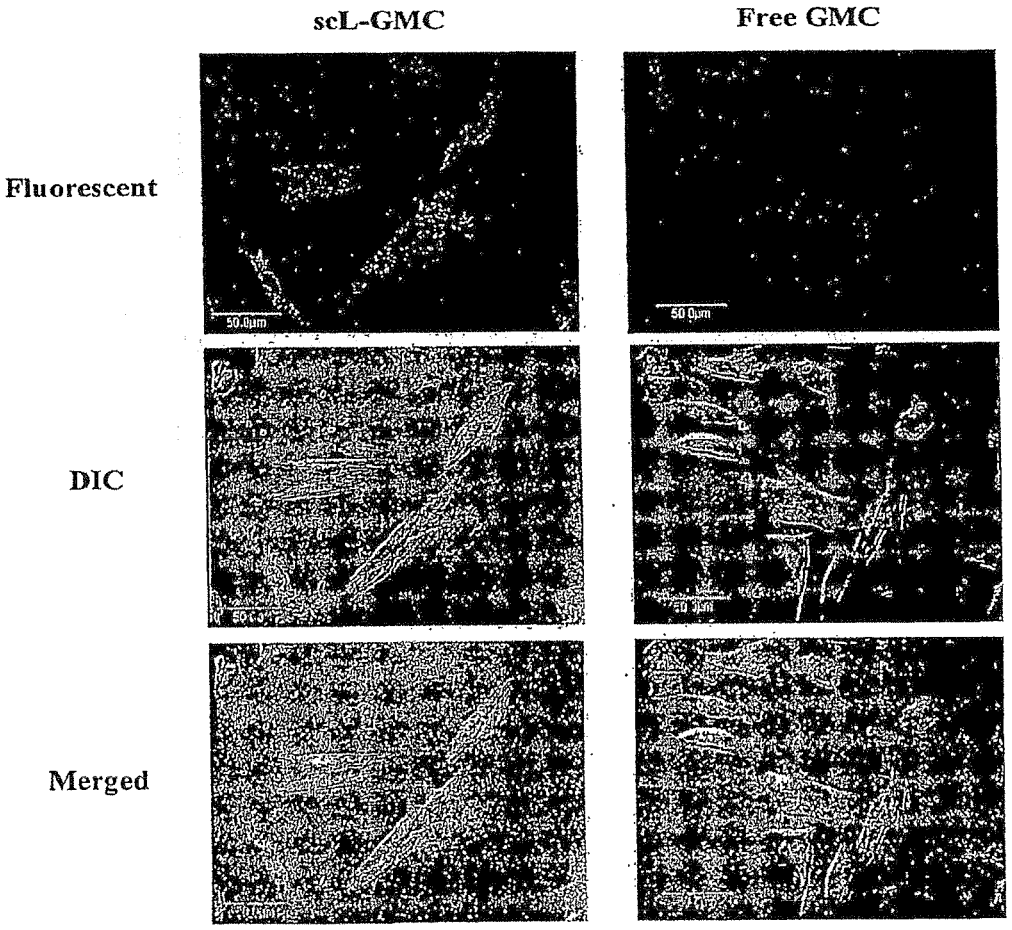


Fig. 19B

***In Vitro* Comparison of Free or Nanoimmunocomplexed (scLHK-GMC) GMC Uptake in MDA-MB-435 Cells**

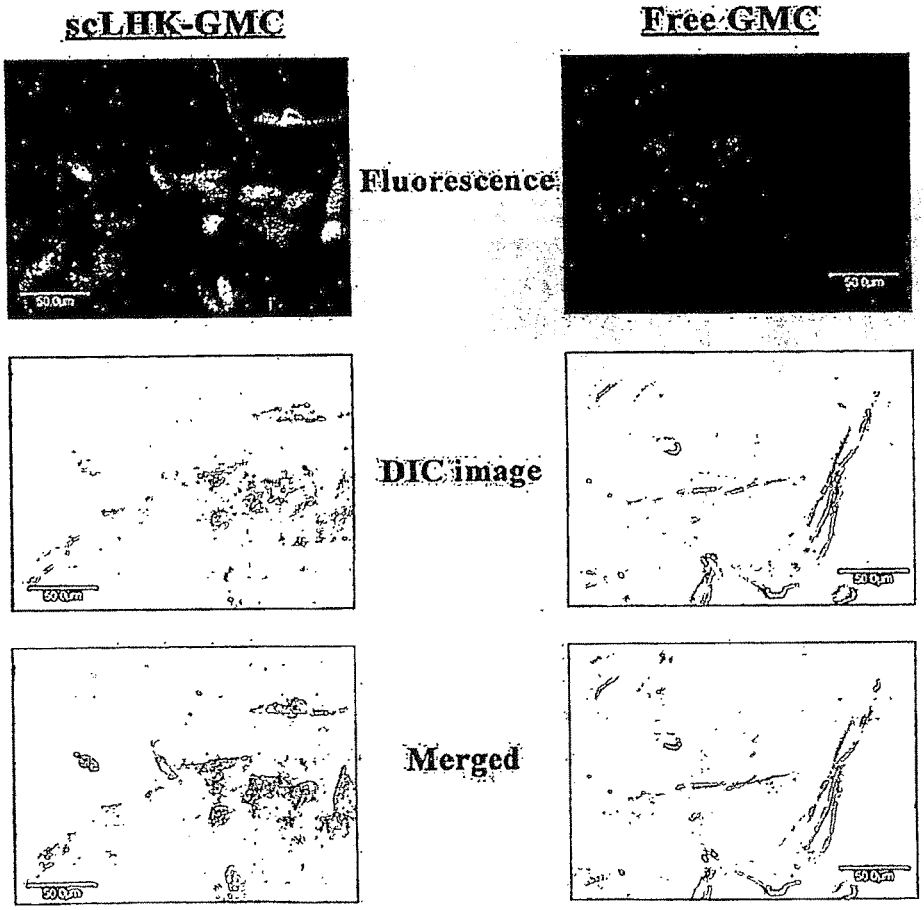
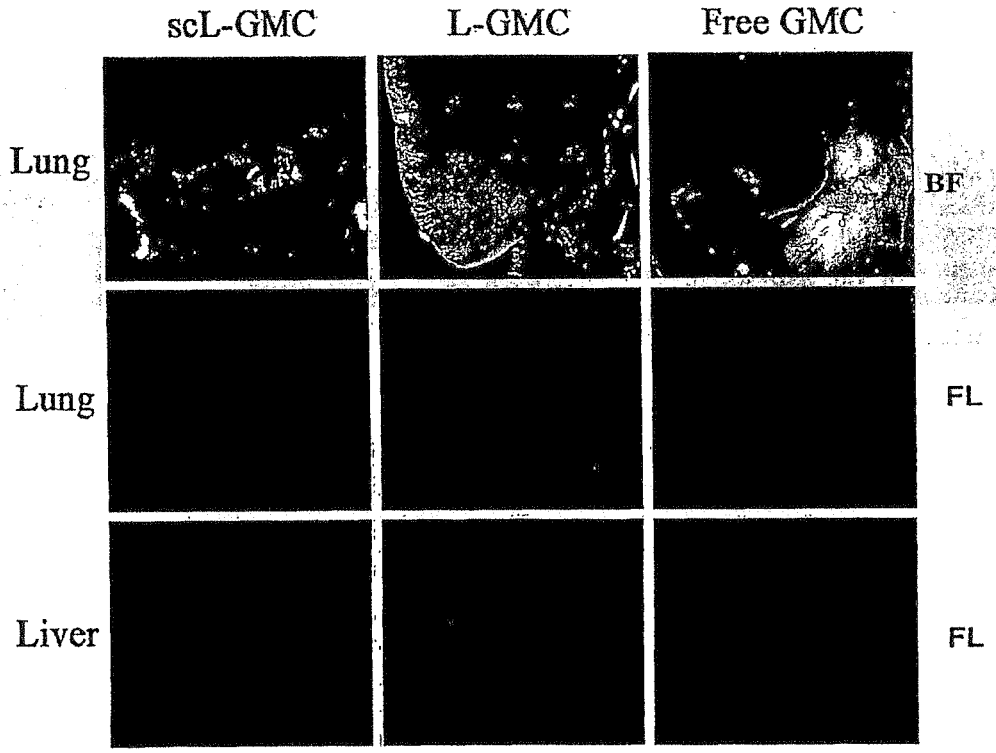


Fig. 20A

Incorporation of a Fluorescent GMC in the Nanoimmunocomplex Enhances Tumor Specific Uptake After Systemic Administration



BF = Brightfield; Fl = Fluorescence of identical area

Fig. 20B

Enhanced Tumor Specific Uptake After Systemic Administration by Incorporation of a Fluorescent Small Molecule in TfRscFv/LipA-HoKC/GMC-5-193 Complex

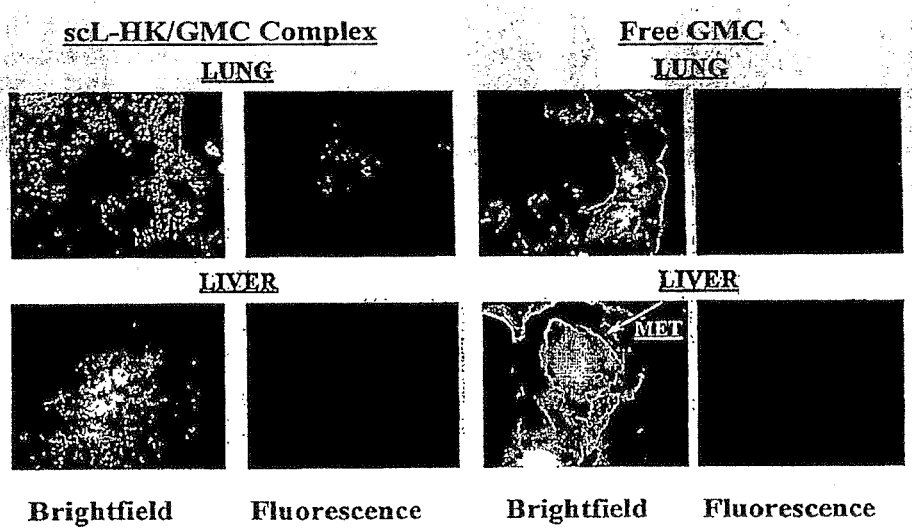


Fig. 20C

Incorporation of a Fluorescent GMC in the Nanoimmunocomplex Enhances Tumor Specific Uptake After Systemic Administration

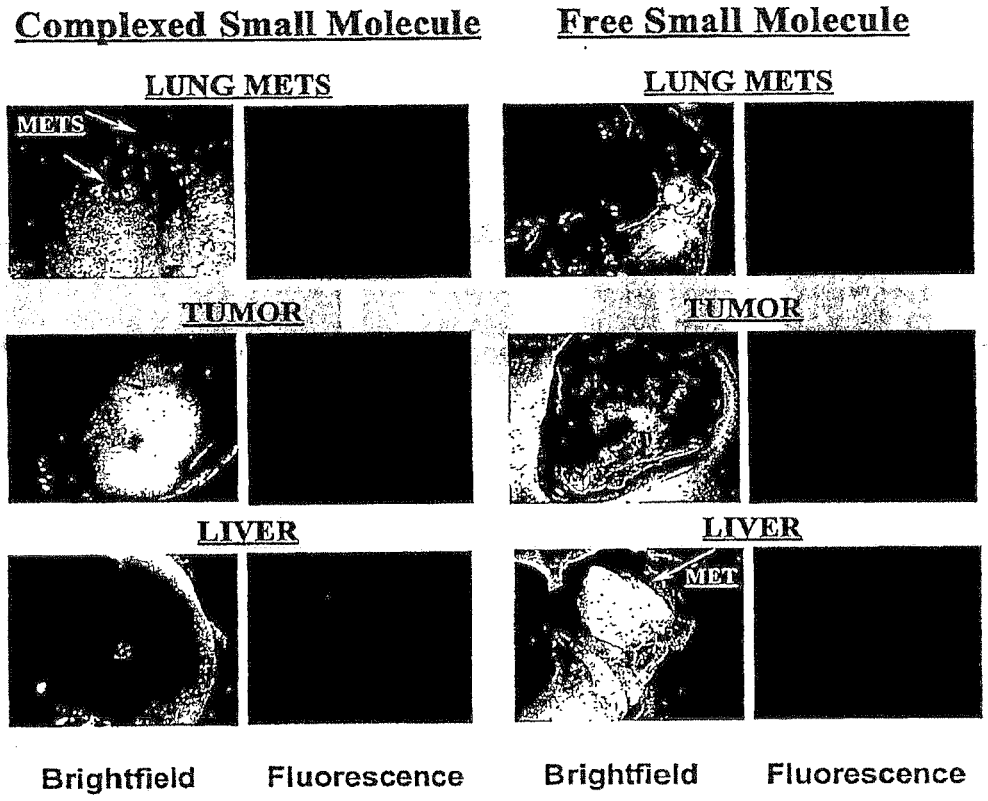


Fig 21A

Inhibition of Melanoma Tumor Growth in Syngeneic Mice after Treatment with the GMC Nanoimmunocomplex (scL-GMC, scLHK-GMC)

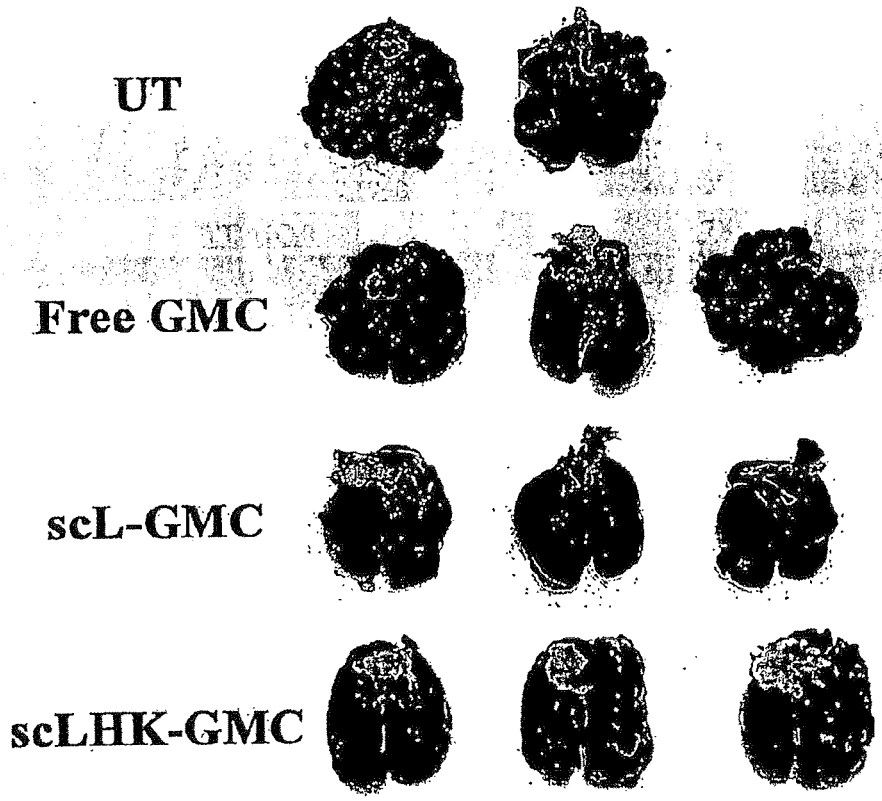


Fig. 21B

Inhibition of Tumor Growth in Tumor (B_{16}/F_{10}) Bearing Syngeneic Mice after Treatment with the Combination of TfRscFv/LipA-HoKC/GMC-5-193 Complex plus CDDP

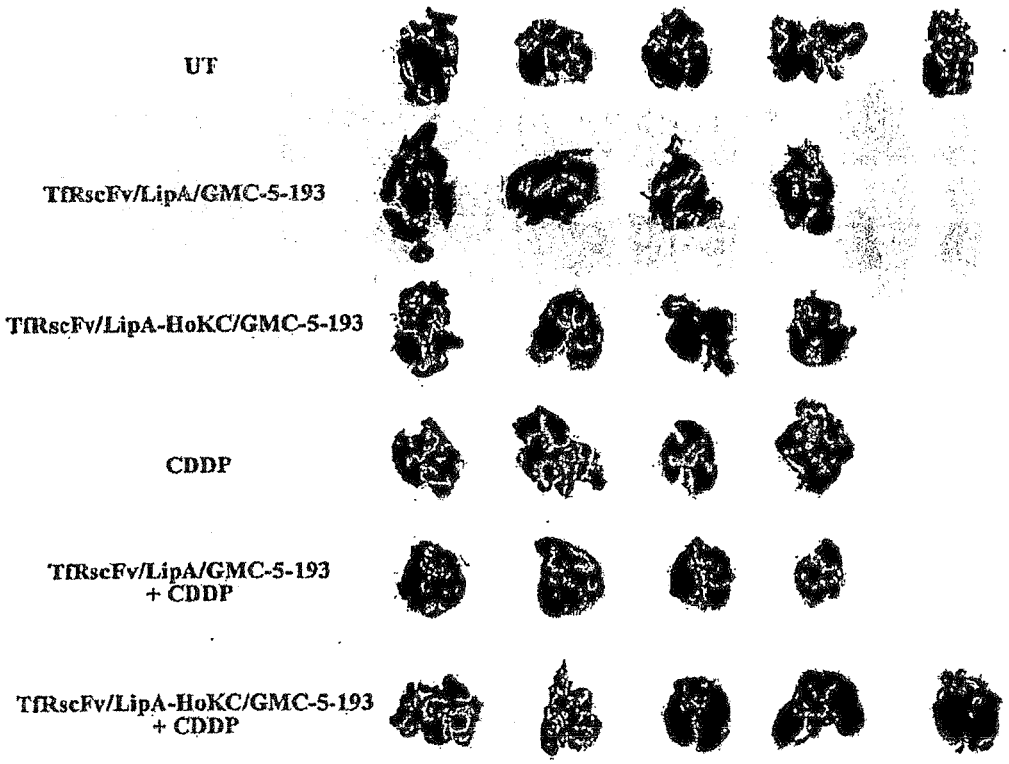


Fig. 21C

Inhibition of Tumor Growth in Tumor Bearing Syngenic Mice after Treatment with the Combination of TfRscFv/LipA/GMC-5-193 Complex plus Cisplatin

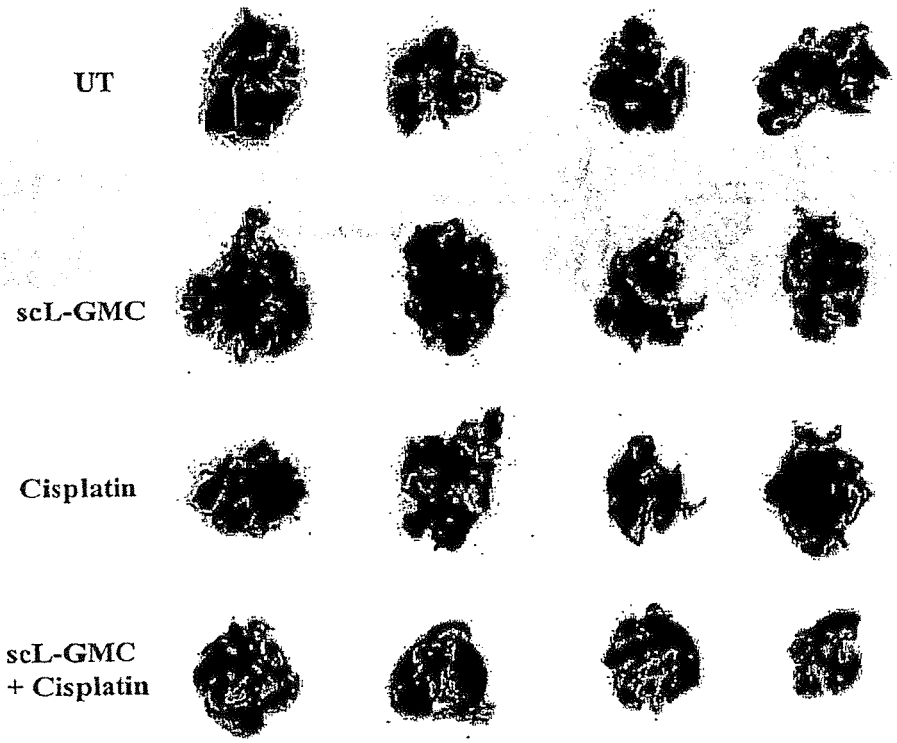


Fig. 22

Cleaved Caspase-3 in the Serum of Tumor Bearing Syngeneic Mice After Treatment with the Combination of TfRscFv/Liposome/GMC-5-193 Complex plus CDDP

