MAb	H4		HS683		A172		T98G		U87-MG	
	%	IFM	%	IFM	%	IFM	%	IFM	%	IFM
mIgG1 CTRL	1+/-1	127+/-1	2+/-2	143+/-11	0+/-0	119+/-11	1+/-1	126+/-1	0+/-0	120+/-2
mDR5-01	90+/-1	284+/-2	87+/-6	264+/-30	94+/-0	296+/-3	94+/-0	299+/-4	75+/-1	226+/-4
mDR5-02	89+/-0	256+/-3	85+/-4	236+/-20	92+/-0	279+/-4	93+/-1	266+/-4	82+/-1	219+/-17
mDR5-04	90+/-0	283+/-4	88+/-2	243+/-13	97+/-1	308+/-10	96+/-1	314+/-6	80+/-3	219+/-13
mDR5-05	77+/-8	239+/-6	79+/-10	214+/-23	89+/-4	268+/-13	89+/-0	255+/-1	70+/-11	169+/-12

Fig. 1

MAb	A704		ACHN		SW948		Caki 1		5637		HCT116		MCF7	
	%	IFM	%	IFM	%	IFM	%	IFM	%	IFM	%	IFM	%	IFM
mIgG1 CTRL	0	136	1	139	1	208	1	165	1	160	1	172	1	176
mDR5-01	92	252	93	244	69	316	79	233	78	263	59	254	51	225
mDR5-05	75	225	82	211	32	245	68	214	51	188	43	224	33	192

Fig. 2

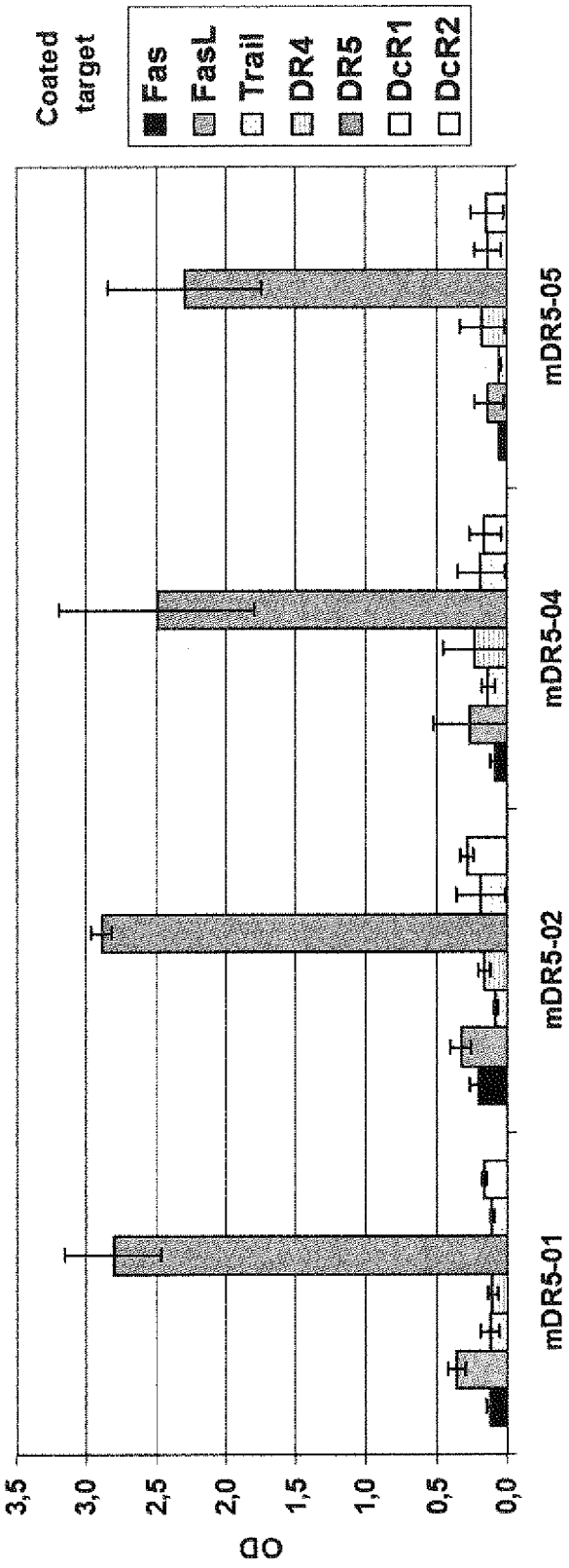

Coated target
Fas
FasL
Trail
DR4
DR5
DcR1
DcR2
OD
3,5
3,0
2,5
2,0
1,5
1,0
0,5
0,0
mDR5-01
mDR5-02
mDR5-04
mDR5-05
Antibody anti-DR5

Fig.3

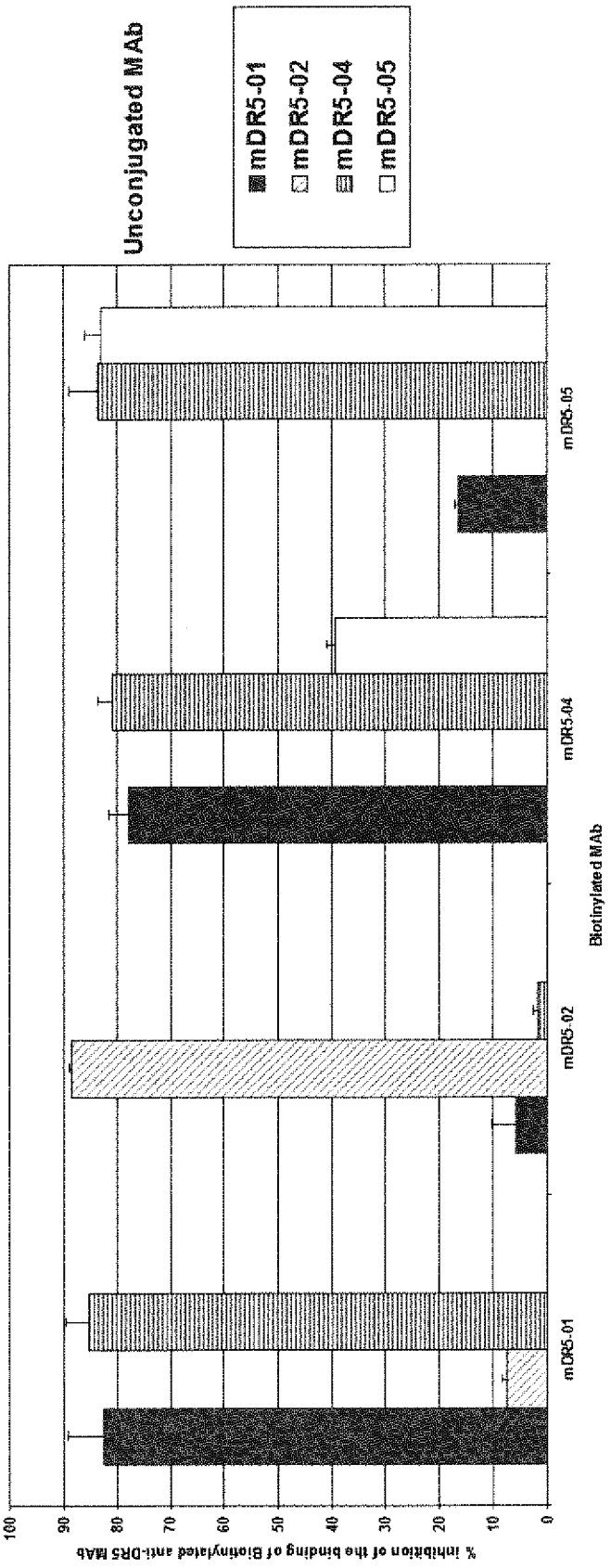

Unconjugated MAb
mDR5-01
mDR5-02
mDR5-04
mDR5-05
% inhibition of the binding of Biotinylated anti-DR5 MAb
100
90
80
70
60
50
40
30
20
10
0
mDR5-01
mDR5-02
mDR5-04
mDR5-05
Biotinylated MAb