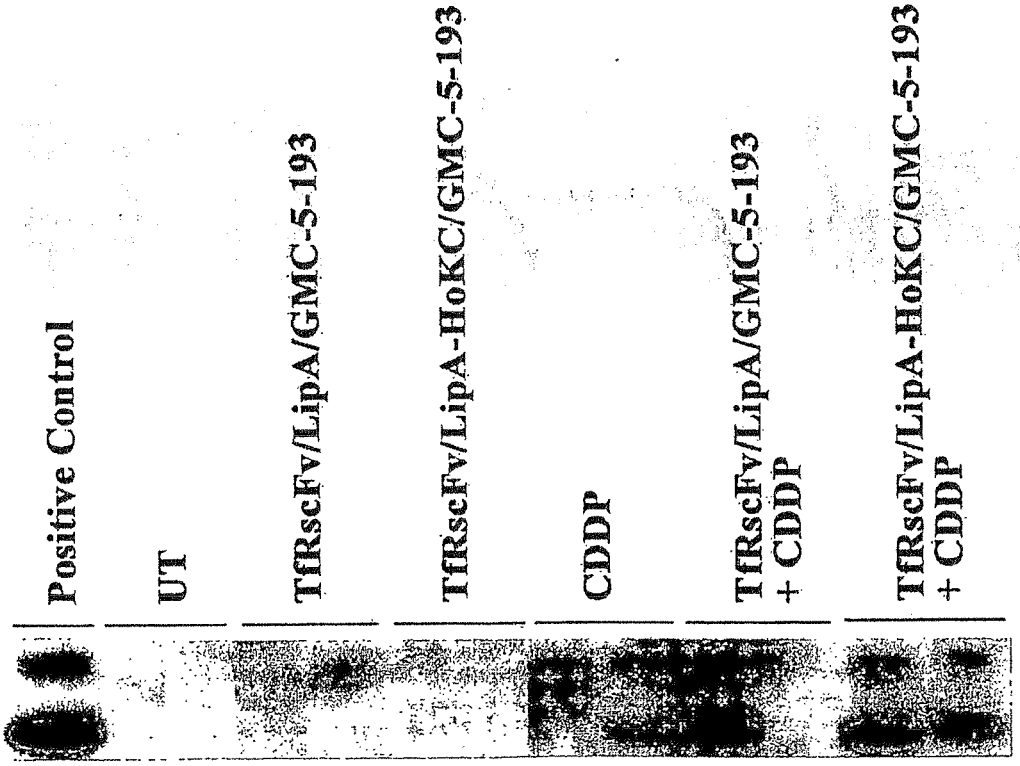
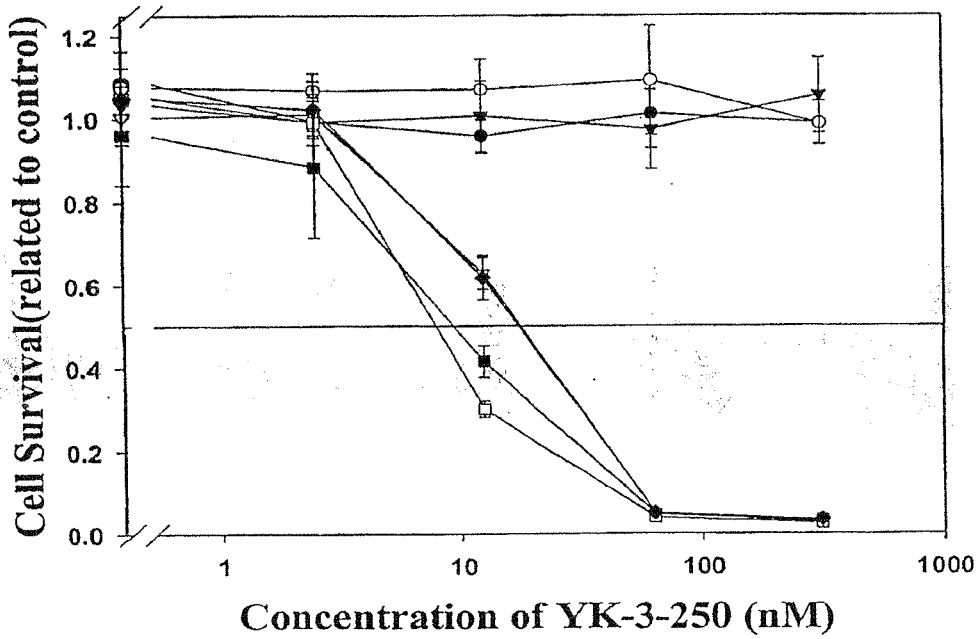


Fig. 23A

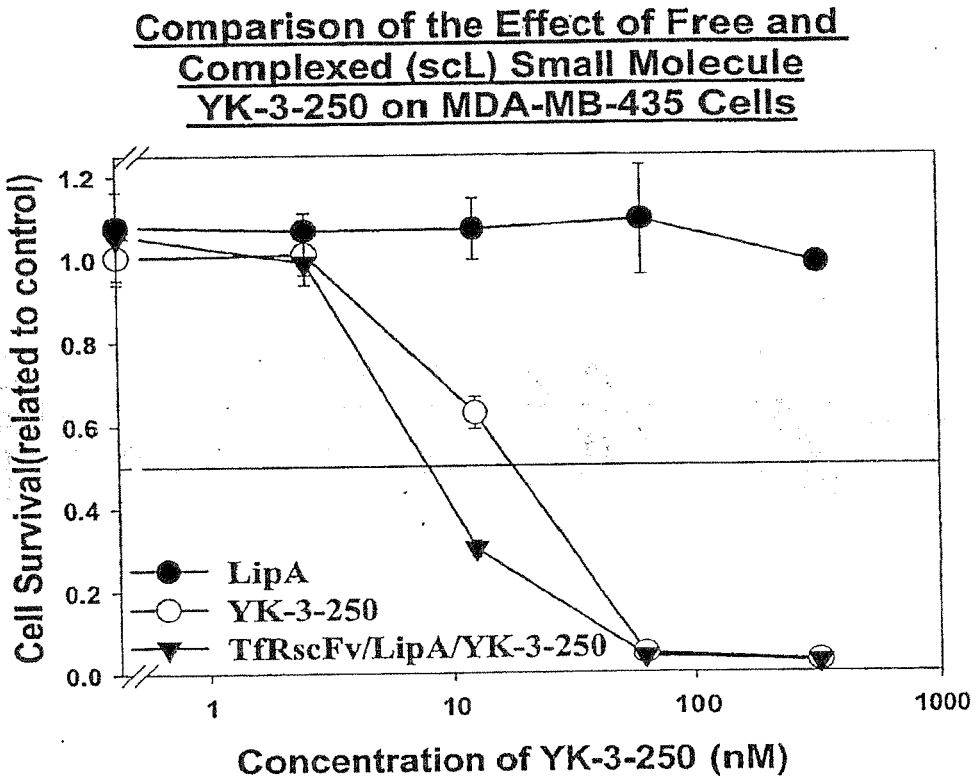
Comparison of Effects of TfRscFv/LipA/YK-3-250 Complexes at Different Ratios of YK-3-250 to LipA in MDA-MB-435 cells



	IC_{50}
LipA (6:7 eq)	>300 nM
LipA (7:7 eq)	>300 nM
LipA (8:7 eq)	>300 nM
YK-3-250	16 nM
YK-3-250/LipA (6:7)	9 nM
YK-3-250/LipA (7:7)	8 nM
YK-3-250/LipA (8:7)	16 nM

092205-435G plate1,2,3

Fig. 23B



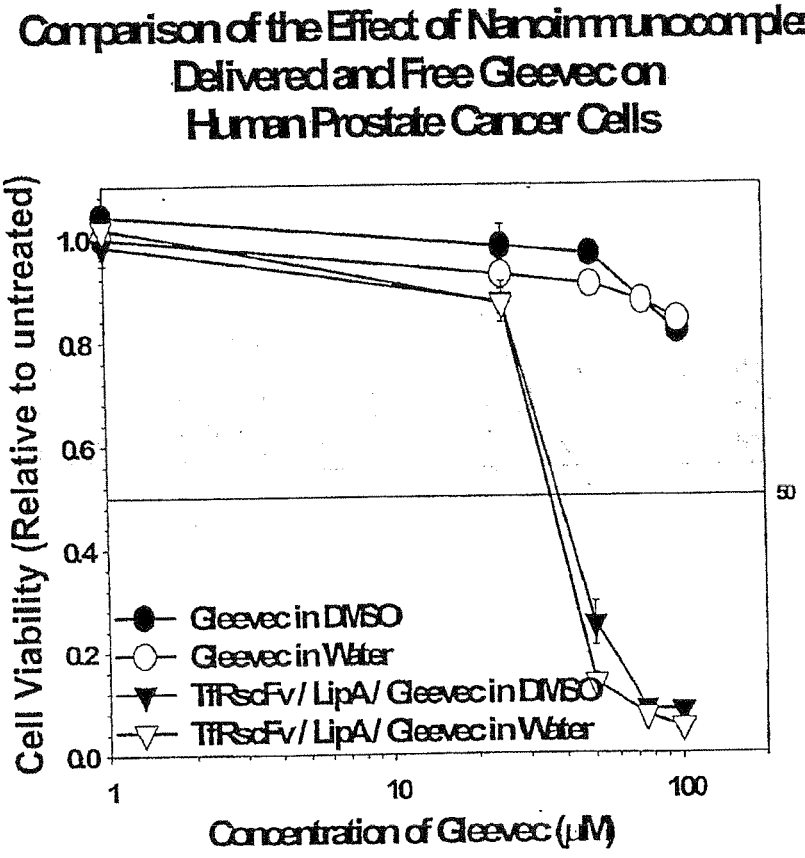
IC_{50} Values

Lip A Only	>1000nM
Free YK-3-250	18nM
TfRscFv/Lipa/YK-3-250	8nM

Fold Sensitization

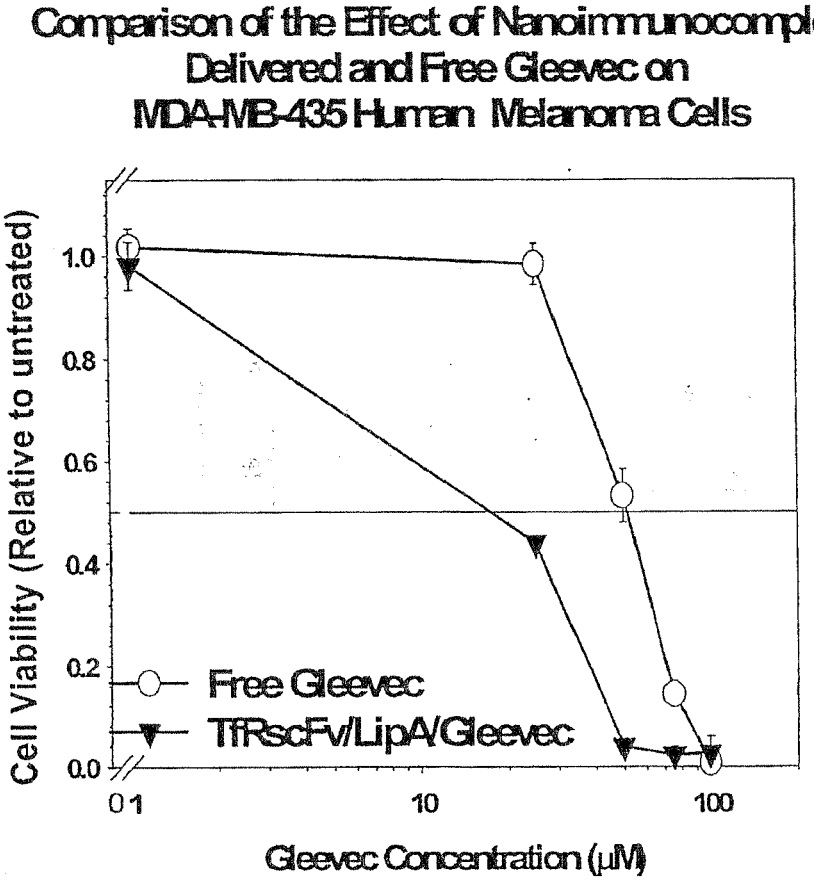
Free YK-3-250 VS TfRscFv/LipA/YK-3-250 = 2.2

Fig. 24A



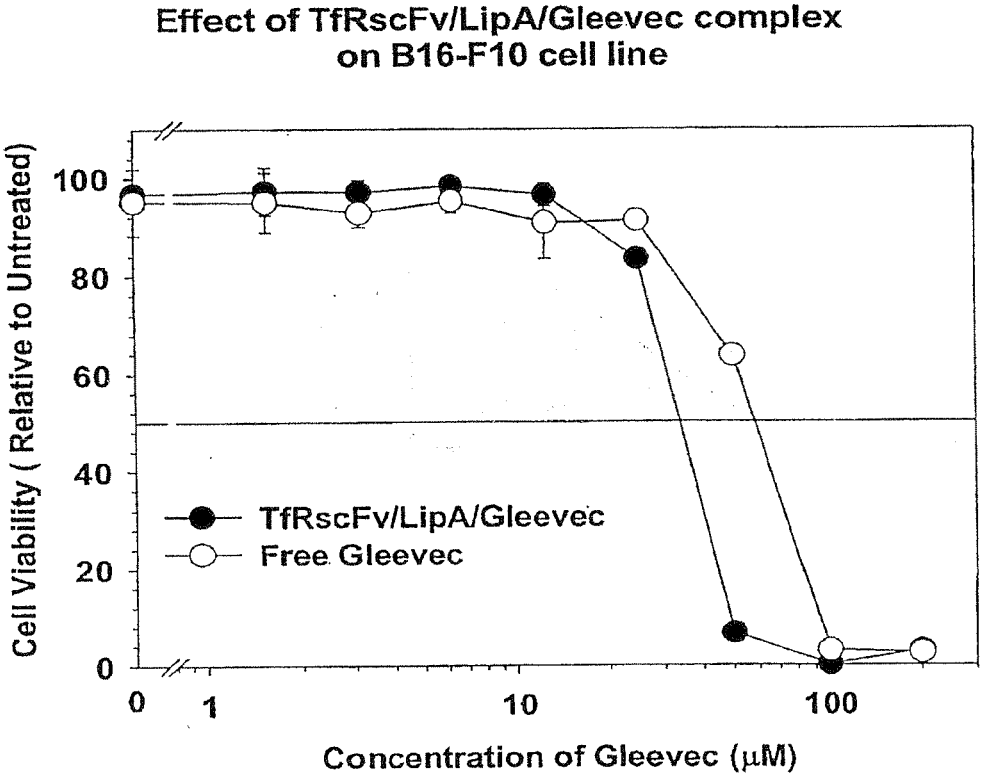
	IC_{50}
Gleevec in DMSO	>200 μM
Gleevec in Water	>200 μM
TfRscFv/LipA/Gleevec in DMSO	38 μM
TfRscFv/LipA/Gleevec in Water	35 μM

Fig. 24B



	IC_{50}
Gleevec in Water	52μM
TfRscFv/LipA/Gleevec in Water	18μM

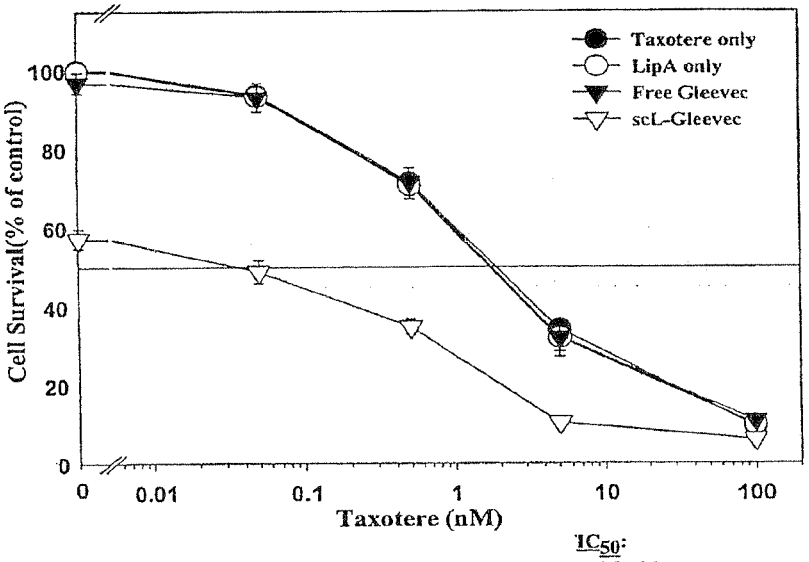
Fig.24C



	IC_{50}
TfRscFv/LipA/Gleevec	32 μM
Gleevec	60 μM

Fig. 25A

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of MDA-MB 435 Human Melanoma Cells to Taxotere



	IC_{50}:
Taxotere only	1.9 nM
LipA only	1.7 nM
Free Gleevec	1.7 nM
scL-Gleevec	0.04 nM

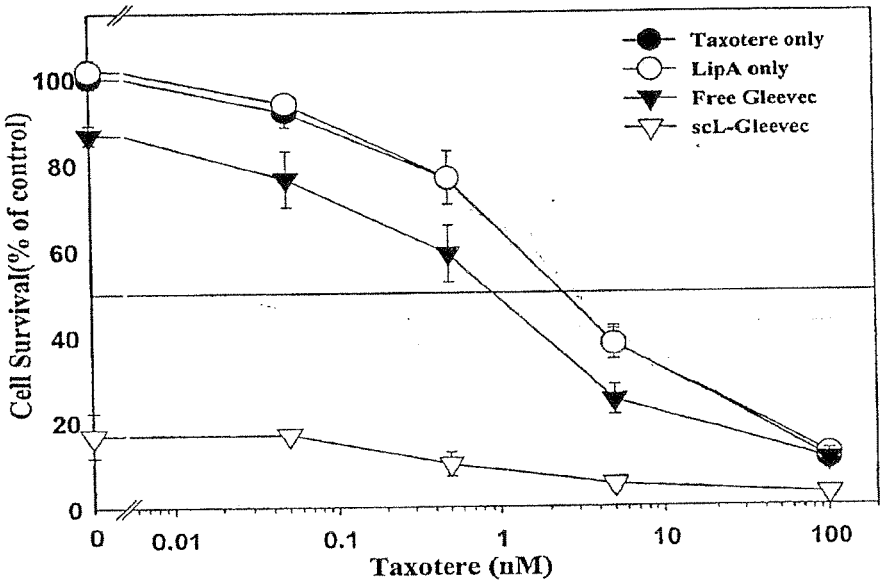
Fold Sensitization(compared to Taxotere)	
LipA only	1.1
Free Gleevec	1.1
scL-Gleevec	47.5