Fig.4

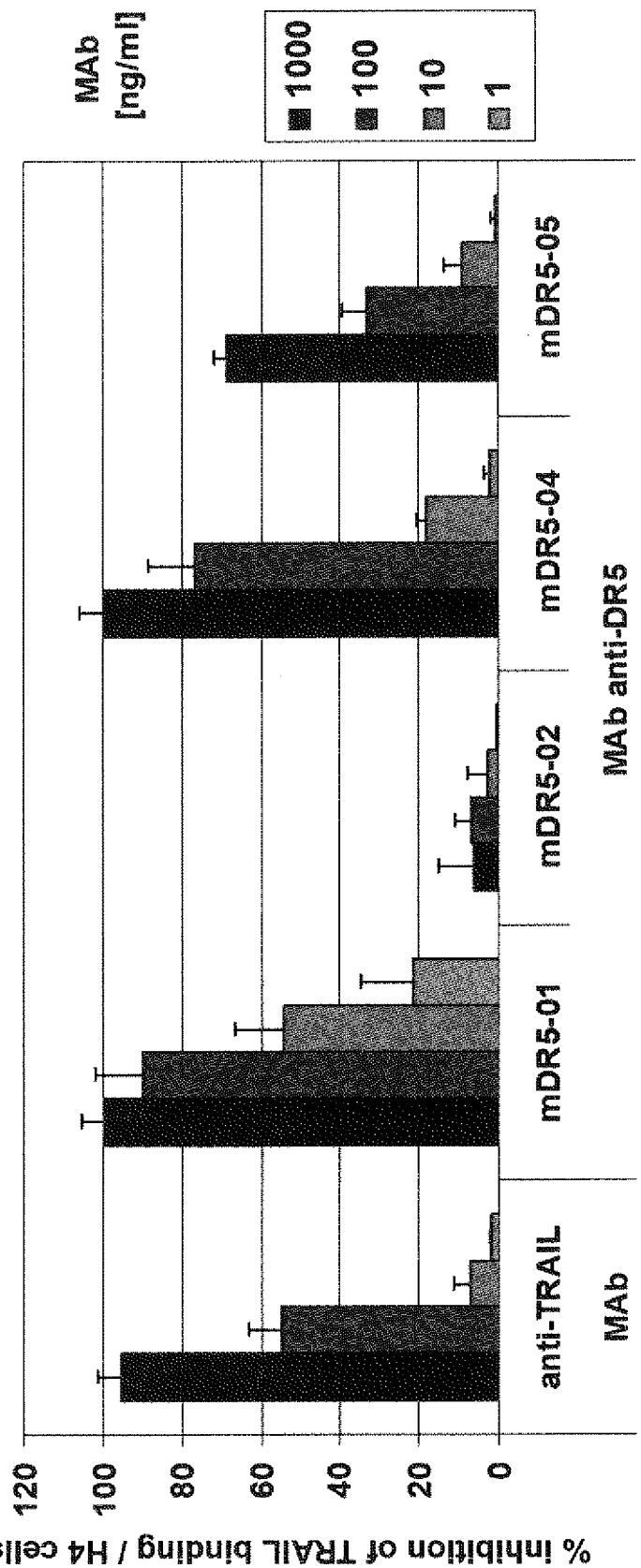

% inhibition of TRAIL binding / H4 cells
120
100
80
60
40
20
0
anti-TRAIL MAb
mDR5-01
mDR5-02
mDR5-04
mDR5-05
MAb anti-DR5
MAb [ng/ml]
1000
100
10
1

Fig.5

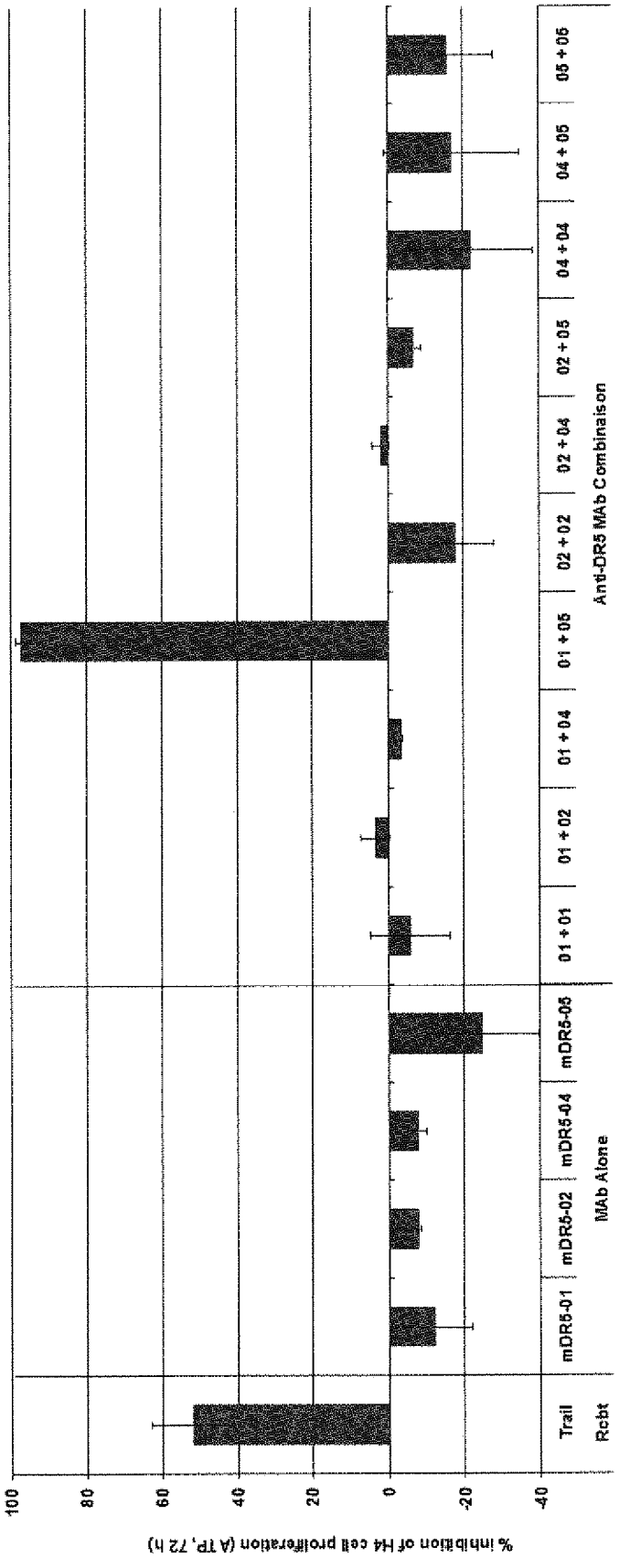

% inhibition of H4 cell proliferation (ΔTP, 72 h)
100
80
60
40
20
0
-20
-40
Trail
Rcbt
mDR5-01
mDR5-02
mDR5-04
mDR5-05
MAb Alone
01 + 01
01 + 02
01 + 04
01 + 05
02 + 02
02 + 04
02 + 05
04 + 04
04 + 05
05 + 05
Anti-DR5 MAb Combinaison

Fig.6

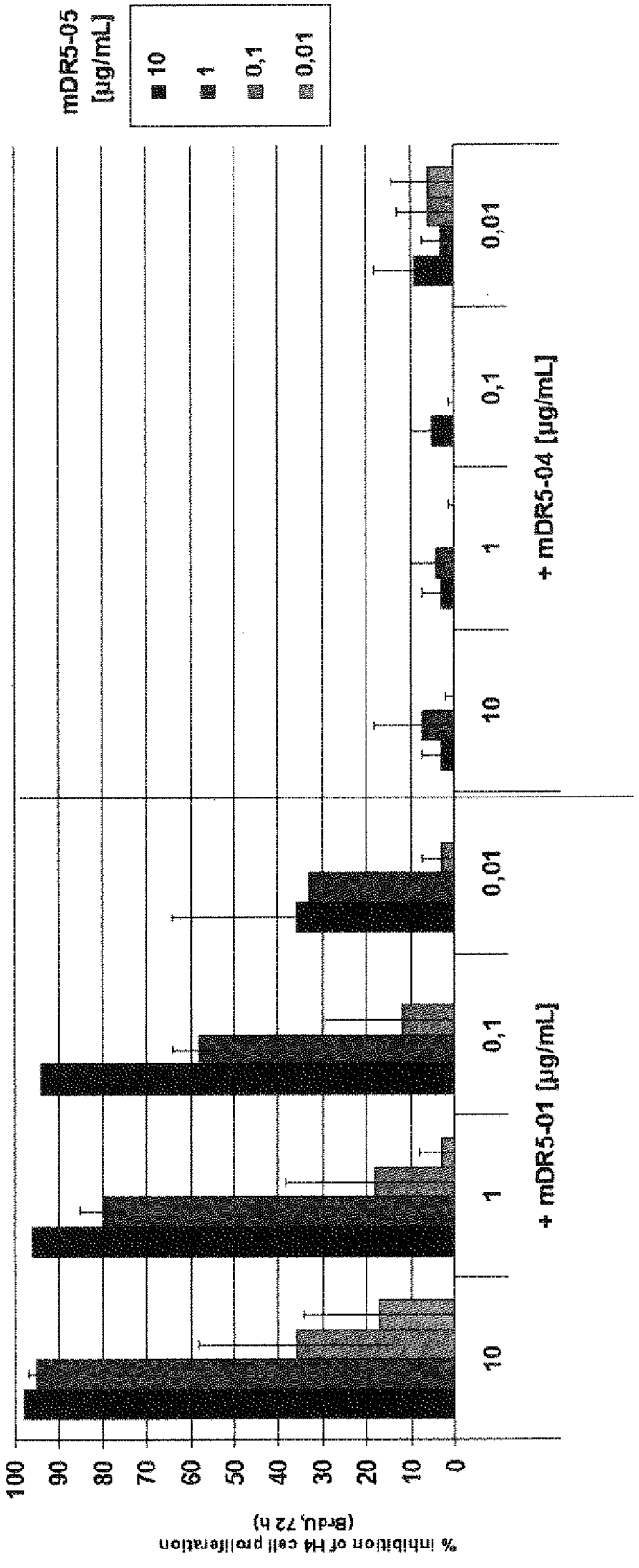

mDR5-05 [µg/mL]
10
1
0,1
0,01
% inhibition of H4 cell proliferation (BrdU, 72 h)
100
90
80
70
60
50
40
30
20
10
0
10
1
0,1
0,01
+ mDR5-01 [µg/mL]
10
1
0,1
0,01
+ mDR5-04 [µg/mL]