Fold Sensitization(compared to Free Gleevec)	
LipA only	1.0
scL-Gleevec	42.5

20uM Gleevec

Fig 25B

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of MDA-MB 435 Human Melanoma Cells to Taxotere



	IC_{50}:
Taxotere only	2.3 nM
LipA only	2.3 nM
Free Gleevec	0.9 nM
scL-Gleevec	

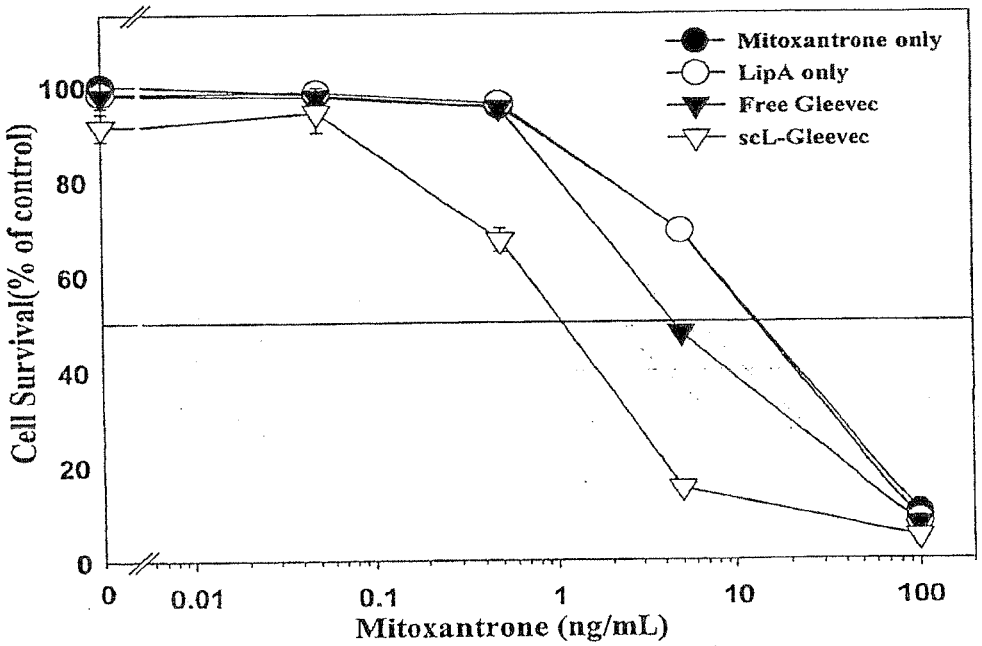
Fold Sensitization(compared to Taxotere)	
LipA only	1.0
Free Gleevec	2.6
scL-Gleevec	

Fold Sensitization(compared to Free Gleevec)	
LipA only	0.4
scL-Gleevec	

30uM Gleevec

Fig. 26A

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of DU145 Human Prostate Cancer Cells to Mitoxantrone



	IC_{50}:
Mitoxantrone only	12.0 ng/mL
LipA only	12.0 ng/mL
Free Gleevec	4.2 ng/mL
scL-Gleevec	1.1 ng/mL

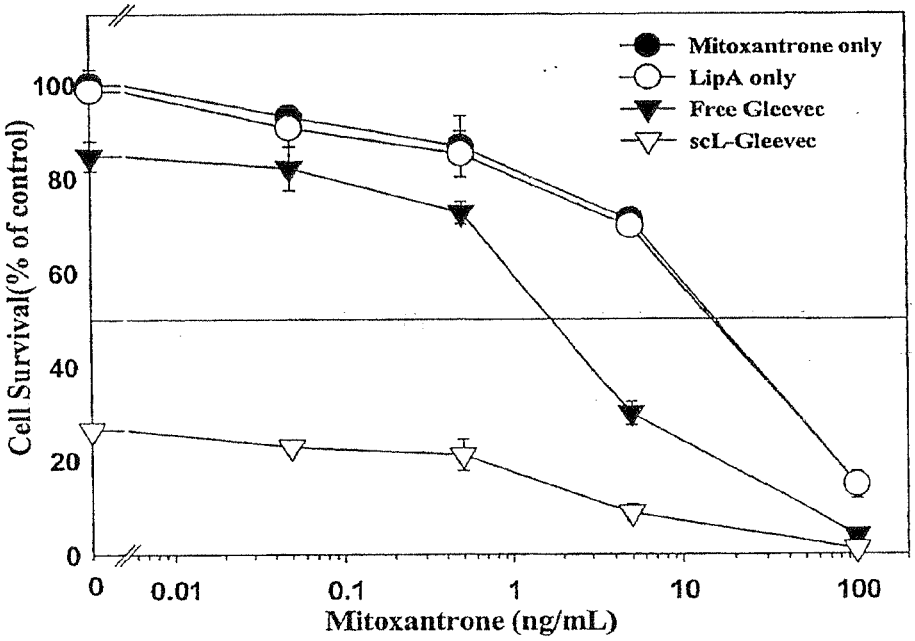
Fold Sensitization(compared to Mitoxantrone)	
LipA only	1.0
Free Gleevec	2.9
scL-Gleevec	10.9

Fold Sensitization(compared to Free Gleevec)	
Lip A only	0.4
scL-Gleevec	3.8

20uM Gleevec

Fig. 26B

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of DU145 Human Prostate Cancer Cells to Mitoxantrone



	IC_{50}:
Mitoxantrone only	14.0 ng/mL
LipA only	14.0 ng/mL
Free Gleevec	1.7 ng/mL
scL-Gleevec	

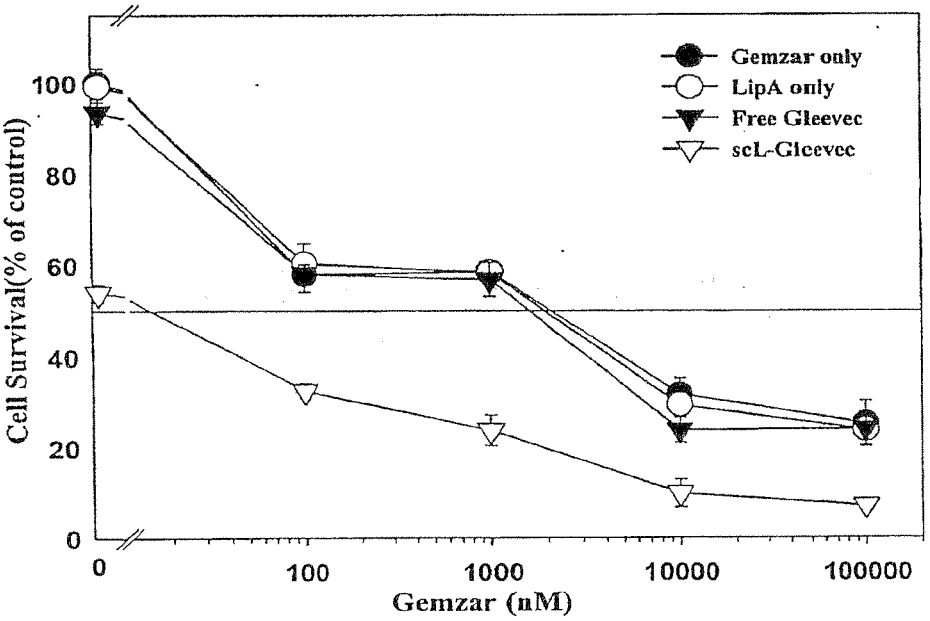
Fold Sensitization(compared to Mitoxantrone)	
LipA only	1.0
Free Gleevec	8.2
scL-Gleevec	

Fold Sensitization(compared to Free Gleevec)	
Lip A only	0.1
scL-Gleevec	

30uM Gleevec

Fig. 27A

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of Panc-1 Human Pancreatic Cancer Cells to Gemzar

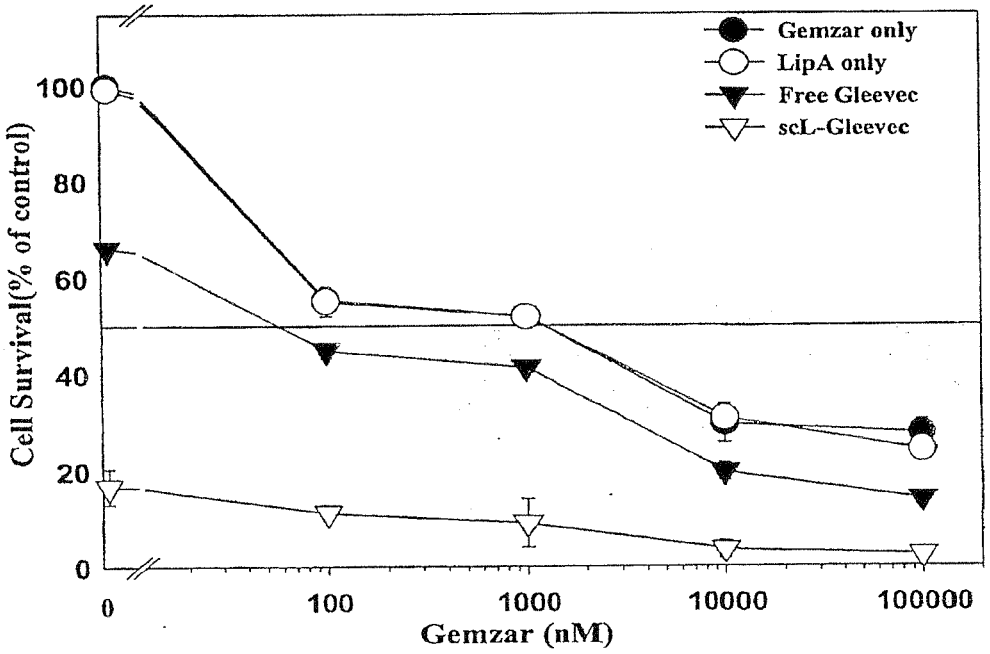


	IC_{50}:
Gemzar only	2100 nM
LipA only	2000 nM
Free Gleevec	1400 nM
scL-Gleevec	14 nM
Fold Sensitization(compared to Gemzar)	
LipA only	1.1
Free Gleevec	1.5
scL-Gleevec	150.0
Fold Sensitization(compared to Free Gleevec)	
LipA only	0.7
scL-Gleevec	100.0

20uM Gleevec

Fig. 27B

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of Panc-1 Human Pancreatic Cancer Cells to Gemzar



	IC_{50}:
Gemzar only	1200 nM
LipA only	1200 nM
Free Gleevec	60 nM
scL-Gleevec	

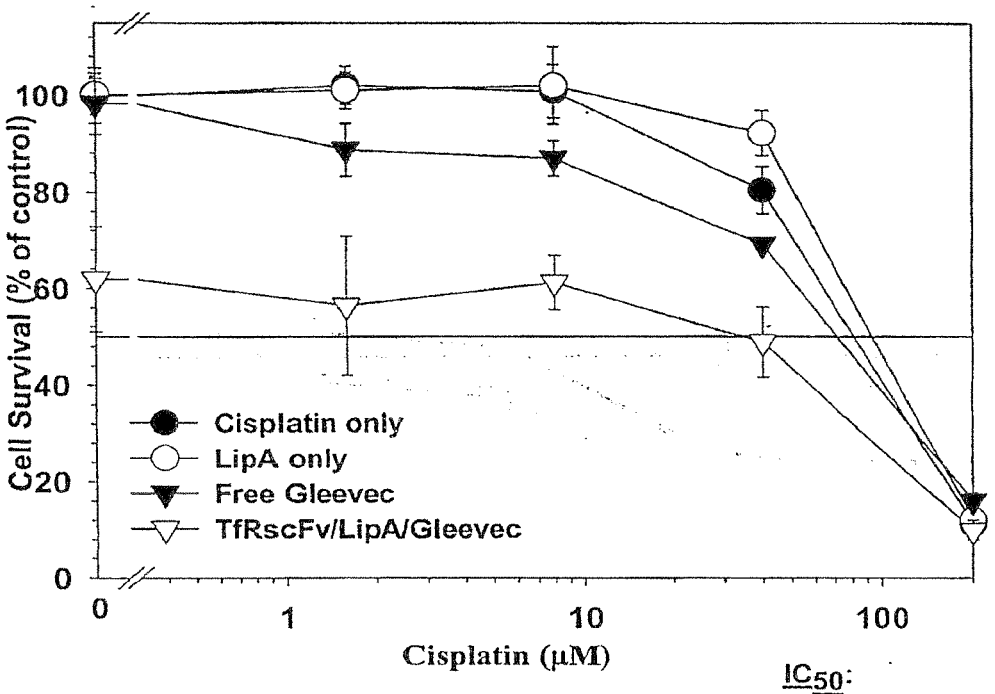
Fold Sensitization(compared to Gemzar)	
LipA only	1.0
Free Gleevec	20.0
scL-Gleevec	

Fold Sensitization(compared to Free Gleevec)	
LipA only	0.05
scL-Gleevec	

30uM Gleevec

Fig. 28A

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of B16-F10 Mouse Melanoma Cells to Cisplatin



	IC_{50}:
Cisplatin only	80 μM
LipA only	90 μM
Free Gleevec	70 μM
TfRscFv/LipA/Gleevec	33 μM

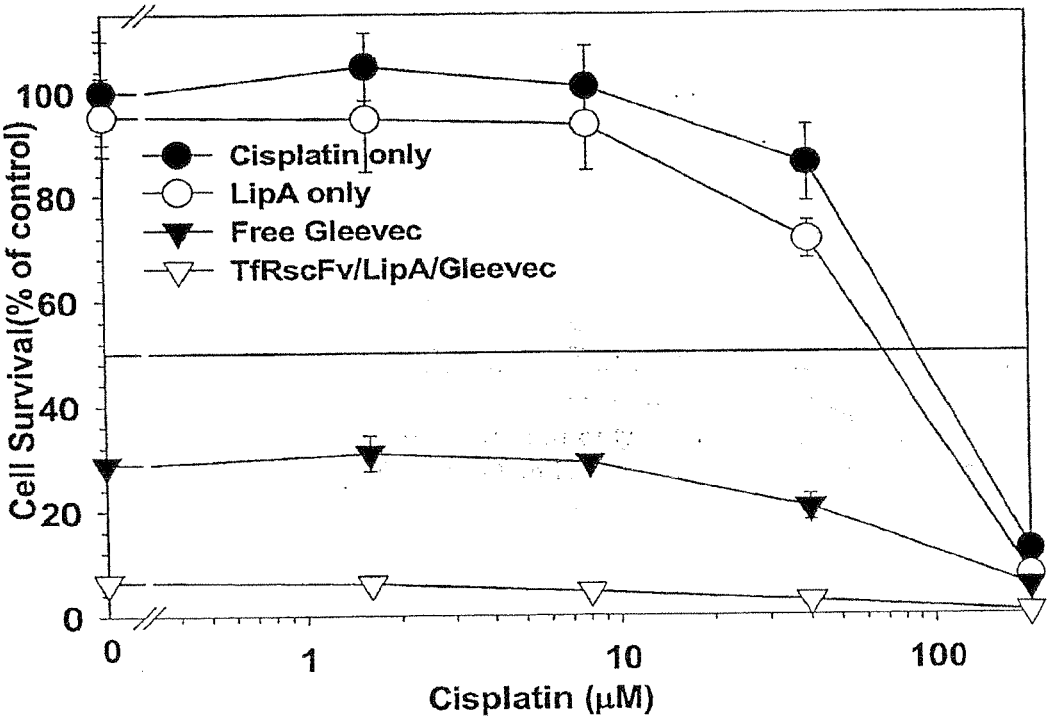
Fold Sensitization(compared to Cisplatin)	
LipA only	0.9
Free Gleevec	1.1
TfRscFv/LipA/Gleevec	2.4

Fold Sensitization(compared to Free Gleevec)	
LipA only	0.8
TfRscFv/LipA/Gleevec	2.1

20uM Gleevec

Fig. 28B

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of B16-F10 Mouse Melanoma Cells to Cisplatin

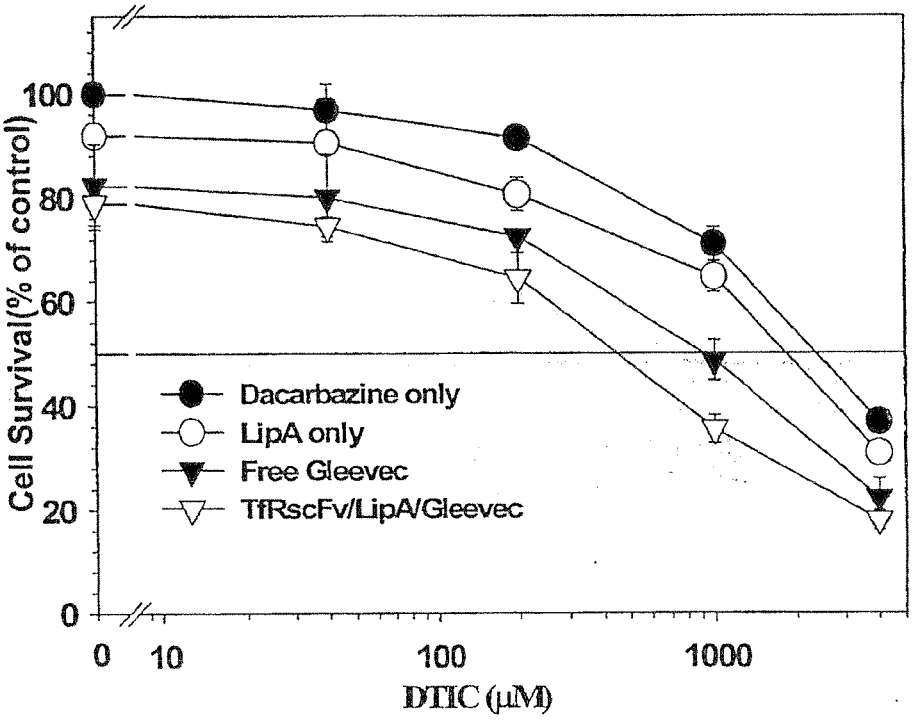


	IC_{50}:
Cisplatin only	89 μM
LipA only	68 μM
Free Gleevec	
TfRscFv/LipA/Gleevec	

30 μM Gleevec

Fig. 29A

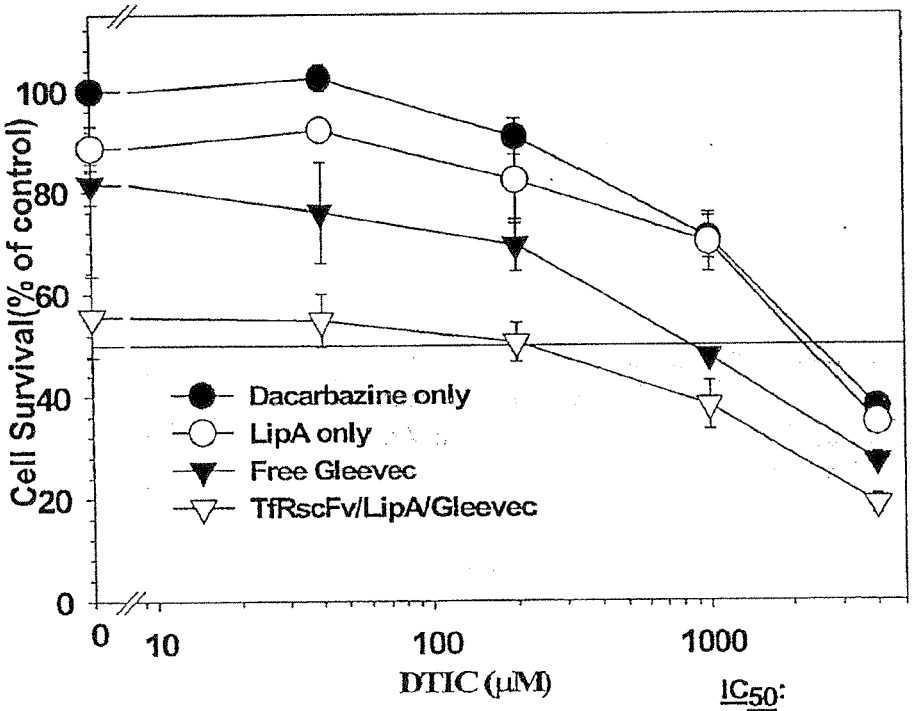
Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of B16-F10 Mouse Melanoma Cells to Dacarbazine (DTIC)