Fig.7

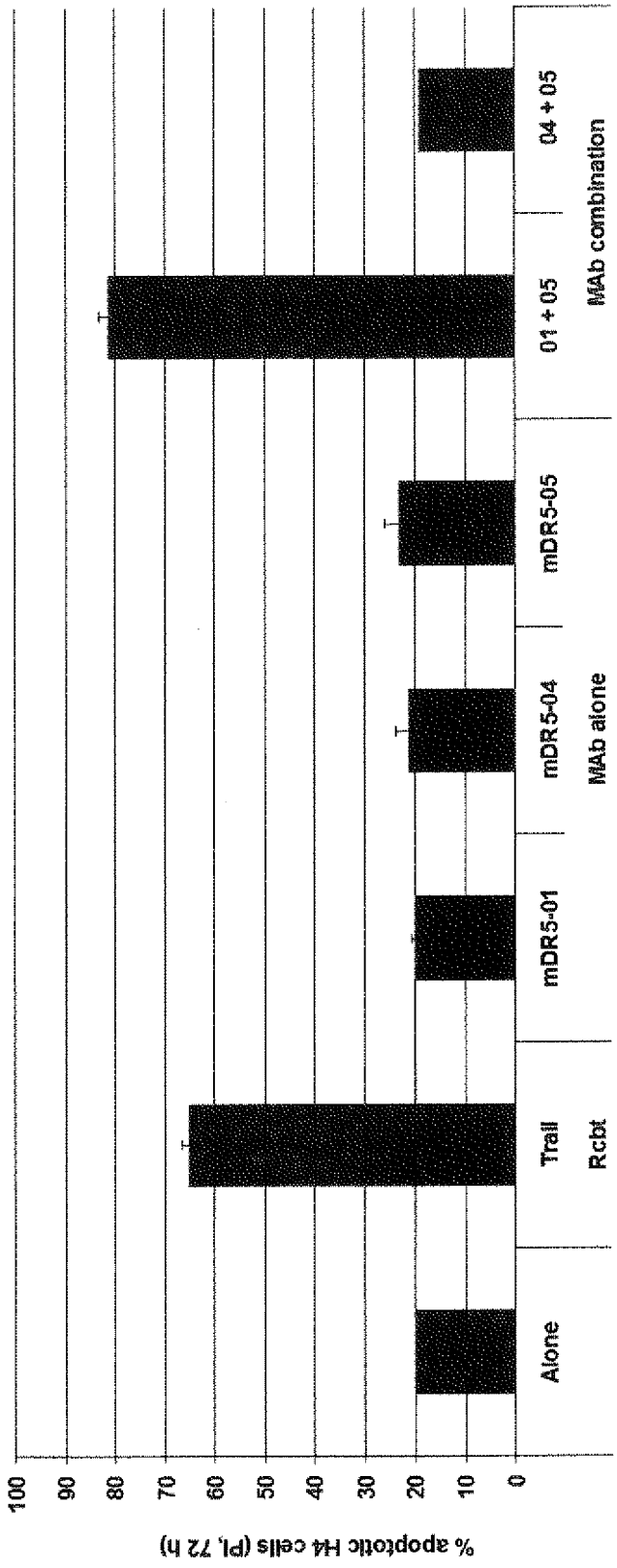

% apoptotic H4 cells (PI, 72 h)
100
90
80
70
60
50
40
30
20
10
0
Alone
Trail
Rcbt
mDR5-01
mDR5-04
mDR5-05
01 + 05
04 + 05
MAb alone
MAb combination

Fig.8

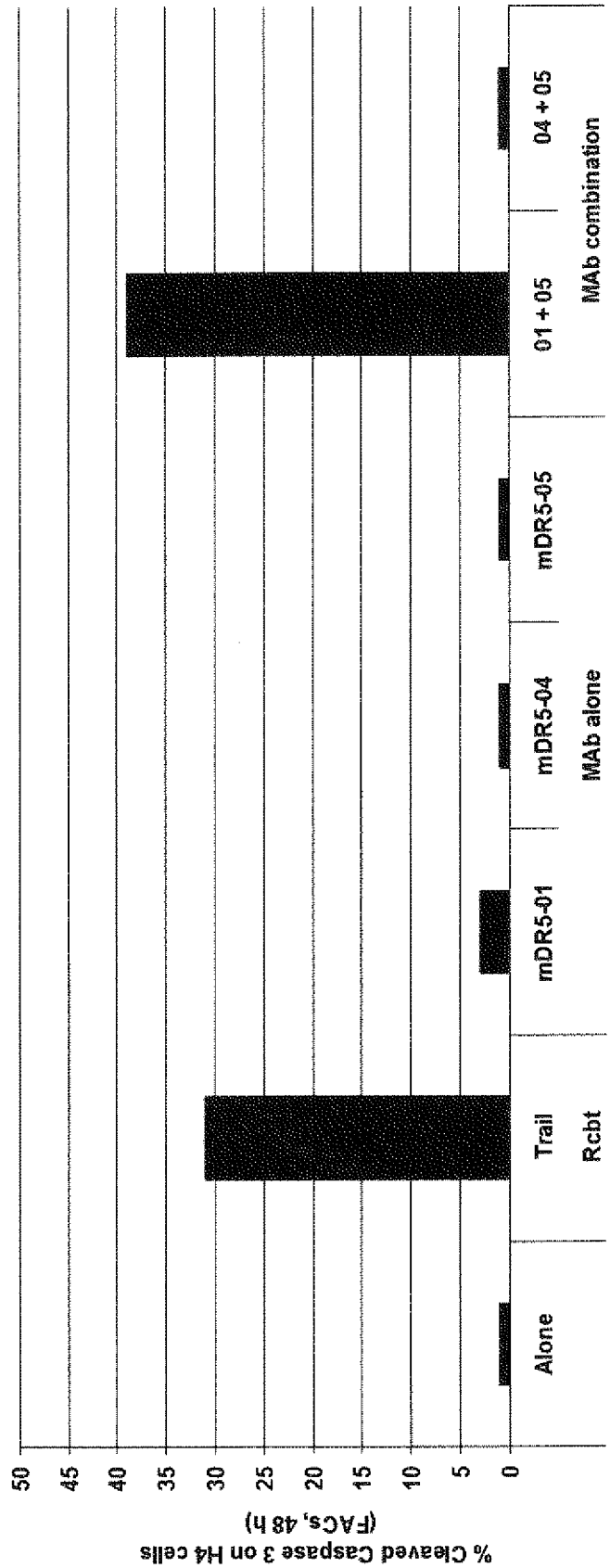

% Cleaved Caspase 3 on H4 cells
(FACs, 48 h)
50
45
40
35
30
25
20
15
10
5
0
Alone
Trail
Rcbt
mDR5-01
mDR5-04
mDR5-05
01 + 05
04 + 05
MAb alone
MAb combination

Fig.9

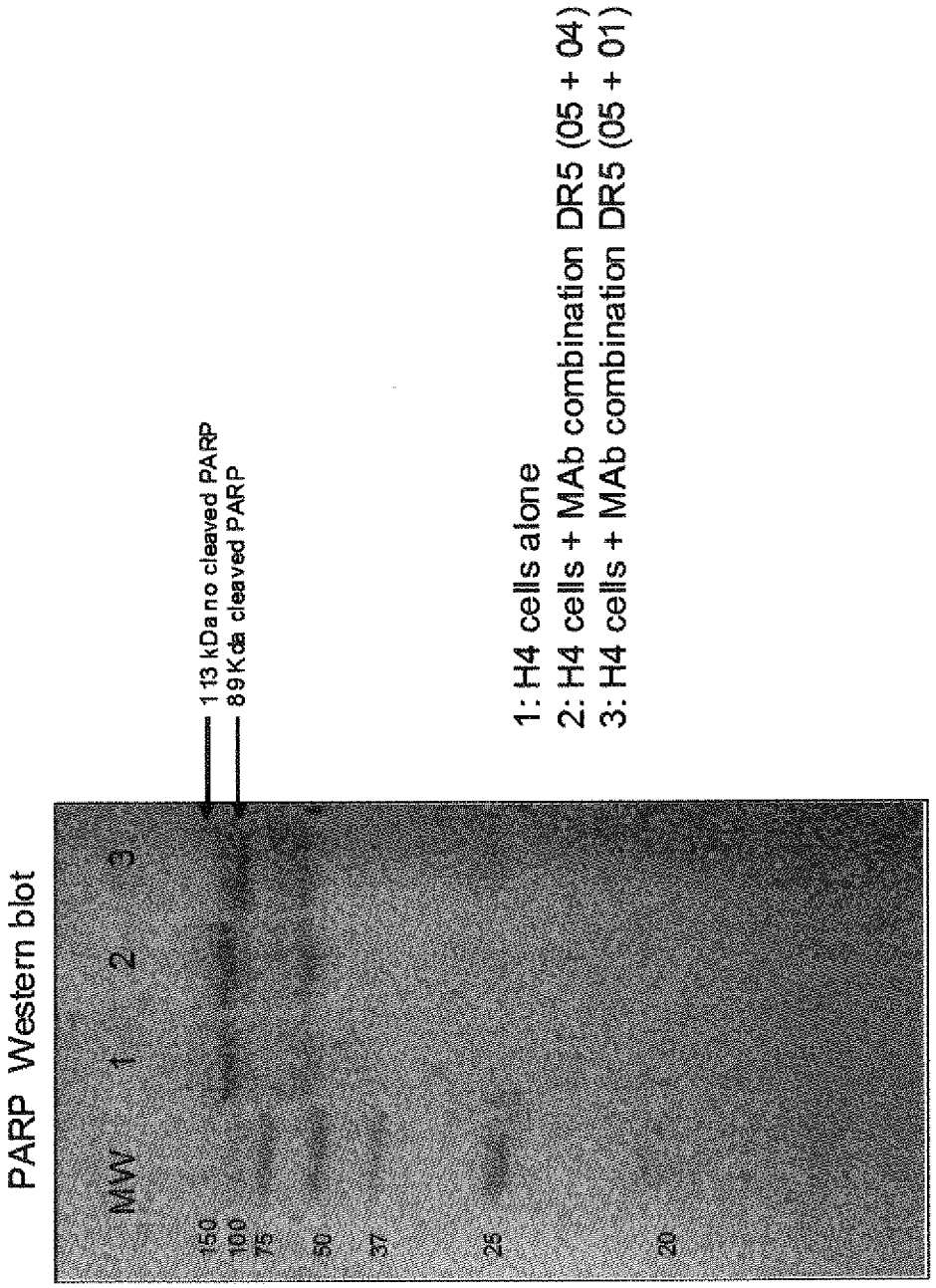

PARP Western blot
MW
1
2
3
150
100
75
50
37
25
20
113 kDa no cleaved PARP
89Kda cleaved PARP
1: H4 cells alone
2: H4 cells + MAb combination DR5 (05 + 04)
3: H4 cells + MAb combination DR5 (05 + 01)

Fig. 10

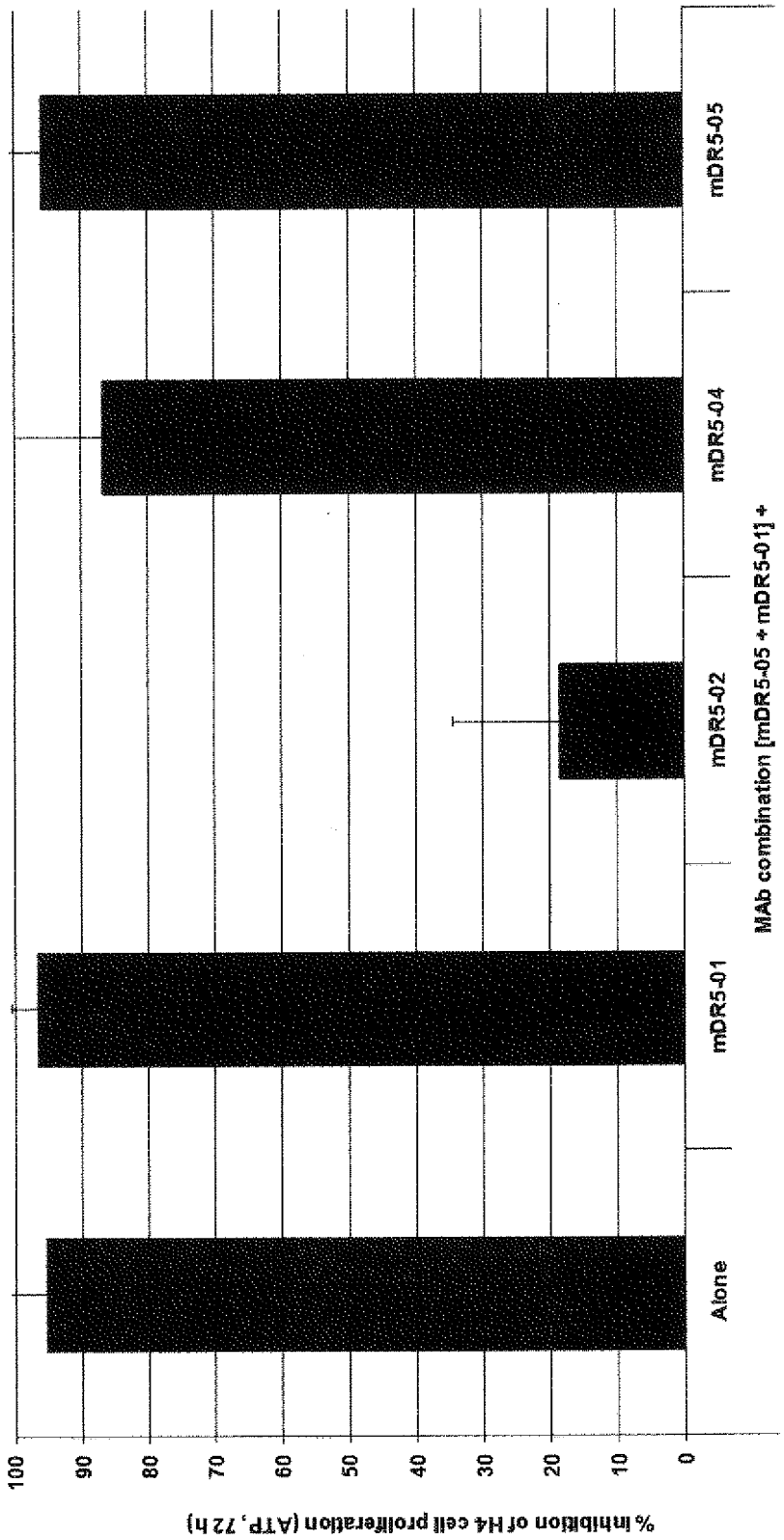

% inhibition of H4 cell proliferation (ATP, 72 h)
100
90
80
70
60
50
40
30
20
10
0
Alone
mDR5-01
mDR5-02
mDR5-04
mDR5-05
MAb combination [mDR5-05 + mDR5-01] +