		IC_{50}:
	DTIC only	2300 μM
	LipA only	1800 μM
	Free Gleevec	900 μM
	TfRscFv/LipA/Gleevec	430 μM
	Fold Sensitization(compared to DTIC)	
	LipA only	1.3
	Free Gleevec	2.6
	TfRscFv/LipA/Gleevec	5.3
	Fold Sensitization(compared to Free Gleevec)	
	LipA only	0.5
15 μM Gleevec	TfRscFv/LipA/Gleevec	2.1

Fig. 29B

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of B16-F10 Mouse Melanoma Cells to Dacarbazine (DTIC)



	IC_{50}:
DTIC only	2300 μM
LipA only	2200 μM
Free Gleevec	830 μM
TfRscFv/LipA/Gleevec	200 μM

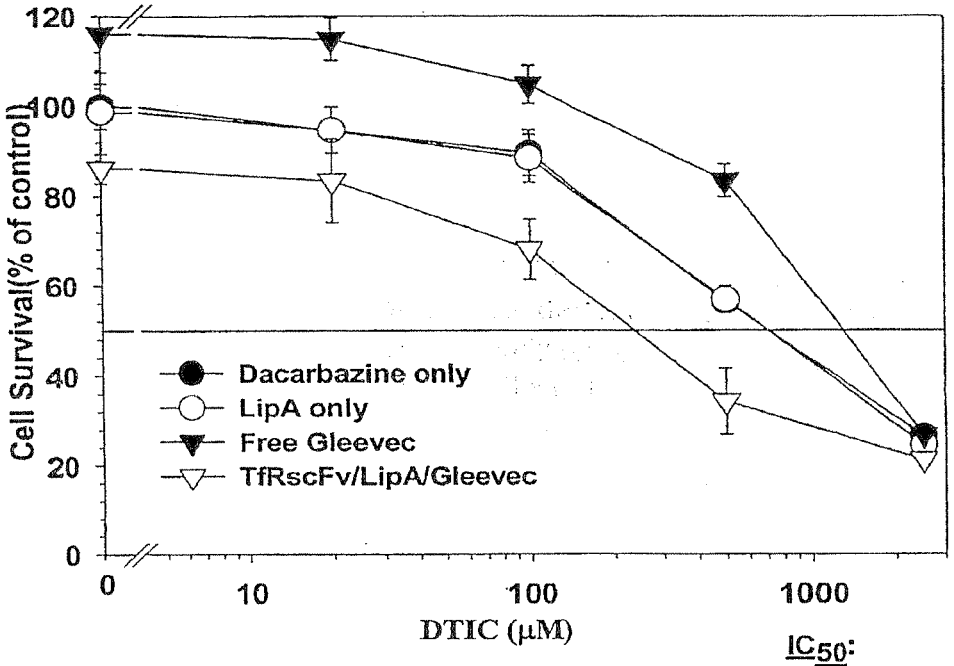
Fold Sensitization(compared to DTIC)	
LipA only	1.0
Free Gleevec	2.8
TfRscFv/LipA/Gleevec	11.5

20 μM Gleevec

Fold Sensitization(compared to Free Gleevec)	
LipA only	0.4
TfRscFv/LipA/Gleevec	4.2

Fig. 29C

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of B16-F10 Mouse Melanoma Cells to Dacarbazine (DTIC)

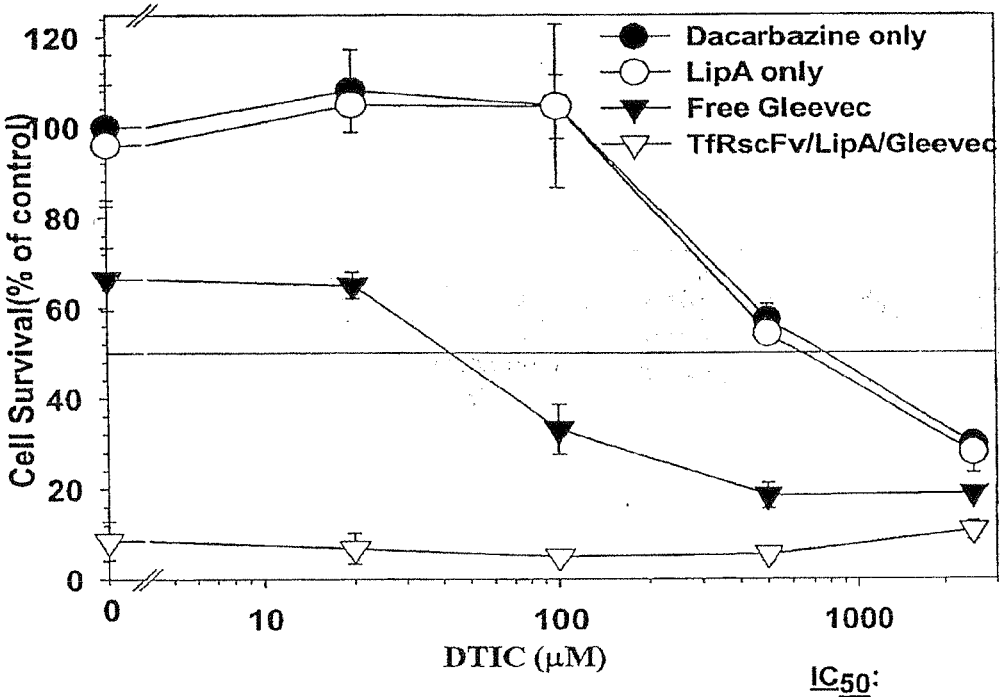


15 μM Gleevec

	IC_{50}:
DTIC only	700 μM
LipA only	700 μM
Free Gleevec	1300 μM
TfRscFv/LipA/Gleevec	230 μM
Fold Sensitization(compared to DTIC)	
LipA only	1.0
Free Gleevec	0.5
TfRscFv/LipA/Gleevec	3.0
Fold Sensitization(compared to Free Gleevec)	
LipA only	1.9
TfRscFv/LipA/Gleevec	5.7

Fig. 29D

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of B16-F10 Mouse Melanoma Cells to Dacarbazine (DTIC)



20 μM Gleevec

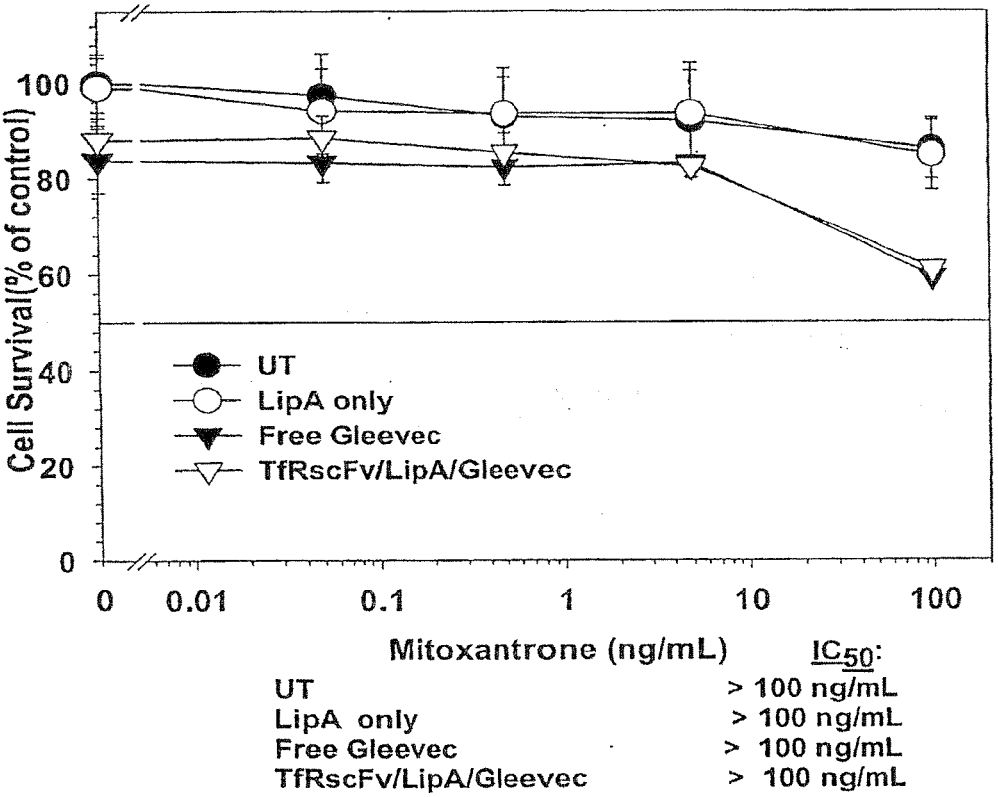
	IC_{50}:
DTIC only	740 μM
LipA only	630 μM
Free Gleevec	42 μM
TfRscFv/LipA/Gleevec	

Fold Sensitization(compared to DTIC)	
LipA only	1.2
Free Gleevec	17.6
TfRscFv/LipA/Gleevec	

Fold Sensitization(compared to Free Gleevec)	
LipA only	0.07
TfRscFv/LipA/Gleevec	> 185

Fig. 30A

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of H500 Human Normal Skin Fibroblasts to Mitoxantrone

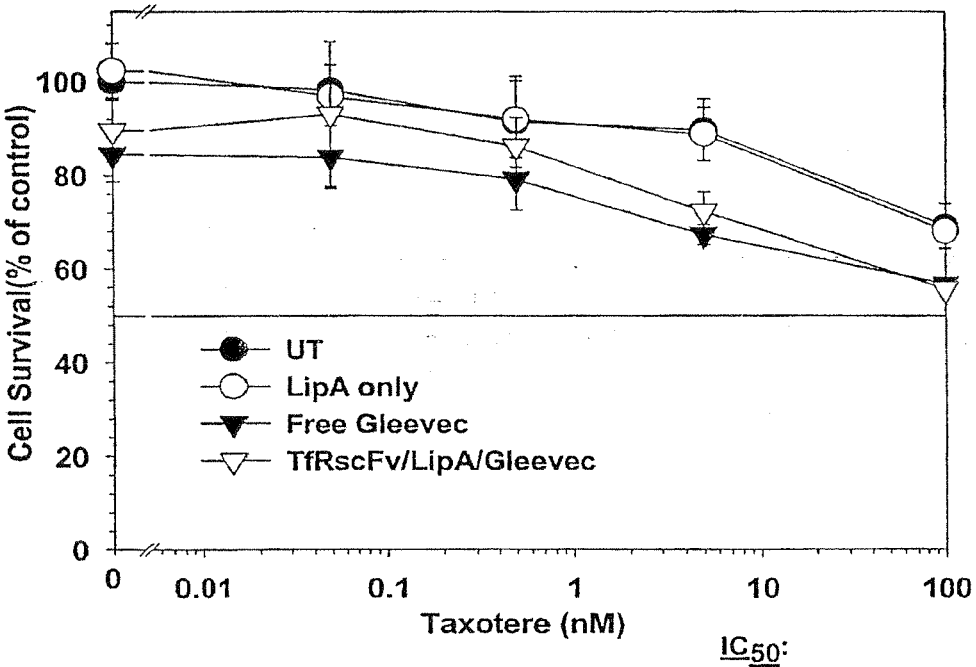


	IC_{50}:
UT	> 100 ng/mL
LipA only	> 100 ng/mL
Free Gleevec	> 100 ng/mL
TfRscFv/LipA/Gleevec	> 100 ng/mL

20 μM Gleevec

Fig. 30B

Effect of Tumor Targeting Liposomal Delivery of Gleevec on Sensitization of H500 Human Normal Skin Fibroblasts to Taxotere



	IC_{50}:
UT	>100 nM
LipA only	>100 nM
Free Gleevec	>100 nM
TfRscFv/LipA/Gleevec	>100 nM

20uM Gleevec

Fig. 31

Tumor Growth Inhibition of Lung Melanoma Metastases by the Combination of scL/Gleevec Plus CDDP

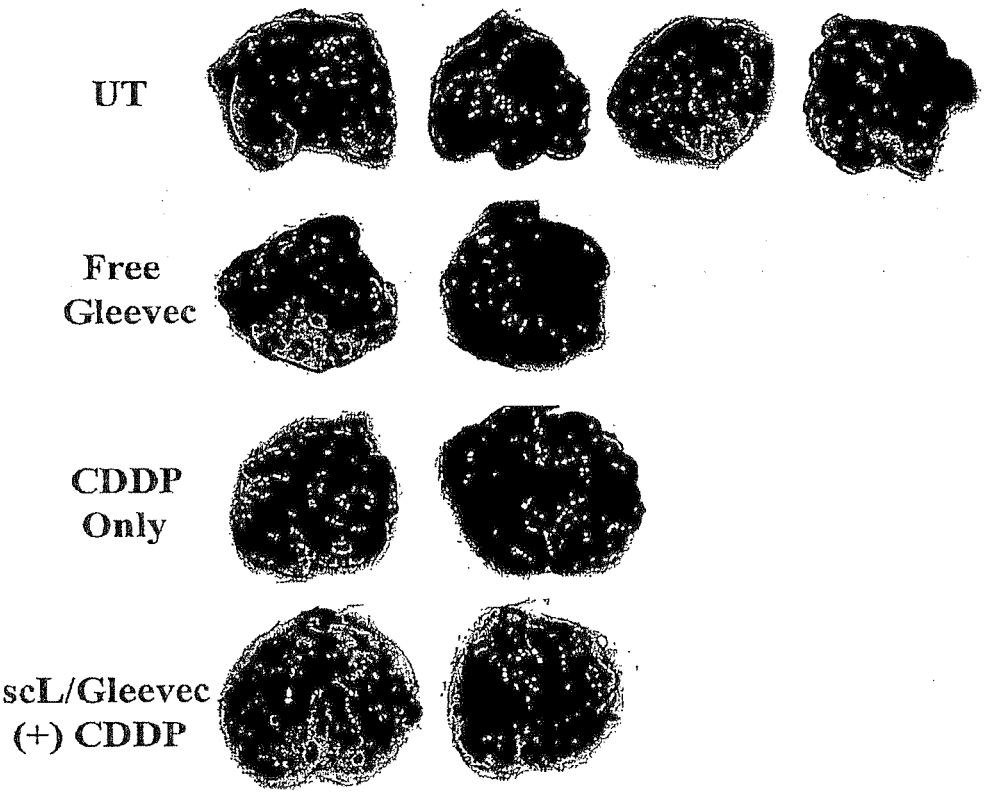
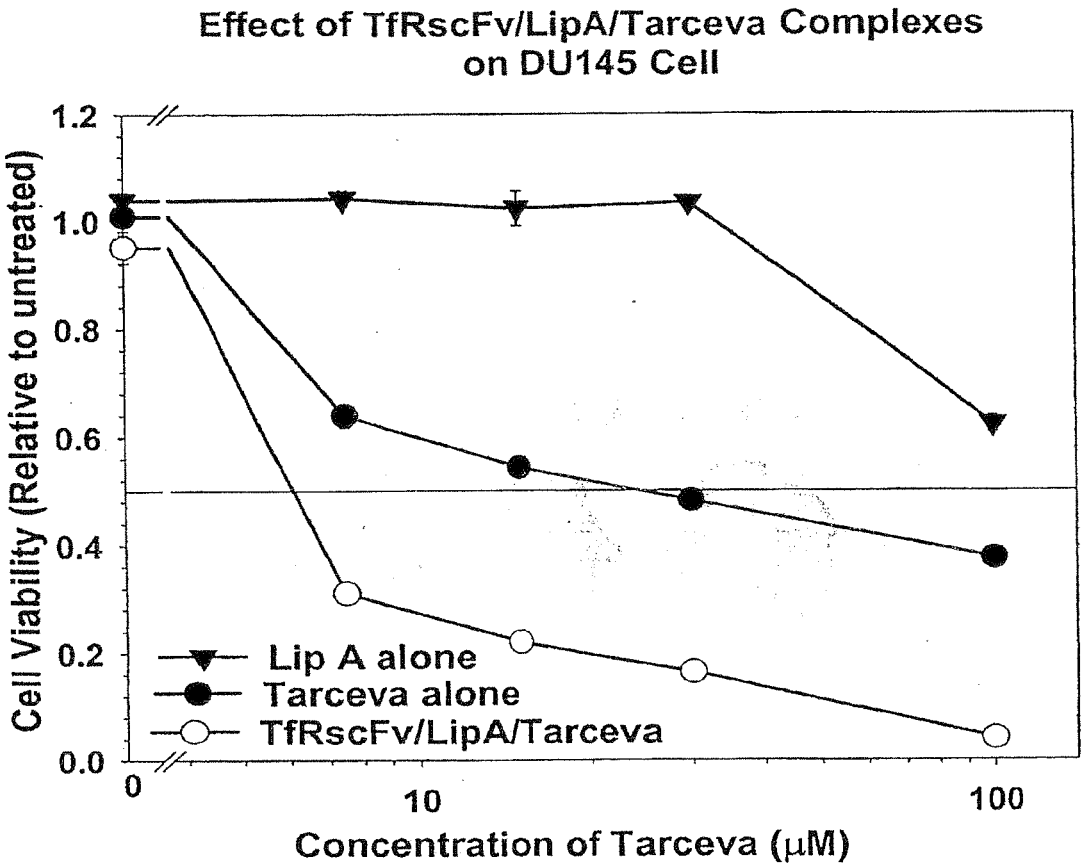
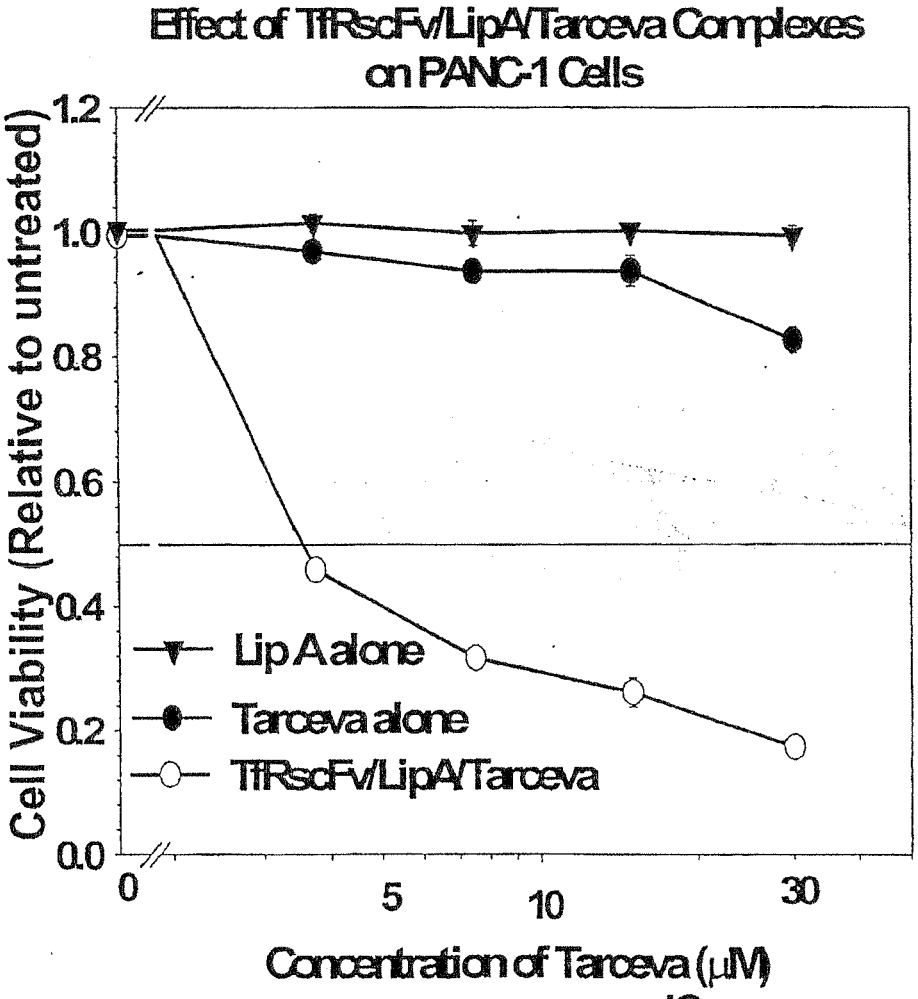