Fig. 11

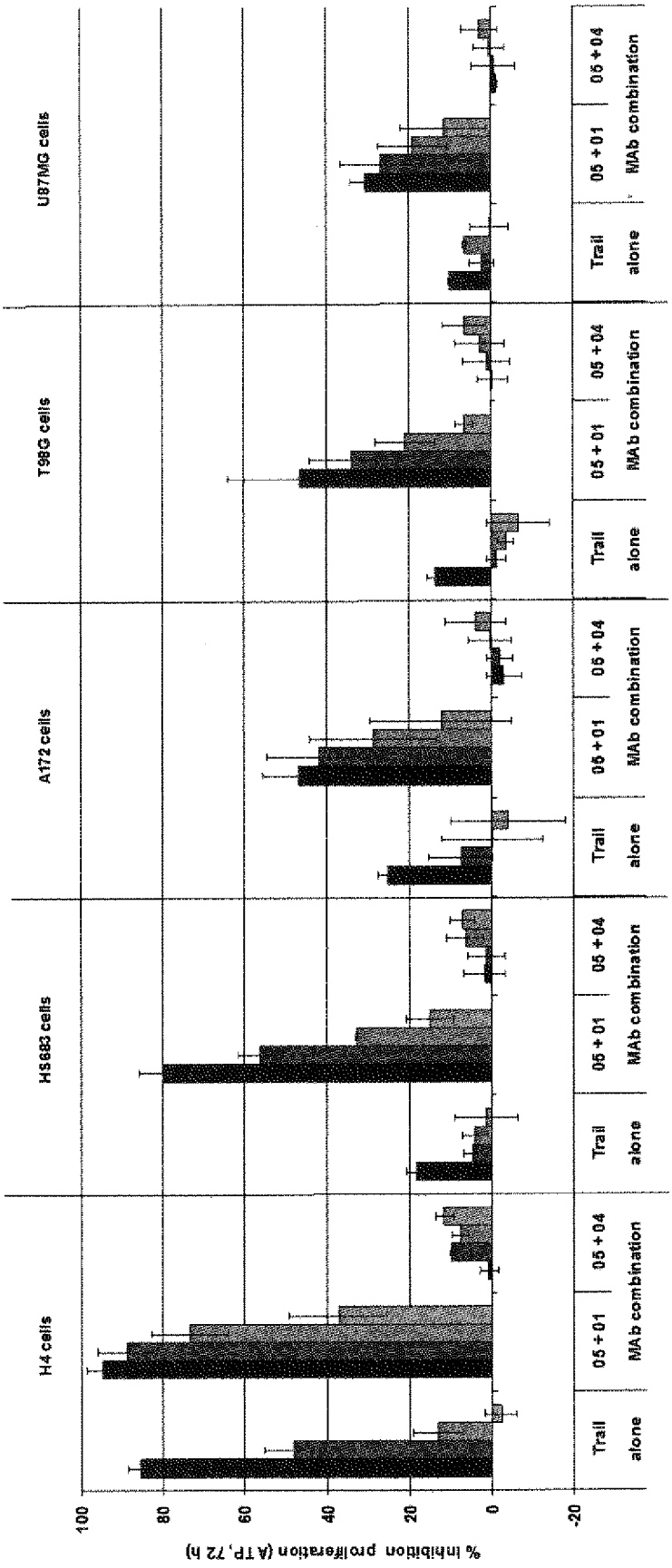

% inhibition proliferation (ΔTP, 72 h)
100
80
60
40
20
0
-20
H4 cells
H5683 cells
A172 cells
T98G cells
U87MG cells
Trail alone
05 + 01
05 + 04
MAb combination

Fig. 12

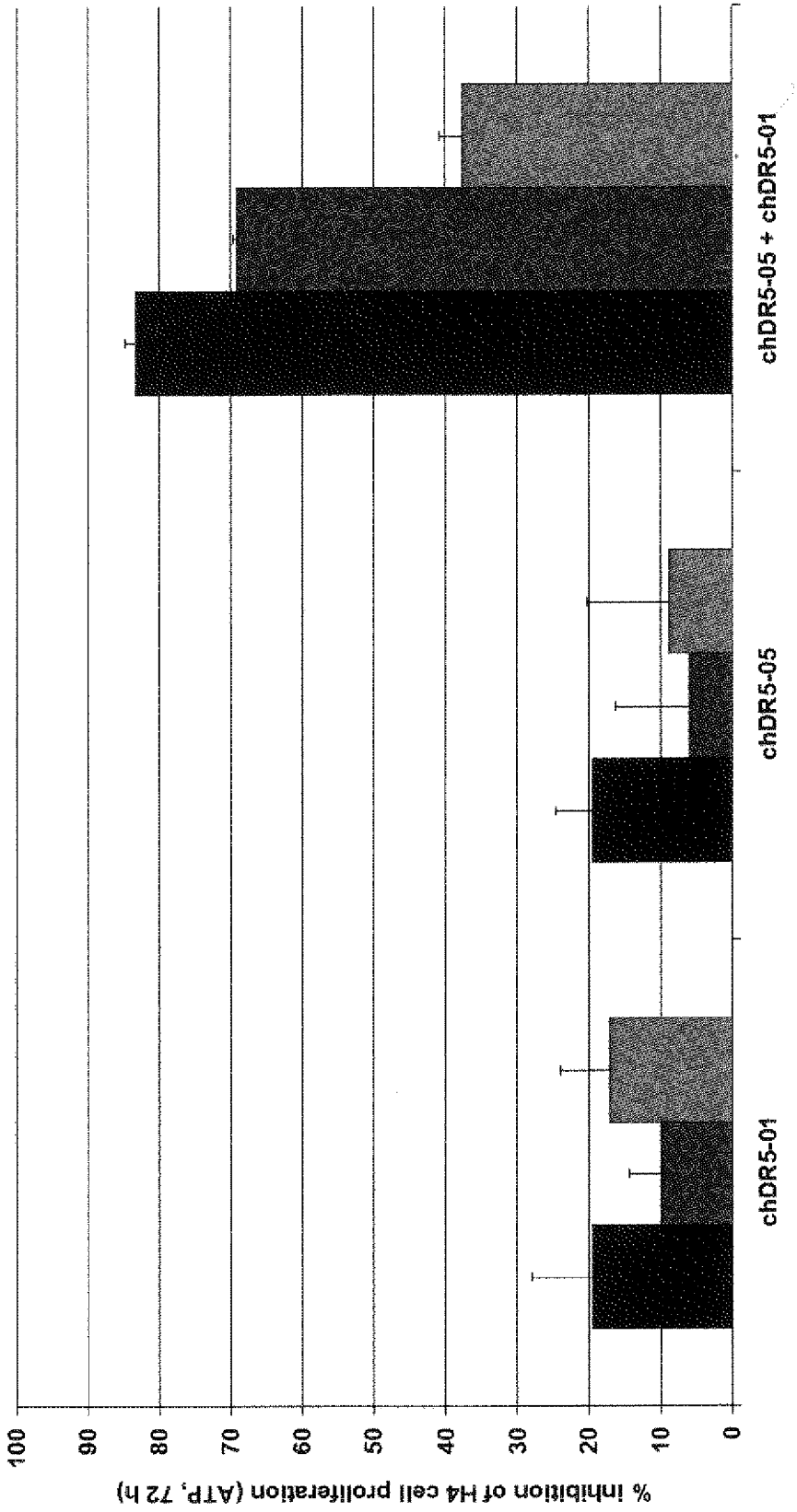

% inhibition of H4 cell proliferation (ATP, 72 h)
100
90
80
70
60
50
40
30
20
10
0
chDR5-01
chDR5-05
chDR5-05 + chDR5-01

Fig. 13

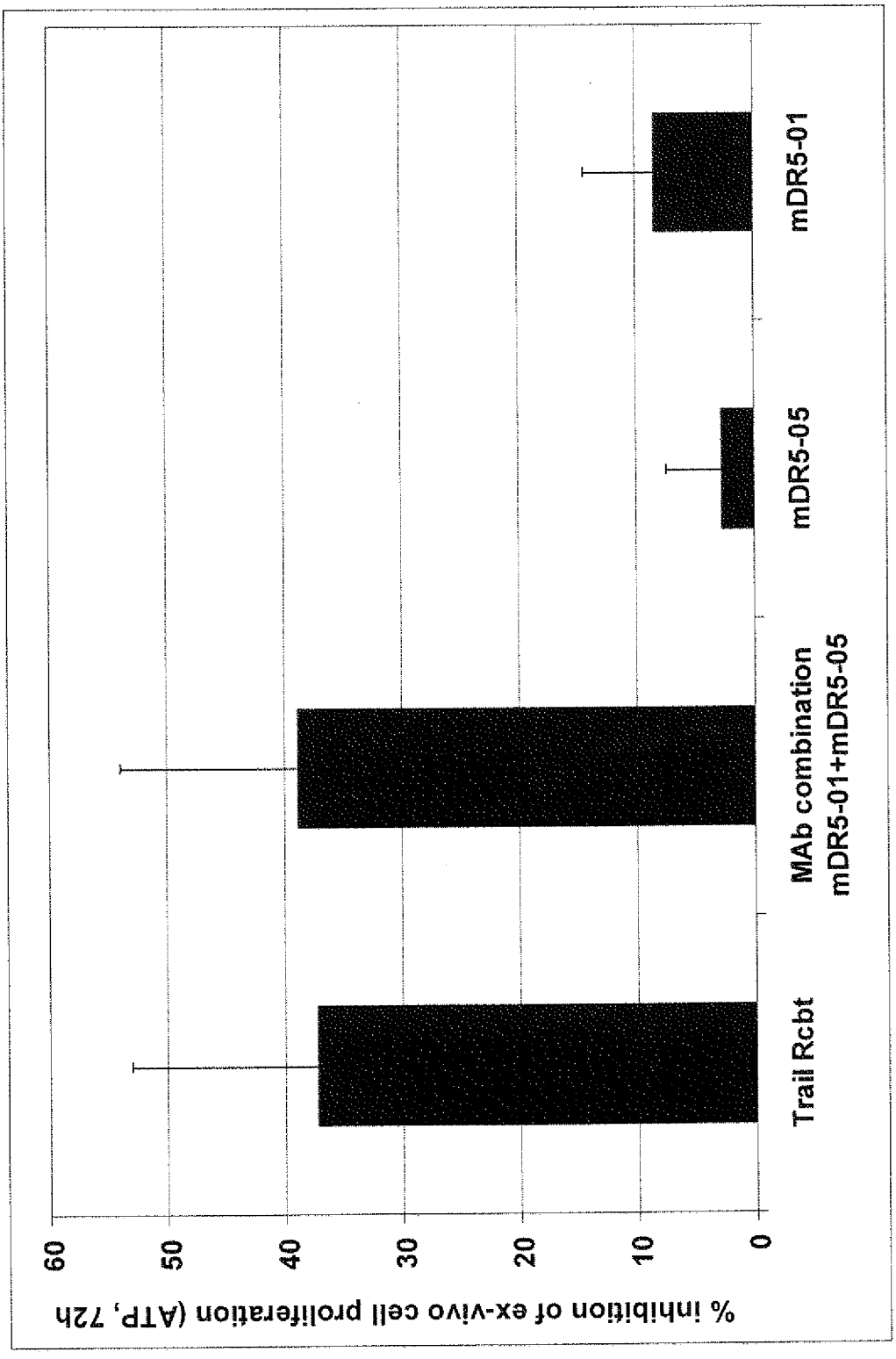

% inhibition of ex-vivo cell proliferation (ATP, 72h
60
50
40
30
20
10
0
Trail Rcbt
MAb combination mDR5-01+mDR5-05
mDR5-05
mDR5-01

Figure 14

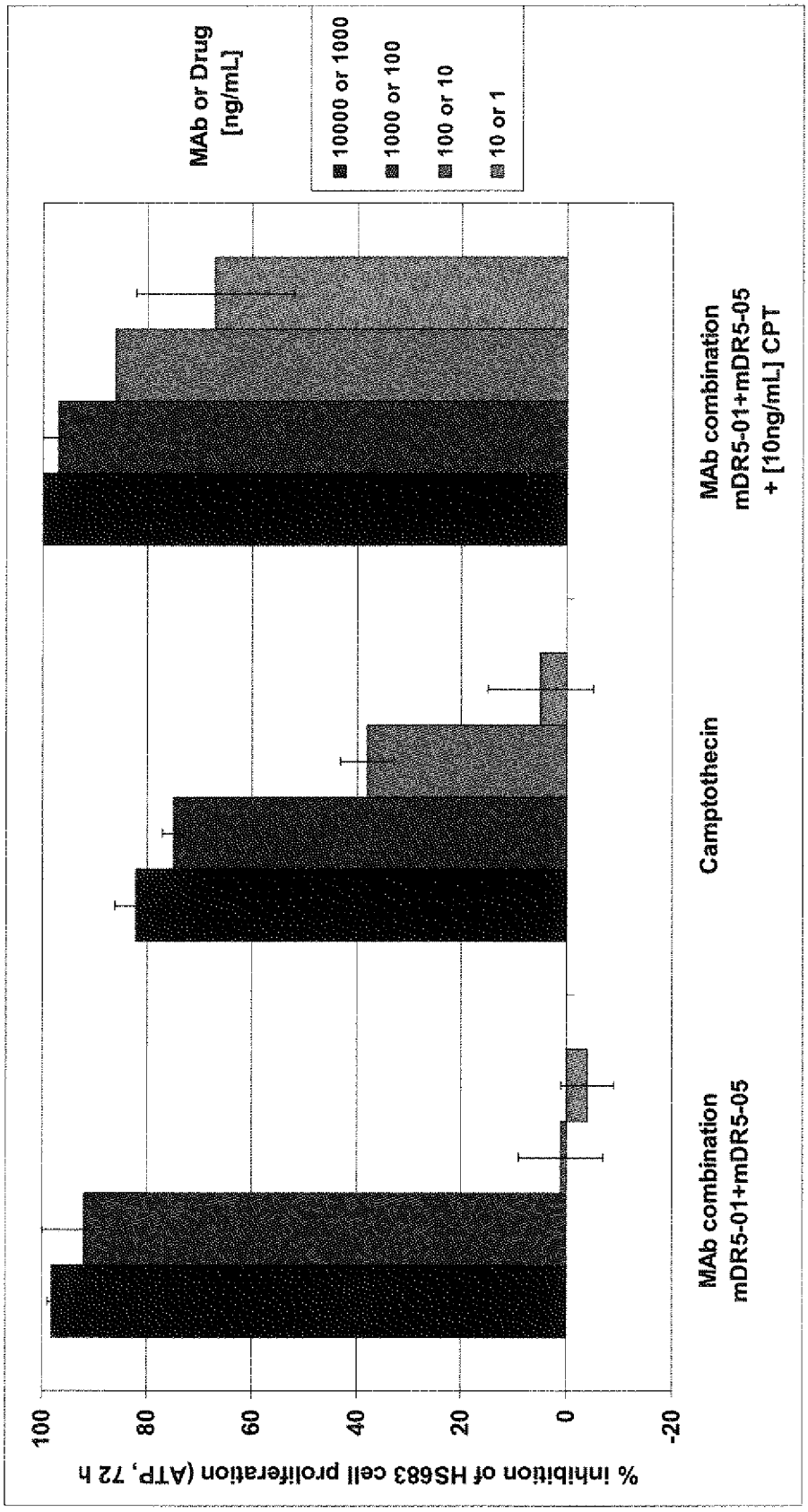

% inhibition of HS683 cell proliferation (ATP, 72 h
100
80
60
40
20
0
-20
MAb combination mDR5-01+mDR5-05
Camptothecin
MAb combination mDR5-01+mDR5-05 + [10ng/mL] CPT
MAb or Drug [ng/mL]
10000 or 1000
1000 or 100
100 or 10
10 or 1

Figure 15

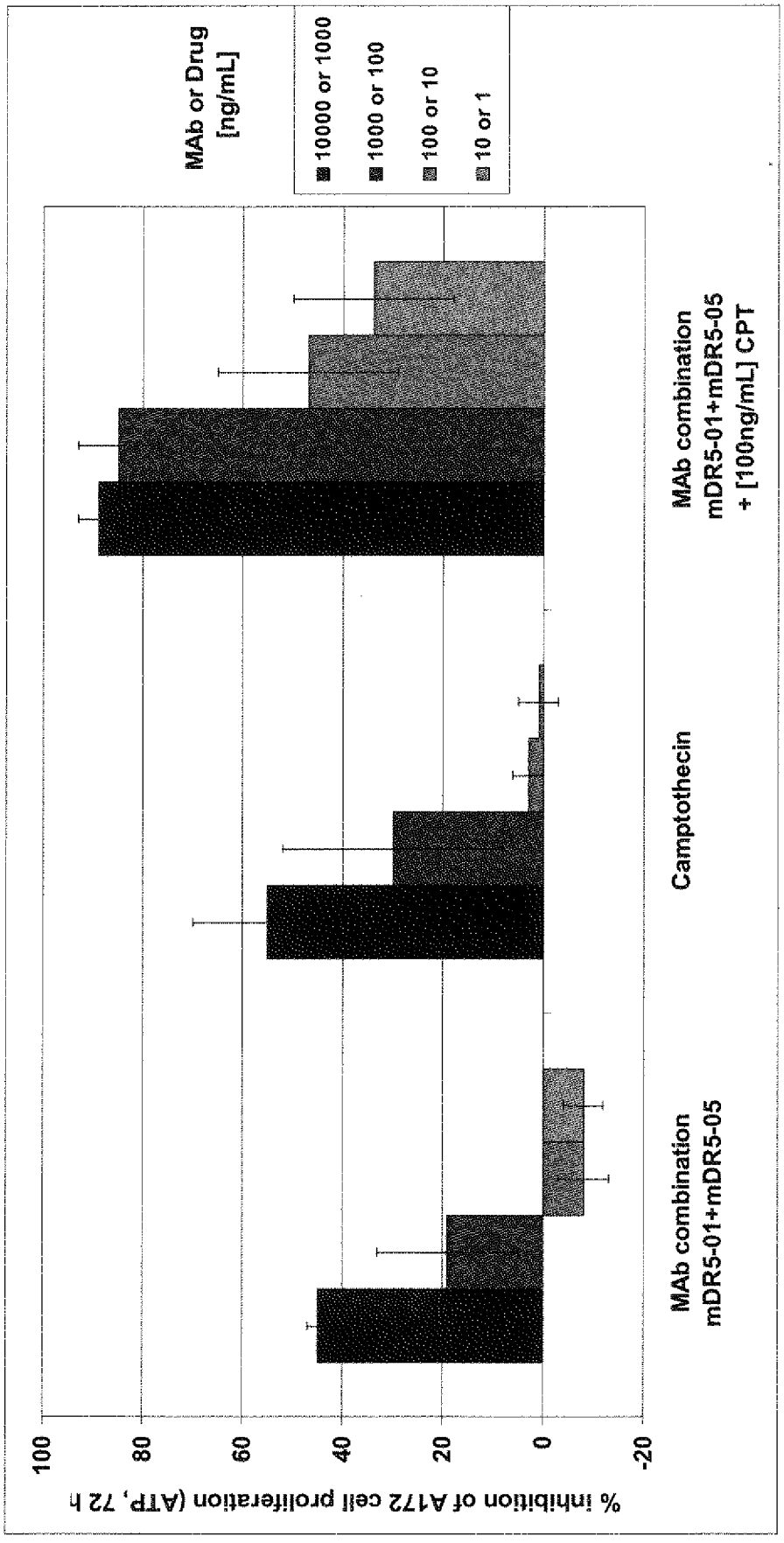

% inhibition of A172 cell proliferation (ATP, 72 h
100
80
60
40
20
0
-20
MAb or Drug [ng/mL]
10000 or 1000
1000 or 100
100 or 10
10 or 1
MAb combination mDR5-01+mDR5-05
Camptothecin
MAb combination mDR5-01+mDR5-05 + [100ng/mL] CPT