Fig. 32A



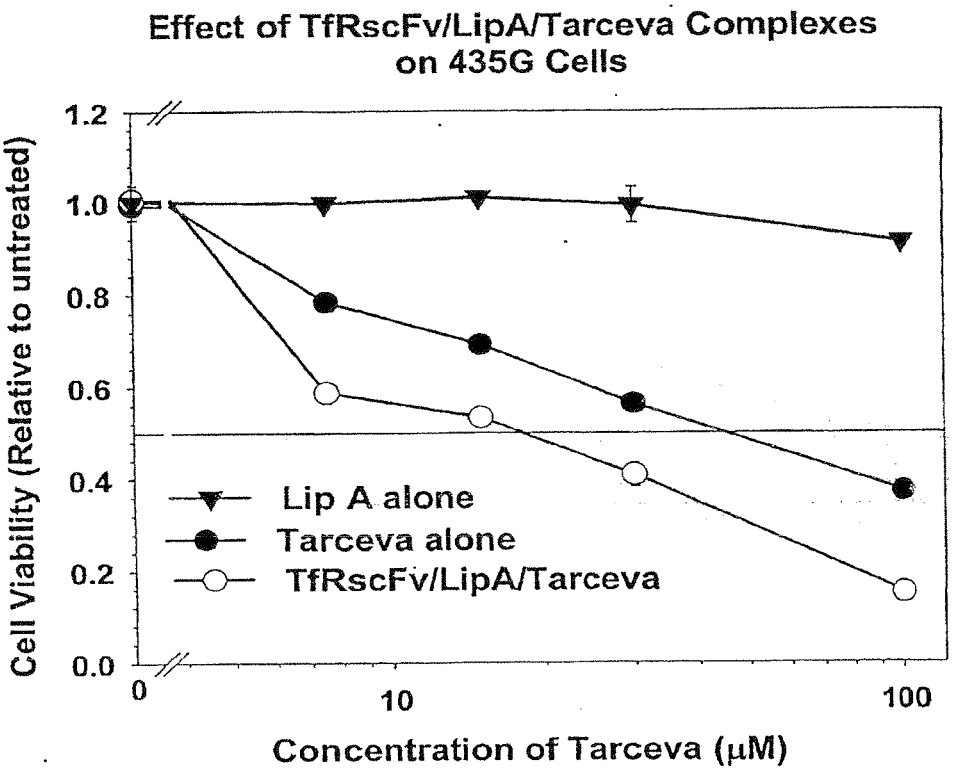
	IC_{50}	
Lip A alone	> 100	μM
Tarceva alone	= 22	μM
TfRscFv/LipA/Tarceva	= 4	μM

Fig. 32B



		IC_{50}
Lip A alone	>	30 μM
Tarceva alone	>	30 μM
TfRscFv/LipA/Tarceva	=	3.5 μM

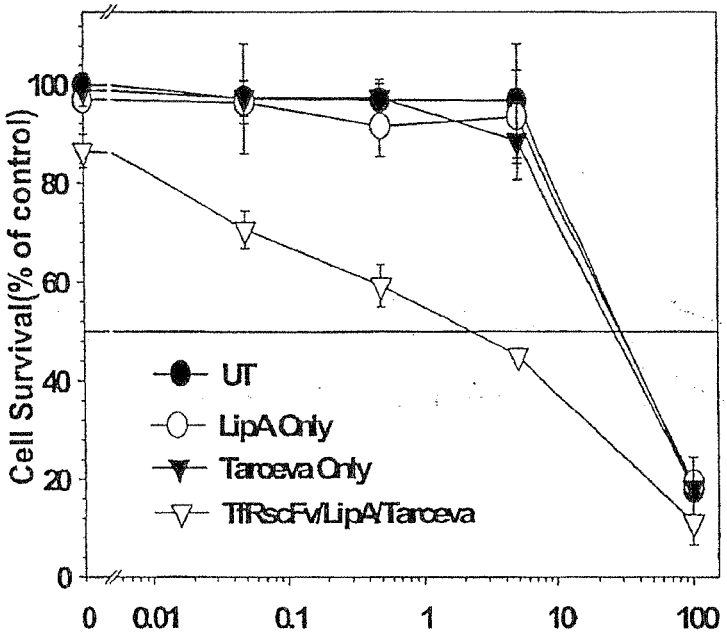
Fig. 32C



	IC_{50}	
Lip A alone	> 100	μM
Tarceva alone	= 40	μM
TfRscFv/LipA/Tarceva	= 18	μM

Fig. 33A

Effect of Tumor Targeting Liposomal Delivery of Tarceva on Sensitization of DU145 Human Prostate Cancer Cells to Mitoxantrone

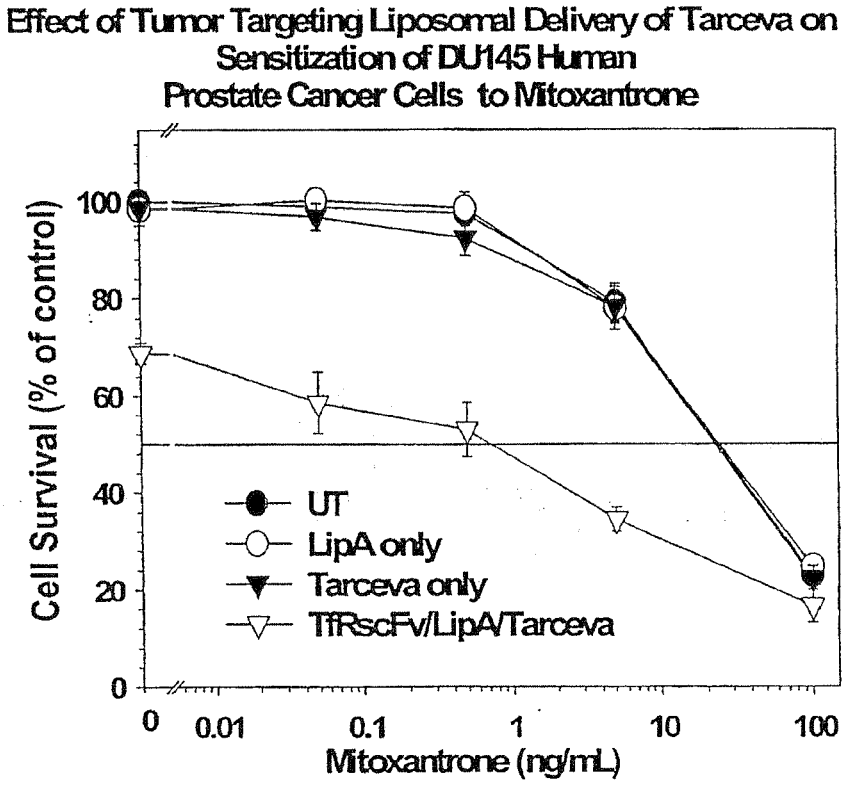


	IC_{50}		Fold Sensitization(compared to UT)
UT	30.0 ng/mL		
LipA only	30.0 ng/mL	LipA only	1.0
Tarceva only	28.0 ng/mL	Tarceva only	1.07
TfRscFv/LipA/Tarceva	2.2 ng/mL	TfRscFv/LipA/Tarceva	13.6

Fold Sensitization(compared to Free Tarceva)	
TfRscFv/LipA/Tarceva	12.7

3.75uM Tarceva

Fig. 33B



	IC_{50}	
UT	22.0	ng/mL
LipA only	24.0	ng/mL
Tarceva only	24.0	ng/mL
TfRscFv/LipA/Tarceva	0.7	ng/mL

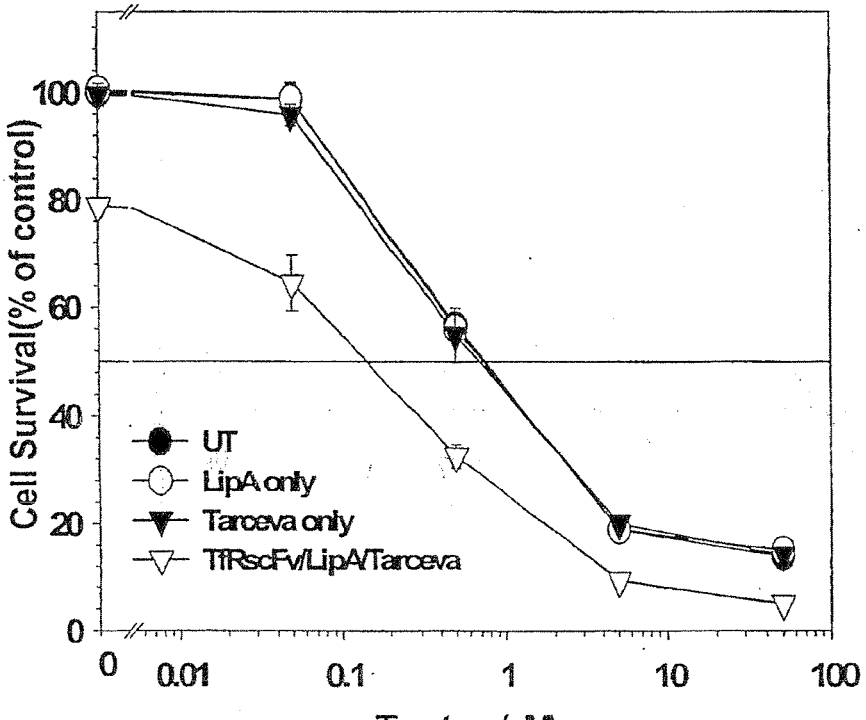
Fold Sensitization(compared to UT)	
LipA only	0.9
Tarceva only	0.9
TfRscFv/LipA/Tarceva	31.4

Fold Sensitization(compared to Free Tarceva)	
TfRscFv/LipA/Tarceva	34.2

7uM Tarceva

Fig. 34A

Effect of Tumor Targeting Liposomal Delivery of Tarceva on Sensitization of MDA-MB-435 Human Melanoma Cells to Taxotere



	IC_{50}:	
UT	0.75	nM
LipA only	0.75	nM
Tarceva only	0.70	nM
TfRscFv/LipA/Tarceva	0.15	nM

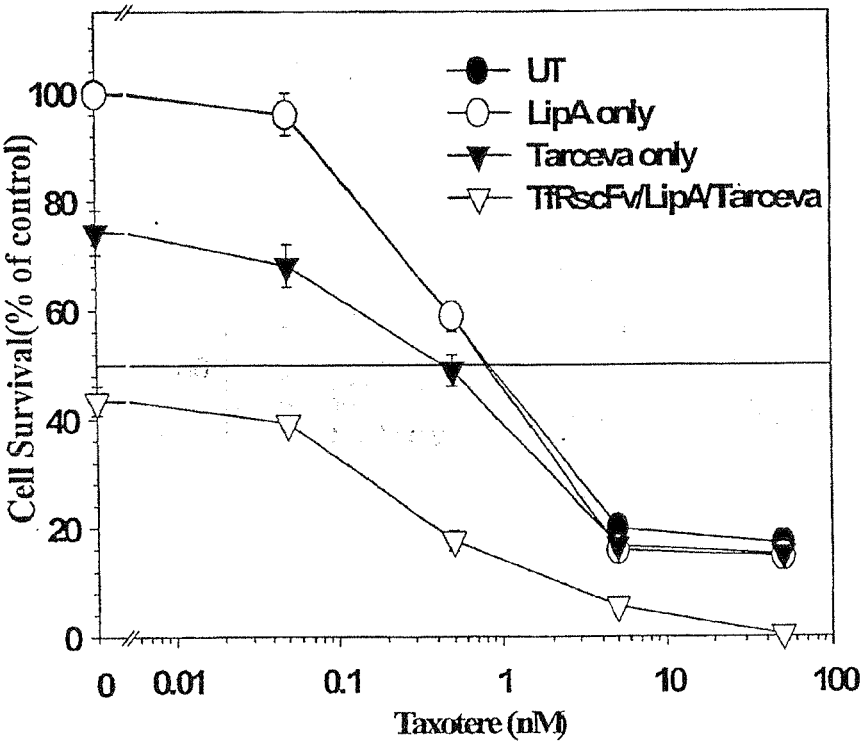
Fold Sensitization(compared to UT)	
LipA only	1.0
Tarceva only	1.07
TfRscFv/LipA/Tarceva	5.0

Fold Sensitization(compared to Free Tarceva)	
TfRscFv/LipA/Tarceva	4.6

3.75uM Tarceva

Fig. 34B

Effect of Tumor Targeting Liposomal Delivery of Tarceva on Sensitization of MDA-MB-435 Human Melanoma to Taxotere

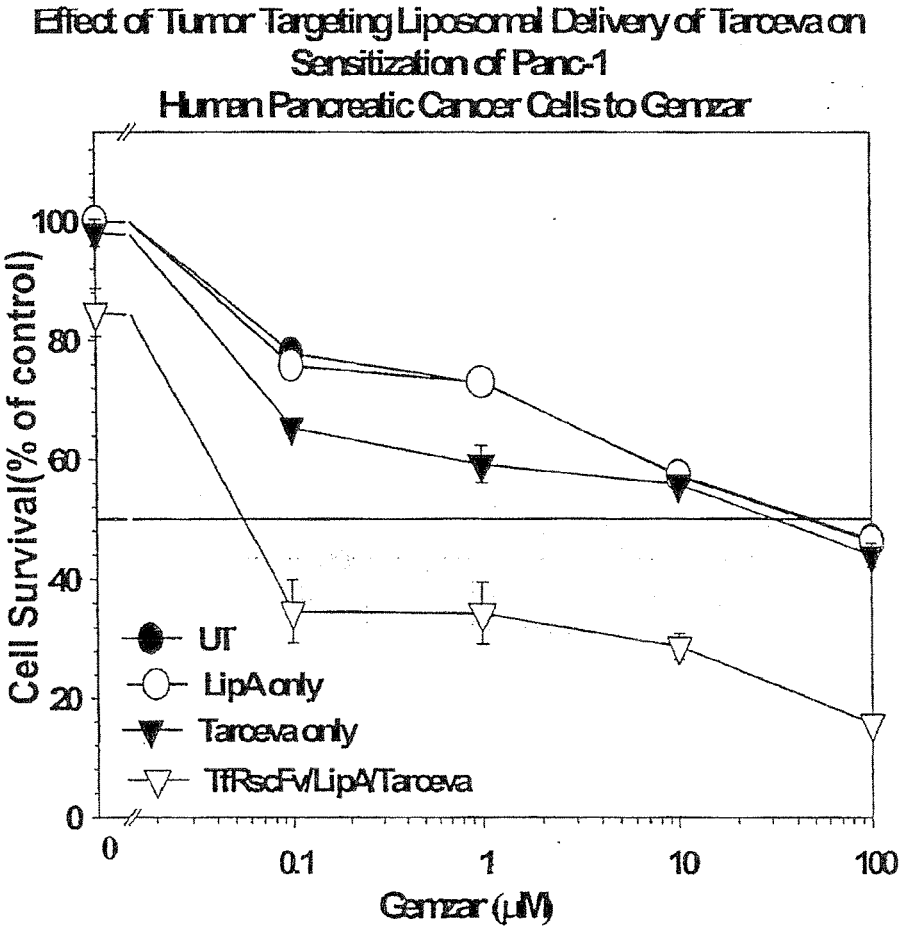


	IC_{50}:
UT	0.85 nM
LipA only	0.80 nM
Tarceva only	0.50 nM
TfRscFv/LipA/Tarceva	<0.006 nM

Fold Sensitization(compared to UT)	
LipA only	1.06
Tarceva only	1.7
TfRscFv/LipA/Tarceva	>140

7.5uM Tarceva

Fig. 35

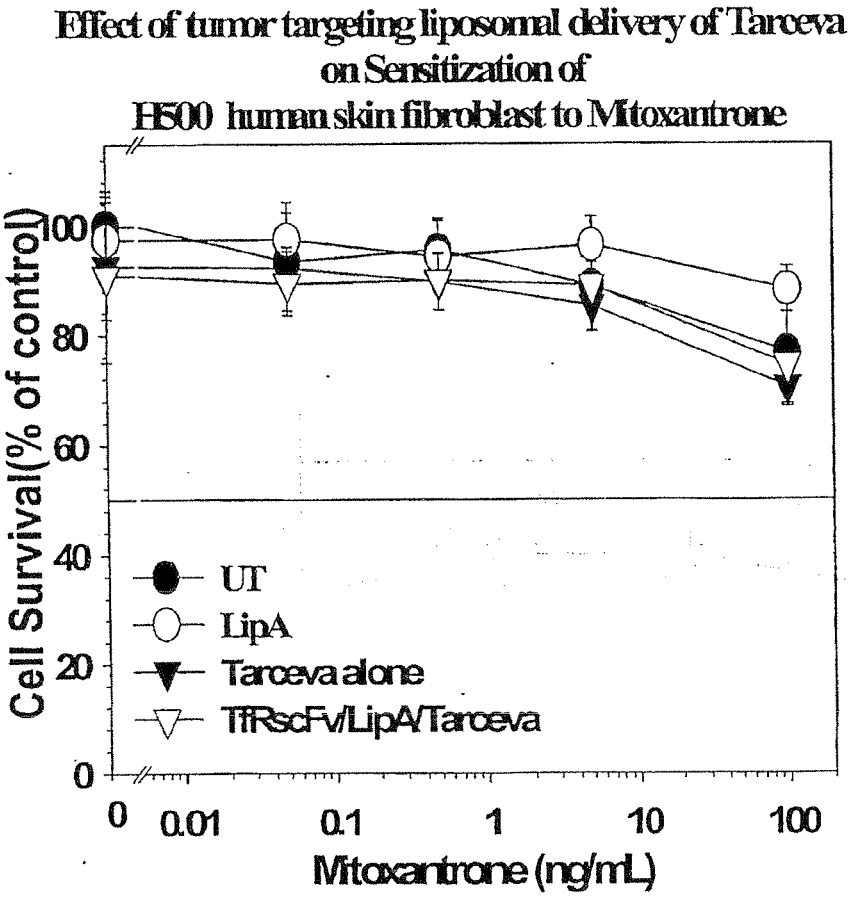


	IC_{50}	Fold Sensitization(compared to UT)	
UT	45.0 μM	LipA only	1.0
LipA only	45.0 μM	Tarceva only	1.5
Tarceva only	30.0 μM	TfRscFv/LipA/Tarceva	818.0
TfRscFv/LipA/Tarceva	0.055 μM		