Figure 16

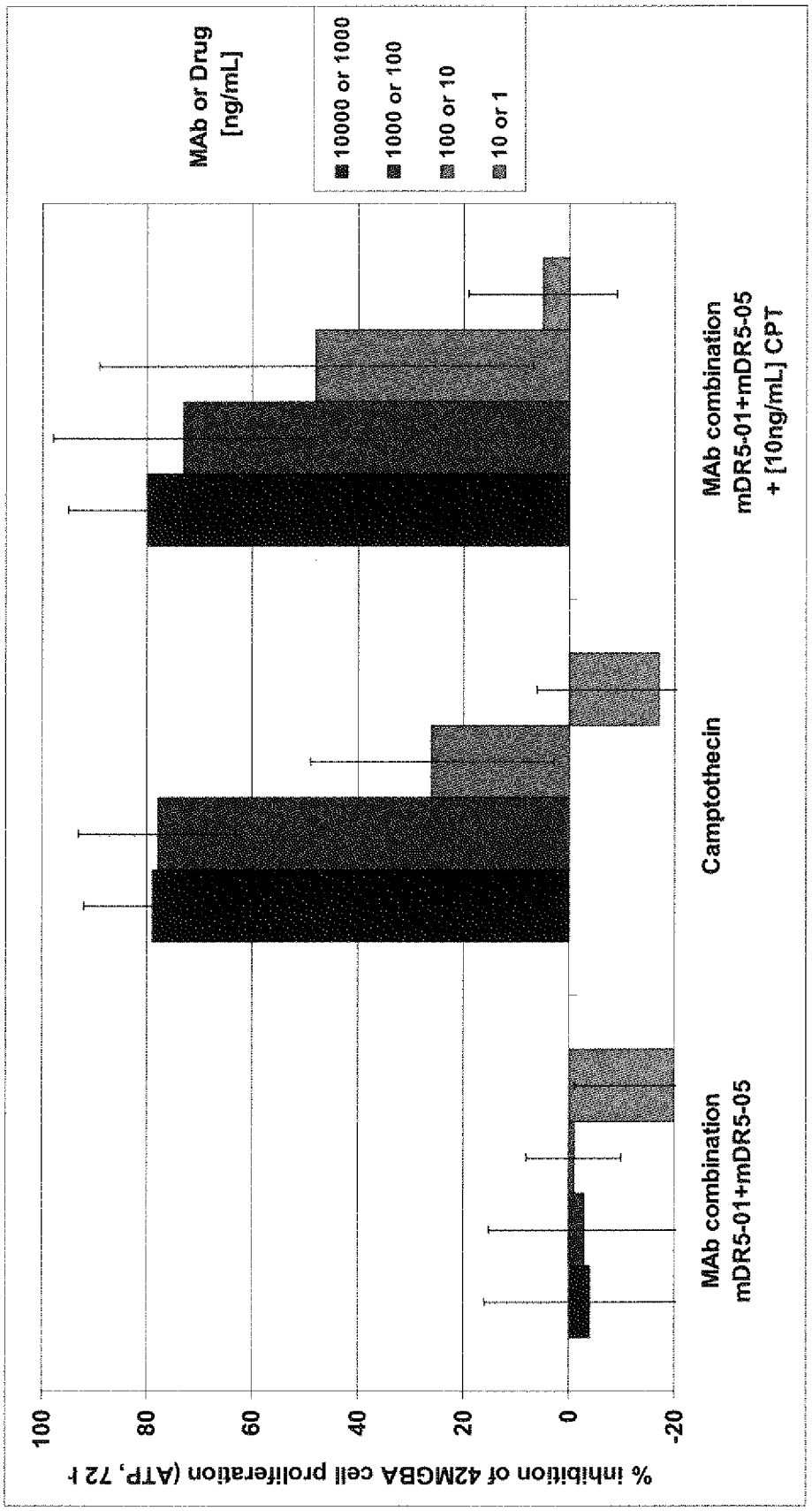

% inhibition of 42MGBA cell proliferation (ATP, 72 h
100
80
60
40
20
0
-20
MAb combination mDR5-01+mDR5-05
Camptothecin
MAb combination mDR5-01+mDR5-05 + [10ng/mL] CPT
MAb or Drug [ng/mL]
10000 or 1000
1000 or 100
100 or 10
10 or 1

Figure 17

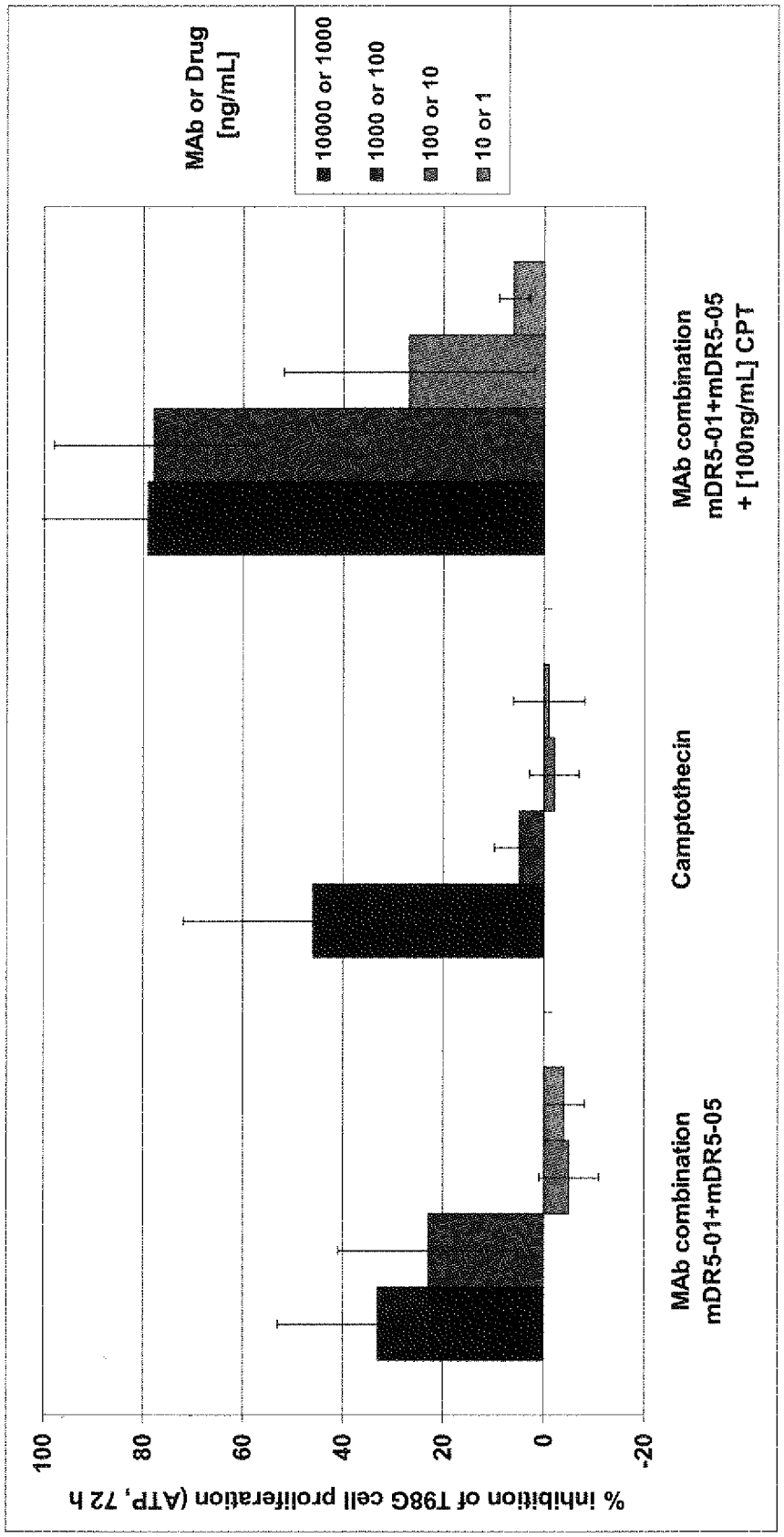

% inhibition of T98G cell proliferation (ATP, 72 h
100
80
60
40
20
0
-20
MAb combination mDR5-01+mDR5-05
Camptothecin
MAb combination mDR5-01+mDR5-05 + [100ng/mL] CPT
MAb or Drug [ng/mL]
10000 or 1000
1000 or 100
100 or 10
10 or 1