Fold Sensitization(compared to Free Tarceva)	
TfRscFv/LipA/Tarceva	545.0

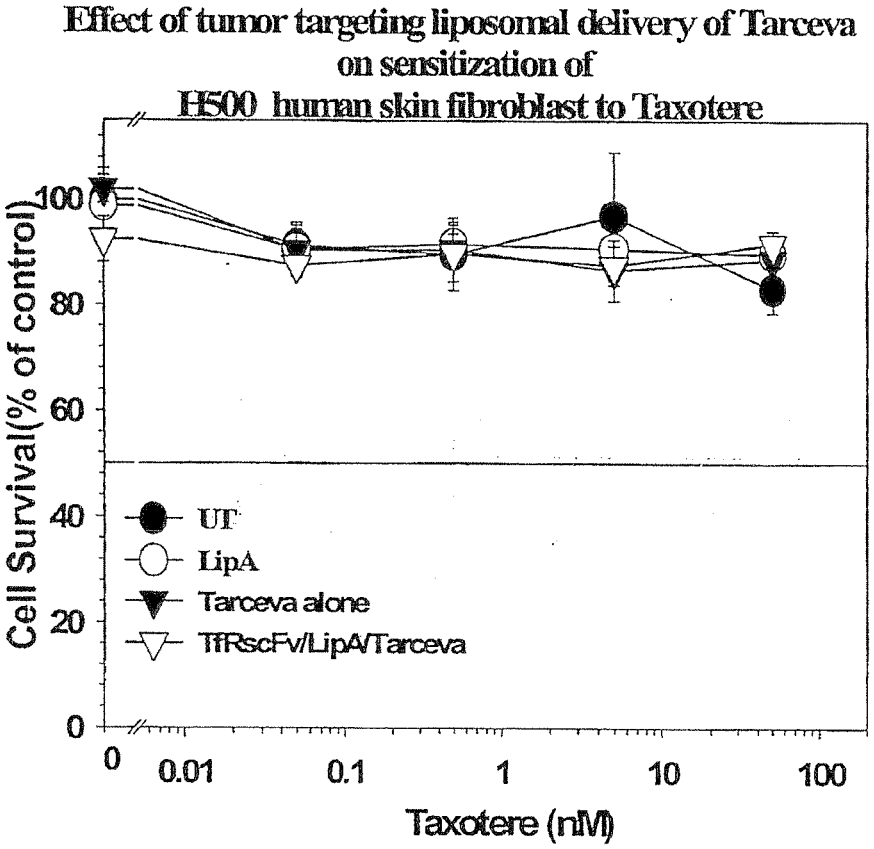
7.5uM Tarceva

Fig. 36A



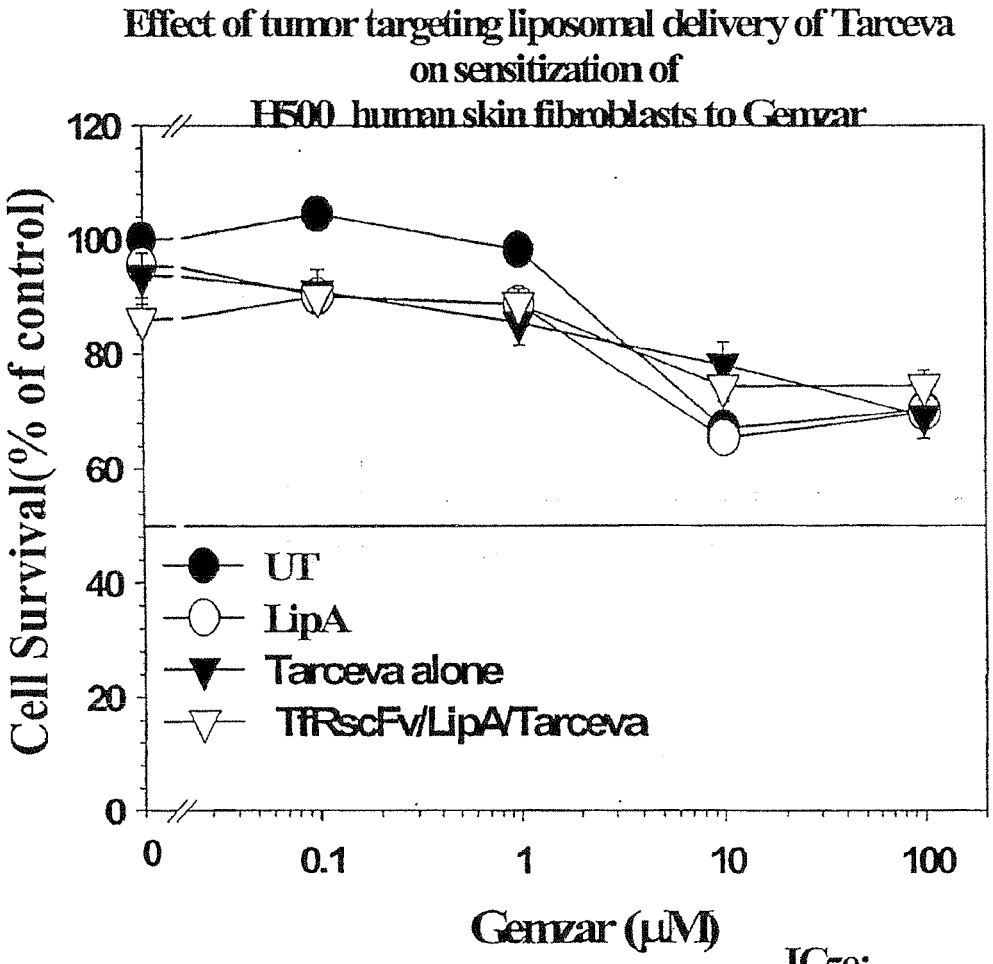
	IC_{50}:
UT	>100 ng/mL
LipA	>100 ng/mL
Tarceva alone	>100 ng/mL
TfRscFv/LipA/Tarceva	>100 ng/mL

Fig. 36B



	IC_{50}:
UT	>50 nM
LipA	>50 nM
Tarceva alone	>50 nM
TfRscFv/LipA/Tarceva	>50 nM

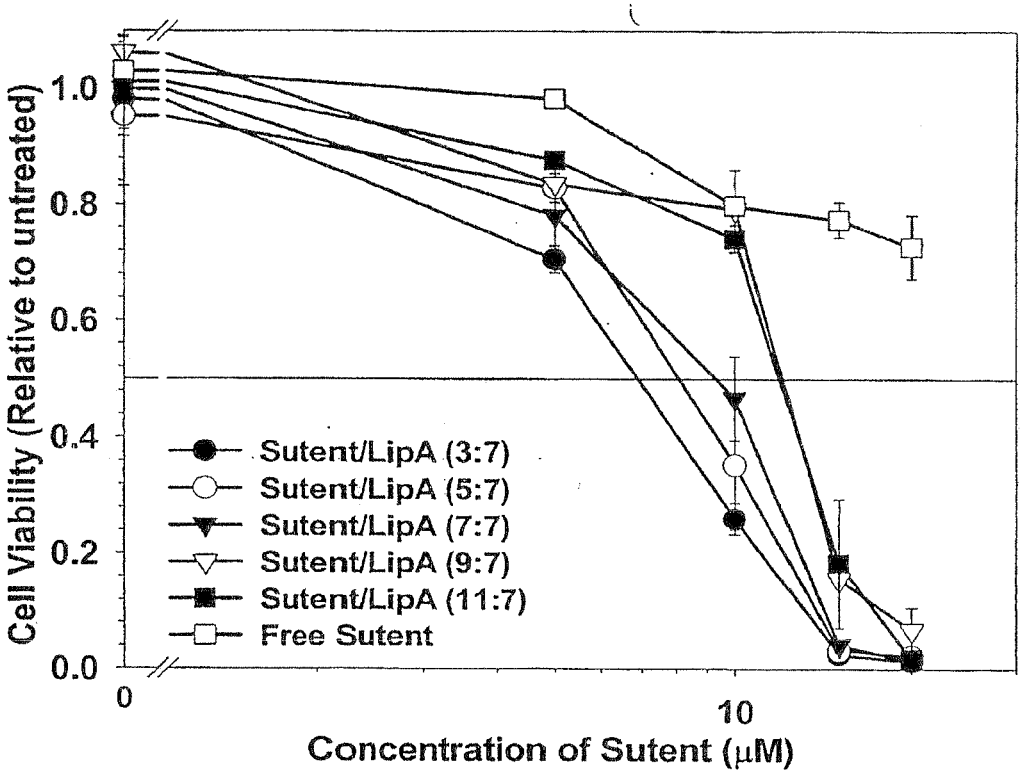
Fig. 36C



	IC_{50}:
UT	>100 μM
LipA	>100 μM
Tarceva alone	>100 μM
TfRscFv/LipA/Tarceva	>100 μM

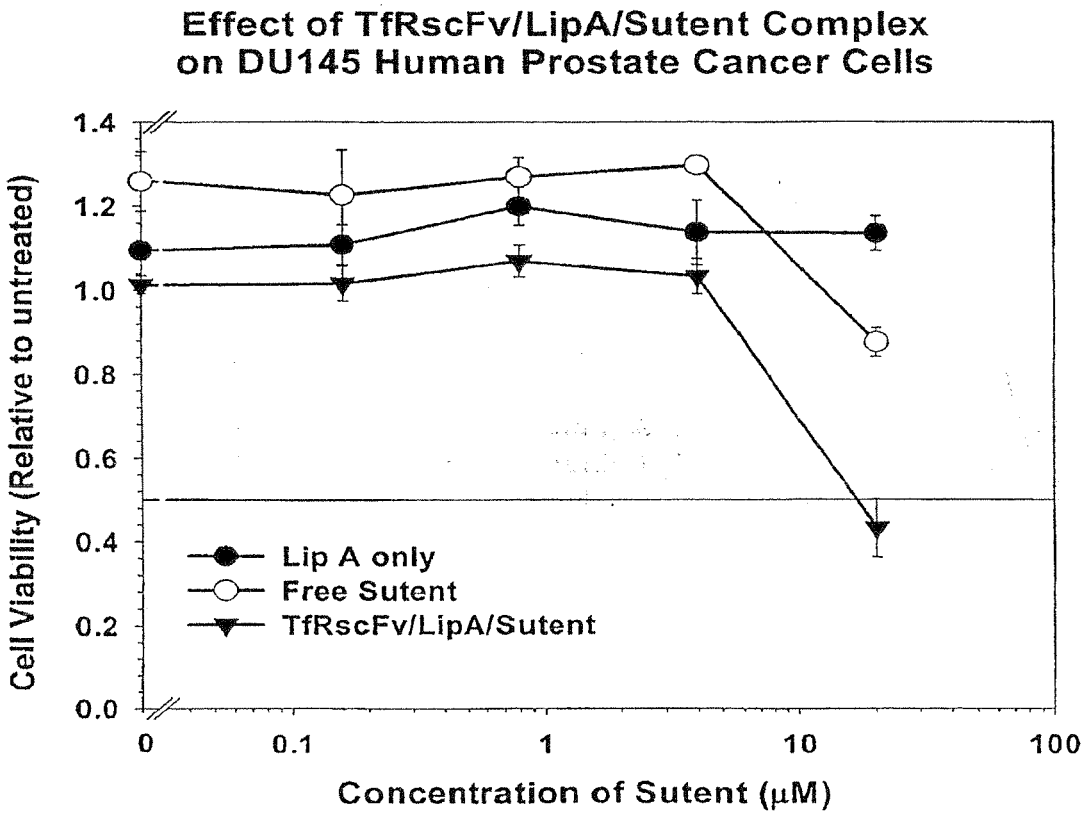
Fig. 37

Effect of Different Sutent/LipA Ratios in the TfRscFv/LipA/Sutent Complex on DU145 Human Prostate Cancer Cells



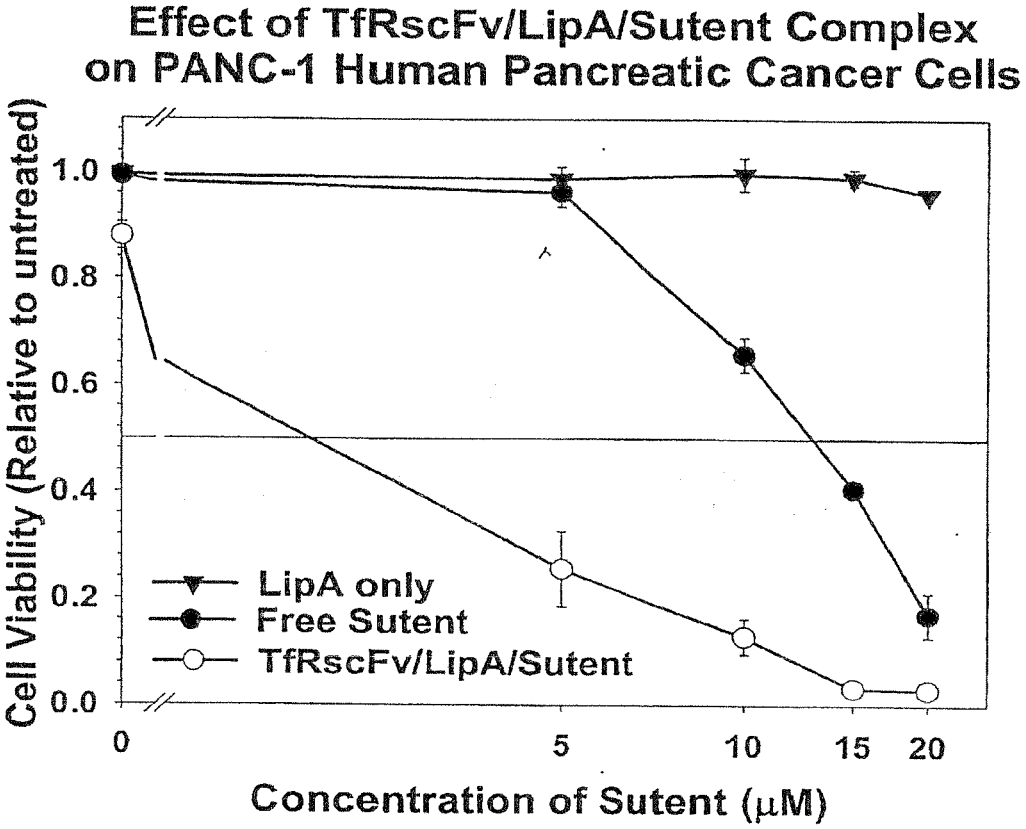
	IC_{50}
Sutent/LipA (3:7)	6.8 μM
Sutent/LipA (5:7)	8.0 μM
Sutent/LipA (7:7)	9.2 μM
Sutent/LipA (9:7)	12 μM
Sutent/LipA (11:7)	12 μM
Free Sutent	>20 μM

Fig. 38A



	IC_{50}
LipA only	>20μM
Free Sutent	>20μM
TfRscFv/LipA/Sutent	15μM

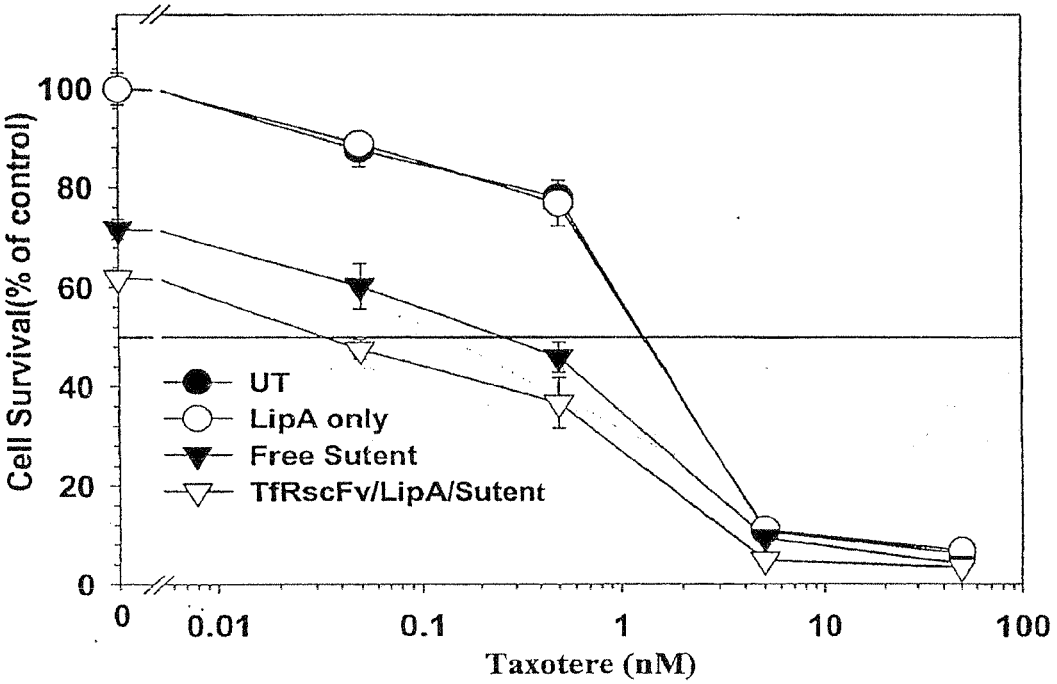
Fig. 38B



	IC_{50}
LipA only	>20 μM
Free Sutent	12 μM
TfRscFv/LipA/Sutent	3 μM

Fig 39A

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of MDA-MB-435 Human Melanoma Cells to Taxotere



	IC_{50}:
UT	1.3 nM
LipA only	1.3 nM
Free Sutent	0.25 nM
TfRscFv/LipA/Sutent	0.03 nM

Fold Sensitization(compared to UT)

LipA only	1.0
Free Sutent	5.2
TfRscFv/LipA/Sutent	43.3

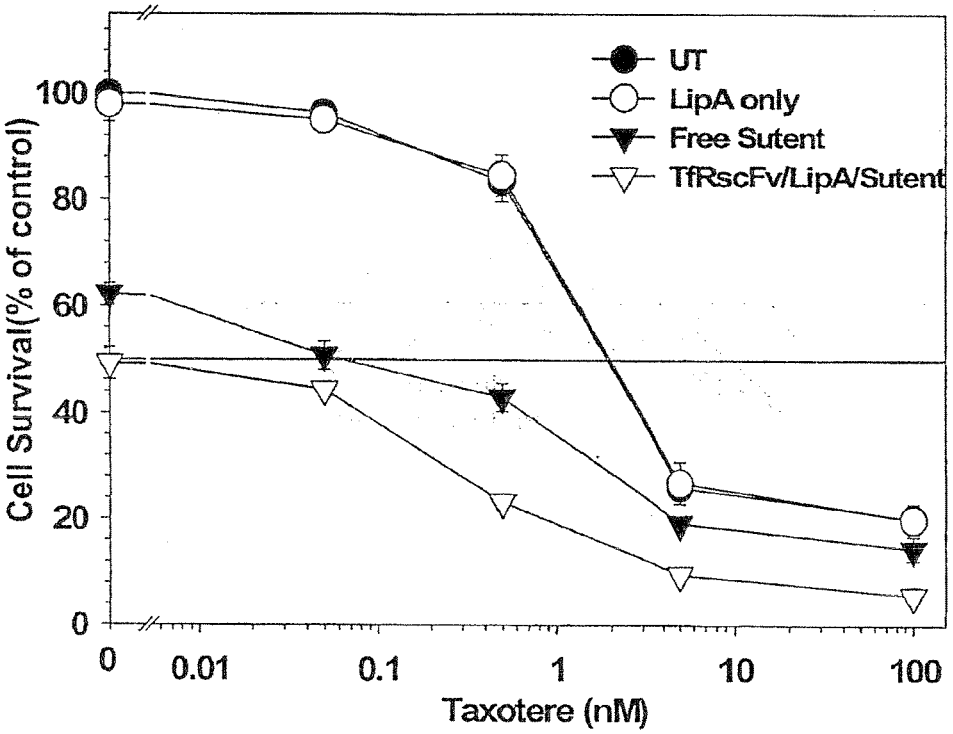
Fold Sensitization(compared to Free Sutent)

TfRscFv/LipA/Sutent	8.3

2.5uM Sutent

Fig. 39B

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of MDA-MB-435G Human Melanoma cells to Taxotere



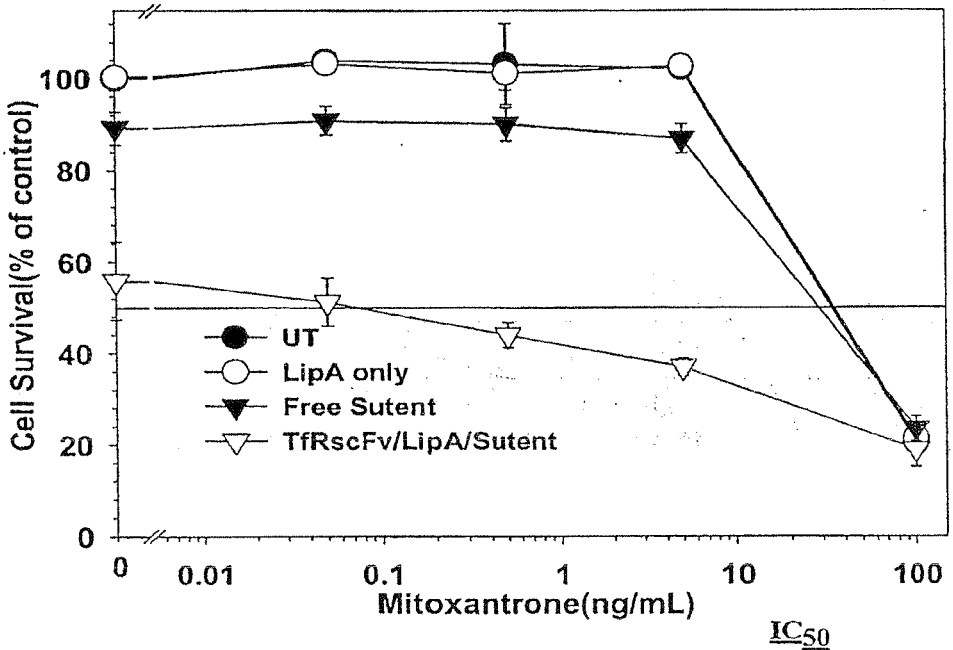
	IC_{50}:
UT	2.0 nM
LipA only	2.0 nM
Free Sutent	0.06 nM
TfRscFv/LipA/Sutent	

Fold Sensitization (Compared to UT)	
LipA only	1.0
Free Sutent	50.0
TfRscFv/LipA/Sutent	>300

5 μM Sutent

Fig. 40

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of DU145 Human Prostate Cancer Cells to Mitoxantrone



	IC_{50}
UT	32.0 ng/mL
LipA only	32.0 ng/mL
Free Sutent	28.0 ng/mL
TfRscFv/LipA/Sutent	0.06 ng/mL

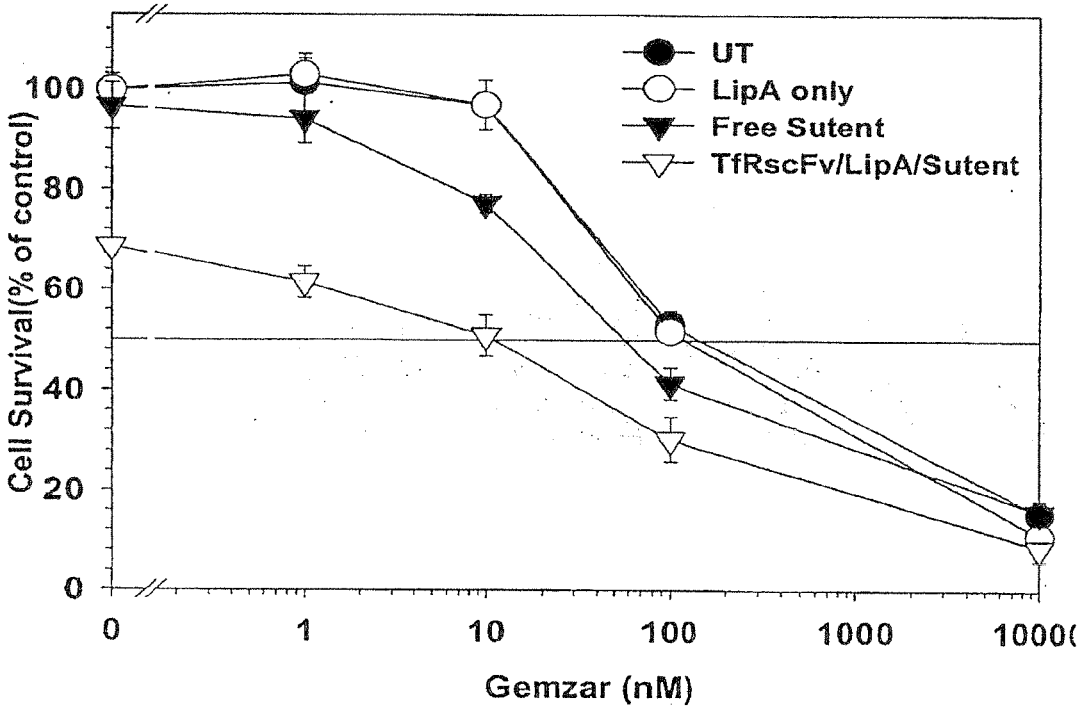
Fold Sensitization (compared to UT)	
LipA only	1.0
Free Sutent	1.14
TfRscFv/LipA/Sutent	533.3

Fold Sensitization(compared to Free Sutent)	
TfRscFv/LipA/Sutent	466.7

5 μM Sutent

Fig. 41

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of Panc-1Human Pancreatic Cancer Cells to Gemzar



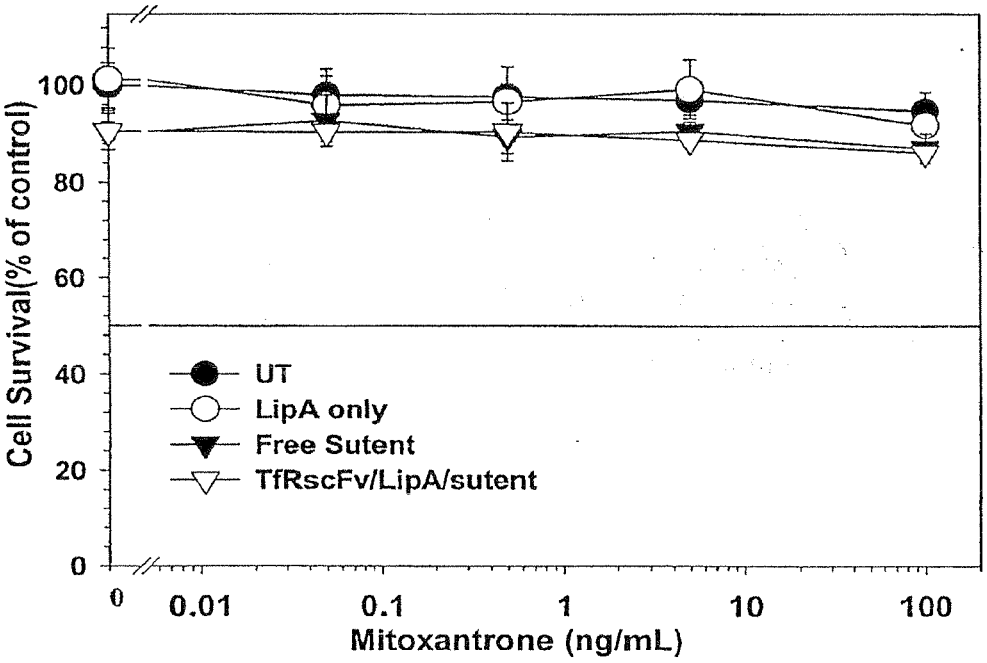
	IC_{50}
UT	150 nM
LipA only	130 nM
Free Sutent	65 nM
TfRscFv/LipA/Sutent	11 nM

Fold Sensitization(compared to UT)	
LipA only	1.2
Free Sutent	2.3
TfRscFv/LipA/Sutent	13.6

Fold Sensitization(compared to Free Sutent)	
TfRscFv/LipA/Sutent	5.9

Fig 42A

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of H500 Human Normal Skin Fibroblasts to Mitoxantrone

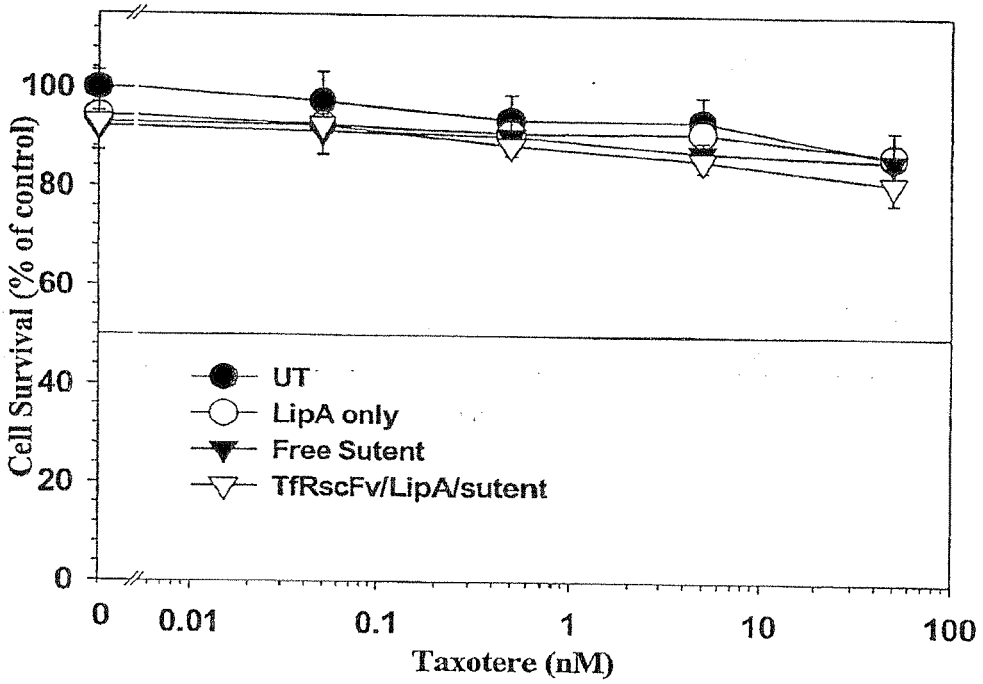


	IC_{50}:
UT	> 100 ng/mL
LipA only	> 100 ng/mL
Free Sutent	> 100 ng/mL
TfRscFv/LipA/sutent	> 100 ng/mL

2.5uM Sutent

Fig. 42B

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of H500 Human Normal Skin Fibroblasts to Taxotere

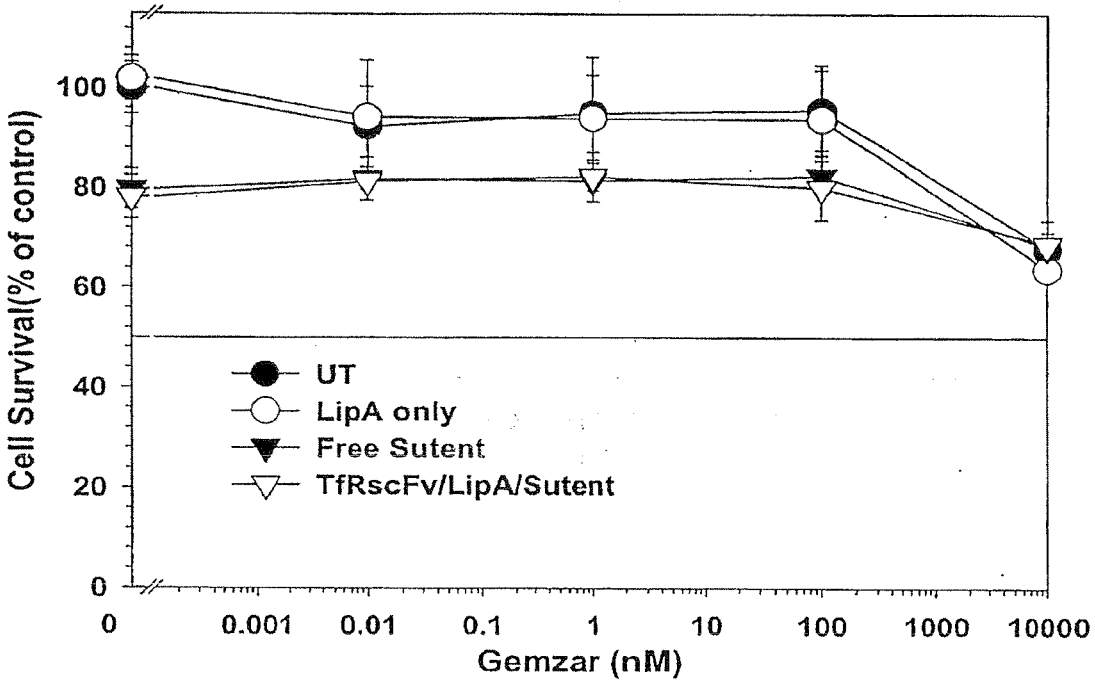


	IC_{50}:
UT	>100 nM
LipA only	>100 nM
Free Sutent	>100 nM
TfRscFv/LipA/sutent	>100 nM

2.5uM Sutent

Fig. 42C

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of H500 Human Normal Skin Fibroblasts to Gemzar

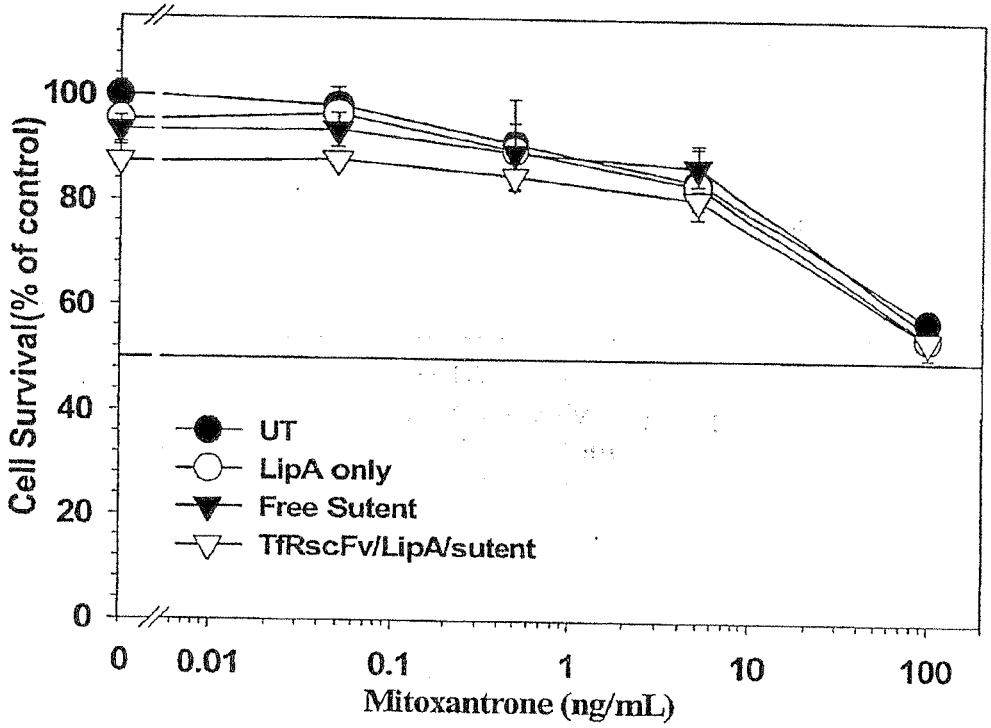


	IC_{50}:
UT	>10000 nM
LipA only	>10000 nM
Free Sutent	>10000 nM
TfRscFv/LipA/Sutent	>10000 nM

5uM Sutent

Fig. 43A

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of IMR-90 Human Normal Lung Fibroblasts to Mitoxantrone

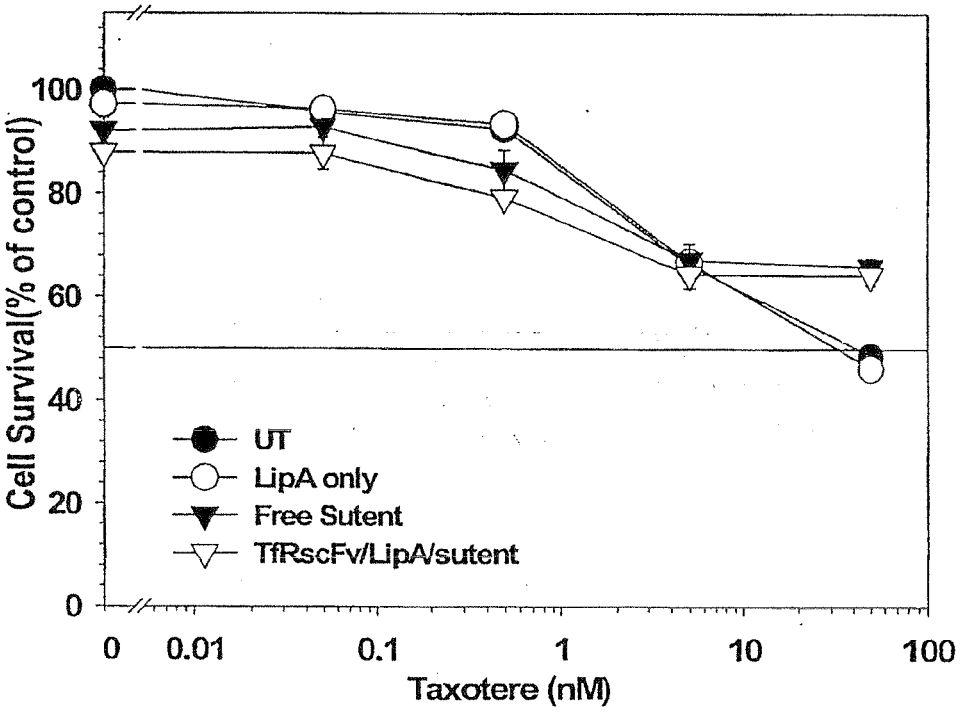


	IC_{50}:
UT	> 100 ng/mL
LipA only	> 100 ng/mL
Free Sutent	> 100 ng/mL
TfRscFv/LipA/sutent	> 100 ng/mL

2.5uM Sutent

Fig. 43B

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of IMR-90 Human Normal Lung Fibroblasts to Taxotere

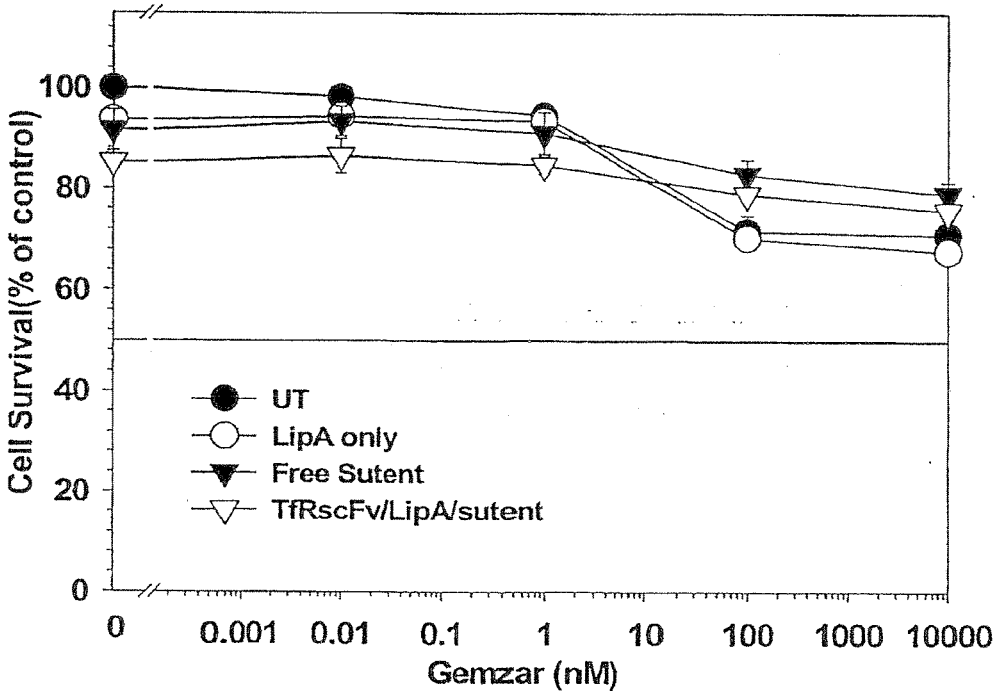


	IC_{50}:
UT	42 nM
LipA only	32 nM
Free Sutent	> 100 nM
TfRscFv/LipA/sutent	> 100 nM

2.5uM Sutent

Fig. 43C

Effect of Tumor Targeting Liposomal Delivery of Sutent on Sensitization of IMR-90 Human Normal Lung Fibroblasts to Gemzar

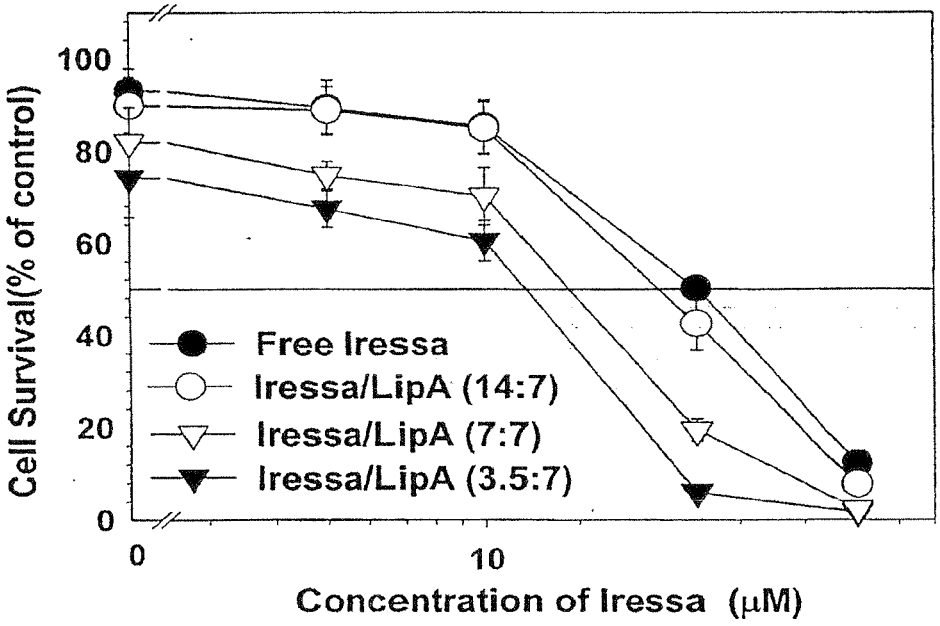


	IC_{50}:
UT	>10000 nM
LipA only	>10000 nM
Free Sutent	>10000 nM
TfRscFv/LipA/sutent	>10000 nM

2.5uM Sutent

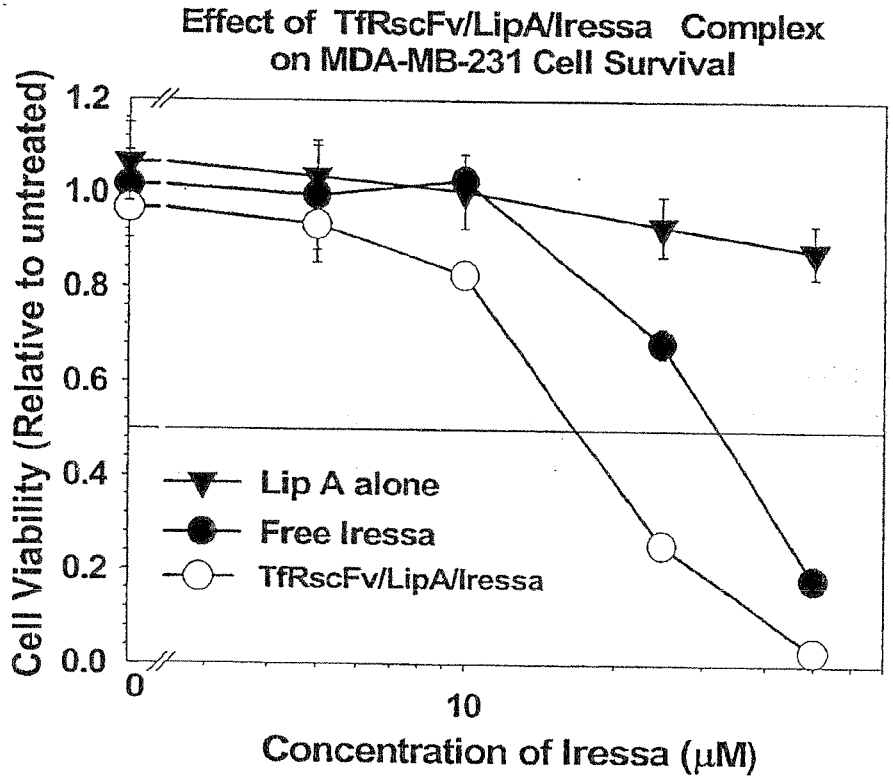
Fig. 44

Comparison of Effects of TfRscFv/LipA/Iressa Complexes at Different Ratios of Iressa to LipA in MDA-MB-231 cells



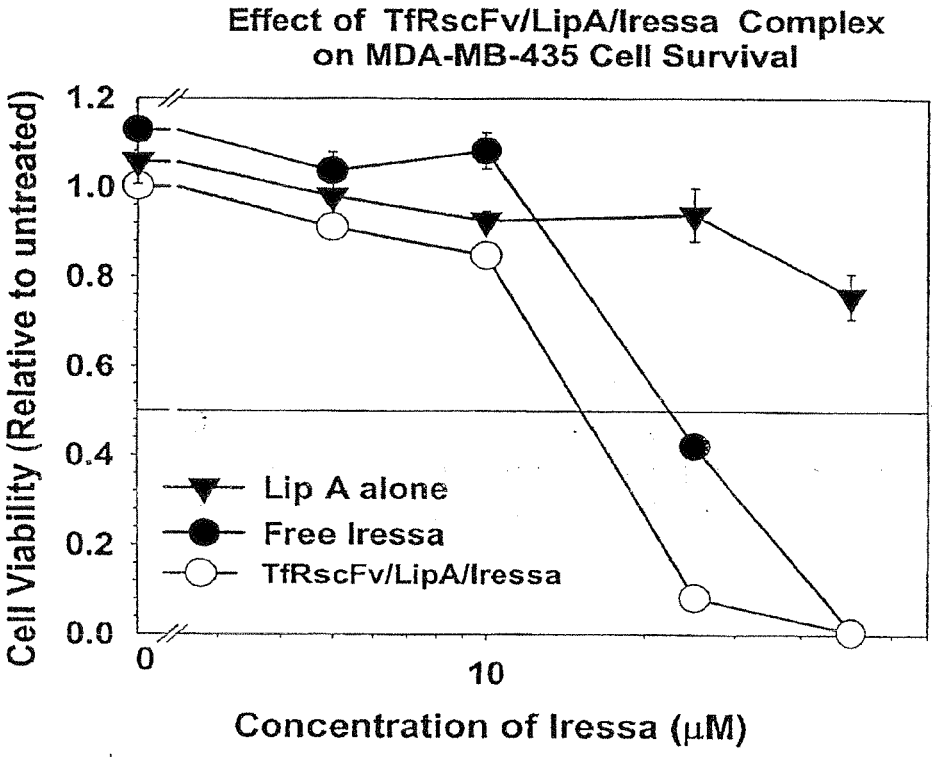
	IC_{50}:
Free Iressa	26 μM
Iressa/LipA (14:7)	22 μM
Iressa/LipA (7:7)	14 μM
Iressa/LipA (3.5:7)	12 μM

Fig. 45A



	IC_{50}
Lip A alone	> 50 μM
Free Iressa	= 32 μM
TfRscFv/LipA/Iressa	= 16 μM

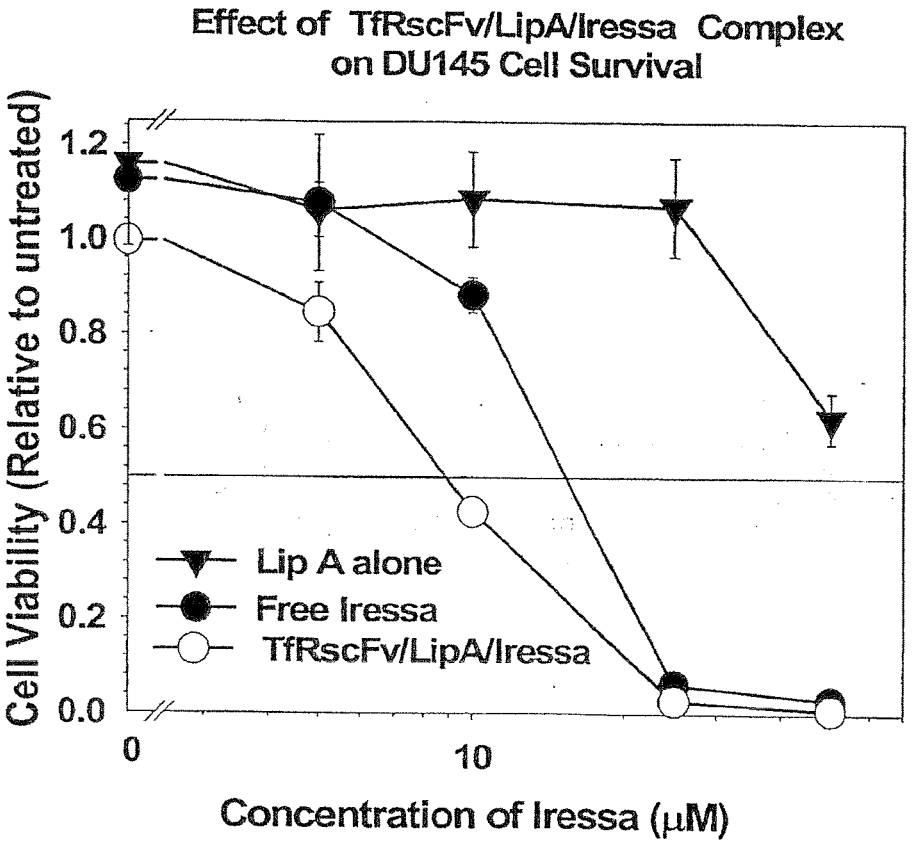
Fig. 45B



	IC_{50}
Lip A alone	> 50 μM
Free Iressa	= 22 μM
TfRscFv/LipA/Iressa	= 15 μM

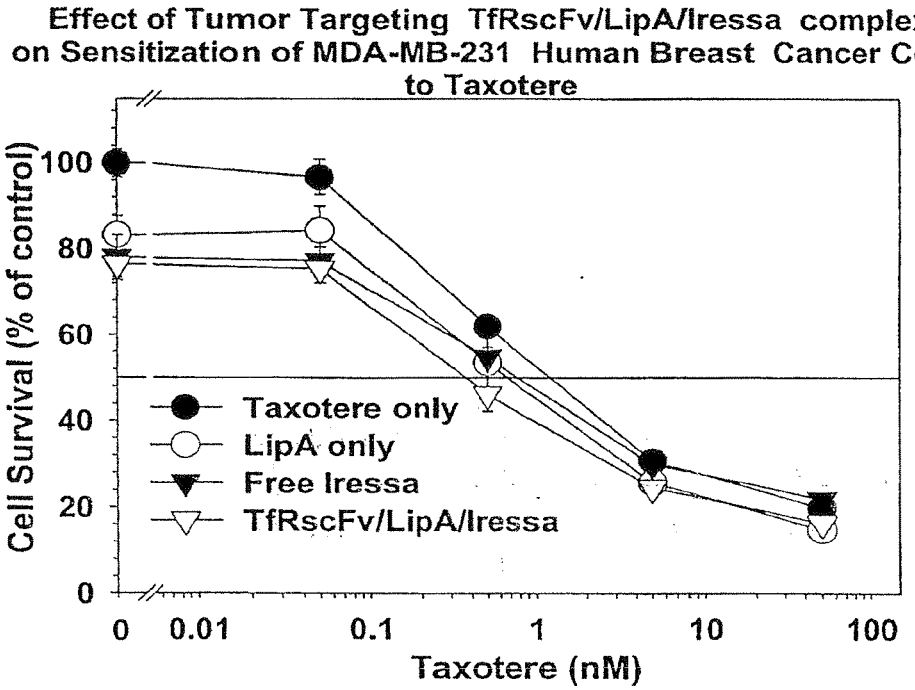
Fig. 45C

FIGURE 6 A



	IC_{50}
Lip A alone	> 50 μM
Free Iressa	= 15 μM
TfRscFv/LipA/Iressa	= 9 μM

Fig. 46A



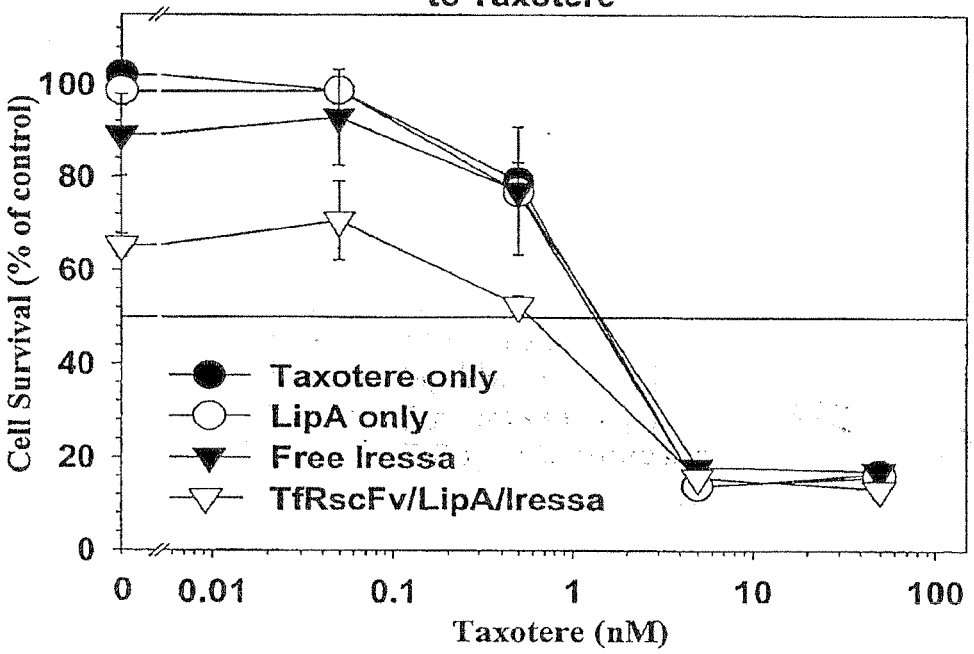
	IC_{50}:
Taxotere only	1.2 nM
LipA only	0.7 nM
Free Iressa	0.8 nM
TfRscFv/LipA/Iressa	0.35 nM

Fold Sensitization (Compare to Taxotere)	
LipA only	1.7
Free Iressa	1.5
TfRscFv/LipA/Iressa	3.4
Fold Sensitization (Compare to Free Iressa)	
TfRscFv/LipA/Iressa	2.3

12uM Iressa

Fig. 46B

Effect of Tumor Targeting TfRscFv/LipA/Iressa Complex on Sensitization of MDA-MB-435 Human Melanoma Cells to Taxotere



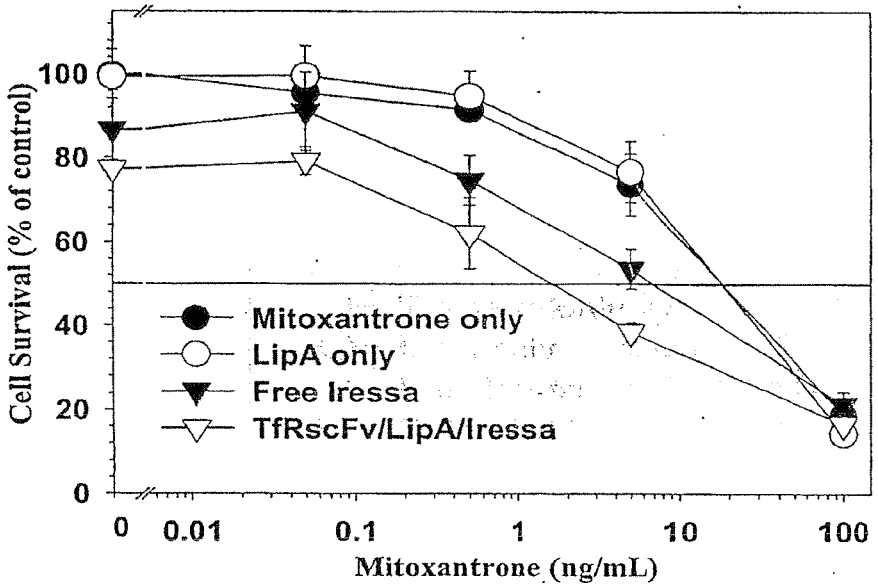
	IC_{50}:
Taxotere only	1.4 nM
LipA only	1.4 nM
Free Iressa	1.3 nM
TfRscFv/LipA/Iressa	0.6 nM

Fold Sensitization (Compare to Taxotere)	
LipA only	1.0
Free Iressa	1.1
TfRscFv/LipA/Iressa	2.3
Fold Sensitization (Compare to Free Iressa)	
TfRscFv/LipA/Iressa	2.2

15uM Iressa

Fig. 46C

Effect of Tumor Targeting TfRscFv/LipA/Iressa Complex on Sensitization of DU 145 Human Prostate Cancer Cells to Mitoxantrone



	IC_{50}:
Mitoxantrone only	17 ng/mL
LipA only	17 ng/mL
Free Iressa	7 ng/mL
TfRscFv/LipA/Iressa	1.5 ng/mL

Fold Sensitization (Compare to Mitoxantrone)	
LipA only	1.0
Free Iressa	2.4
TfRscFv/LipA/Iressa	11.3
Fold Sensitization (Compare to Free Iressa)	
TfRscFv/LipA/Iressa	4.7

8uM Iressa

SEQUENCE LISTING

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<120> Preparation of Antibody or an Antibody Fragment-Targeted Immunoliposomes for Systemic Administration of Therapeutic or Diagnostic Agents and Uses Thereof

<130> 2474.002PC06

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