Figure 18

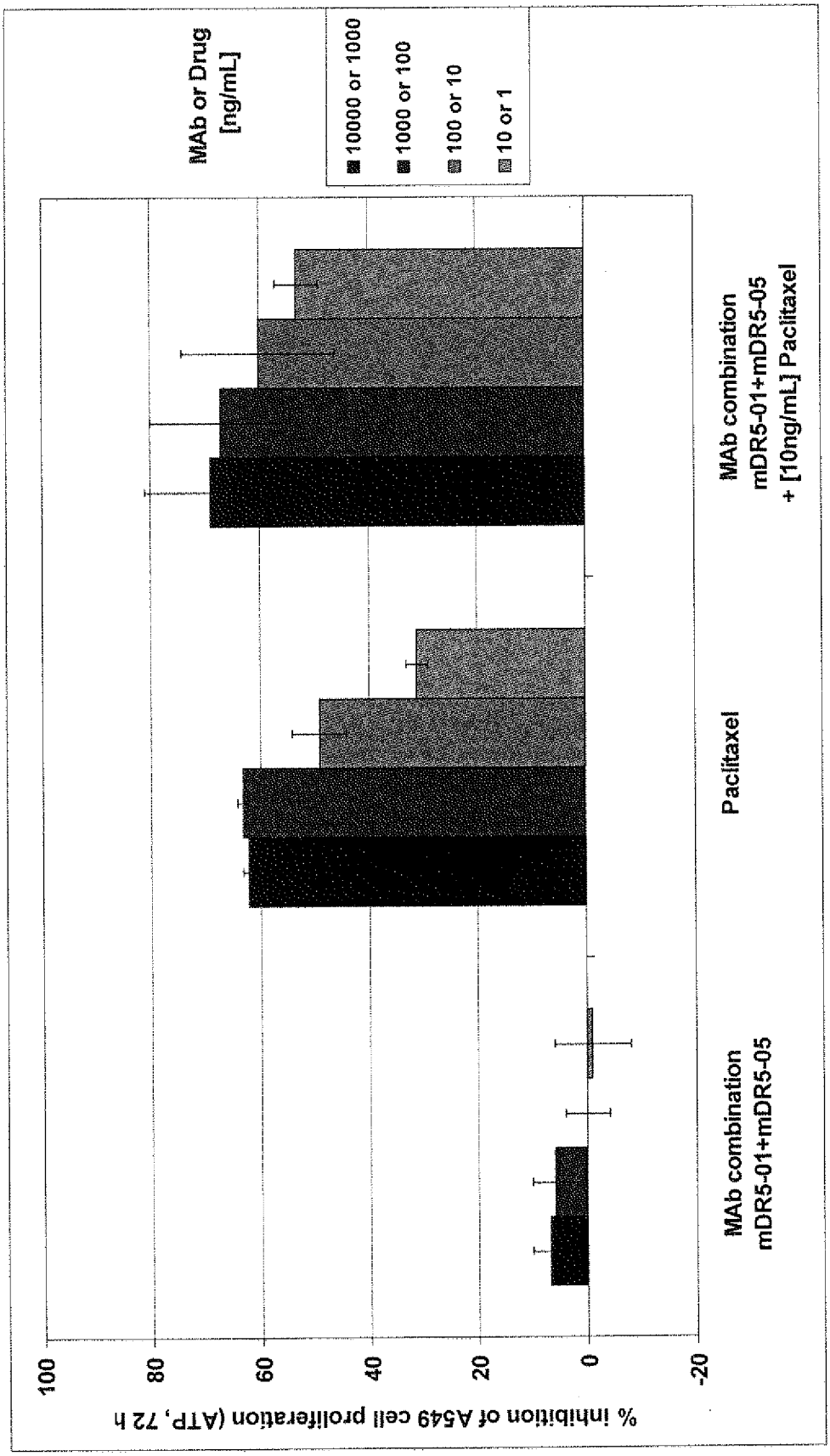

% inhibition of A549 cell proliferation (ATP, 72 h
100
80
60
40
20
0
-20
MAb combination mDR5-01+mDR5-05
Paclitaxel
MAb combination mDR5-01+mDR5-05 + [10ng/mL] Paclitaxel
MAb or Drug [ng/mL]
10000 or 1000
1000 or 100
100 or 10
10 or 1

Figure 19

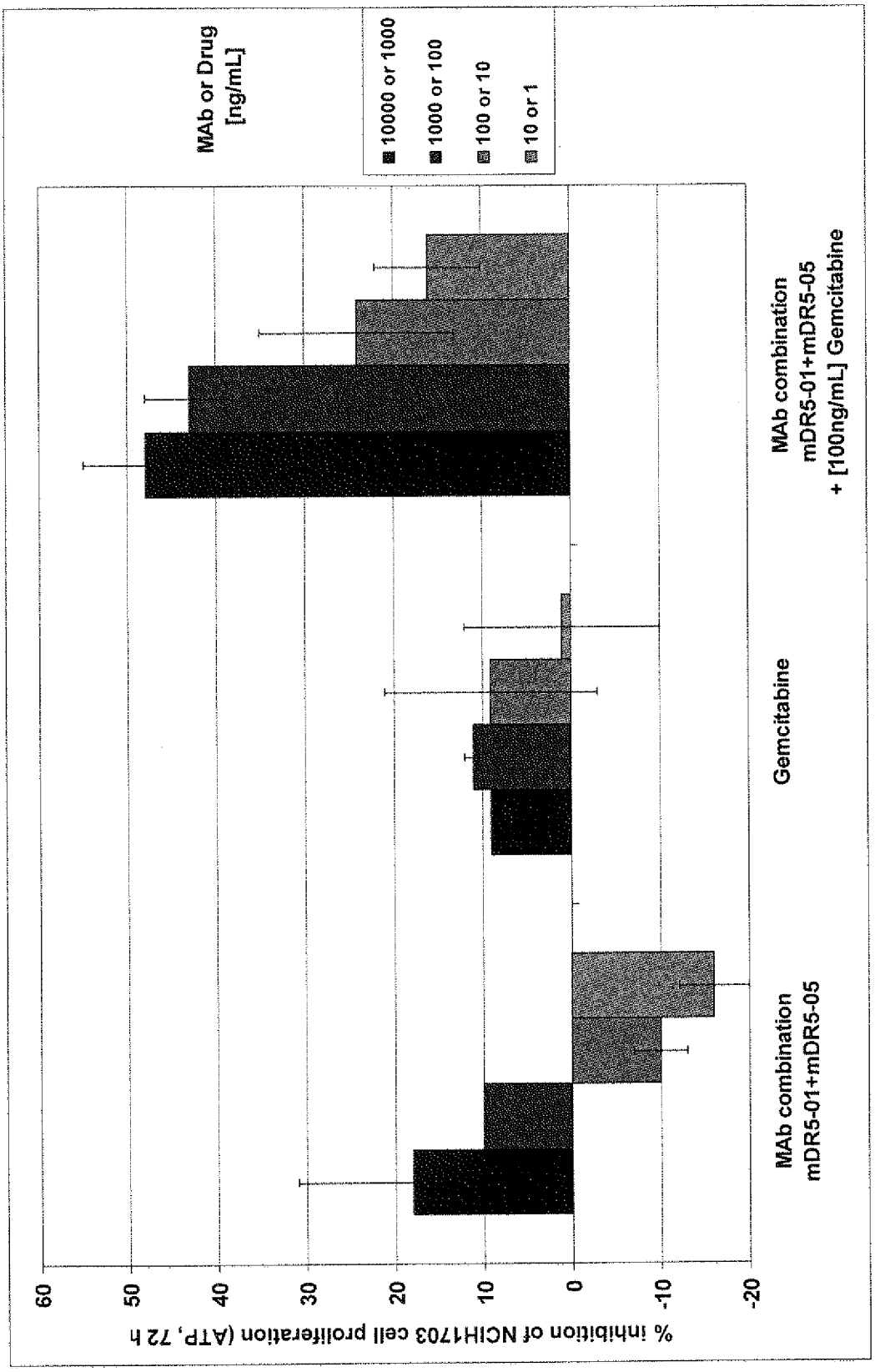

% inhibition of NCIH1703 cell proliferation (ATP, 72 h
60
50
40
30
20
10
0
-10
-20
MAb or Drug [ng/mL]
10000 or 1000
1000 or 100
100 or 10
10 or 1
MAb combination mDR5-01+mDR5-05
Gemcitabine
MAb combination mDR5-01+mDR5-05 + [100ng/mL] Gemcitabine

Figure 20

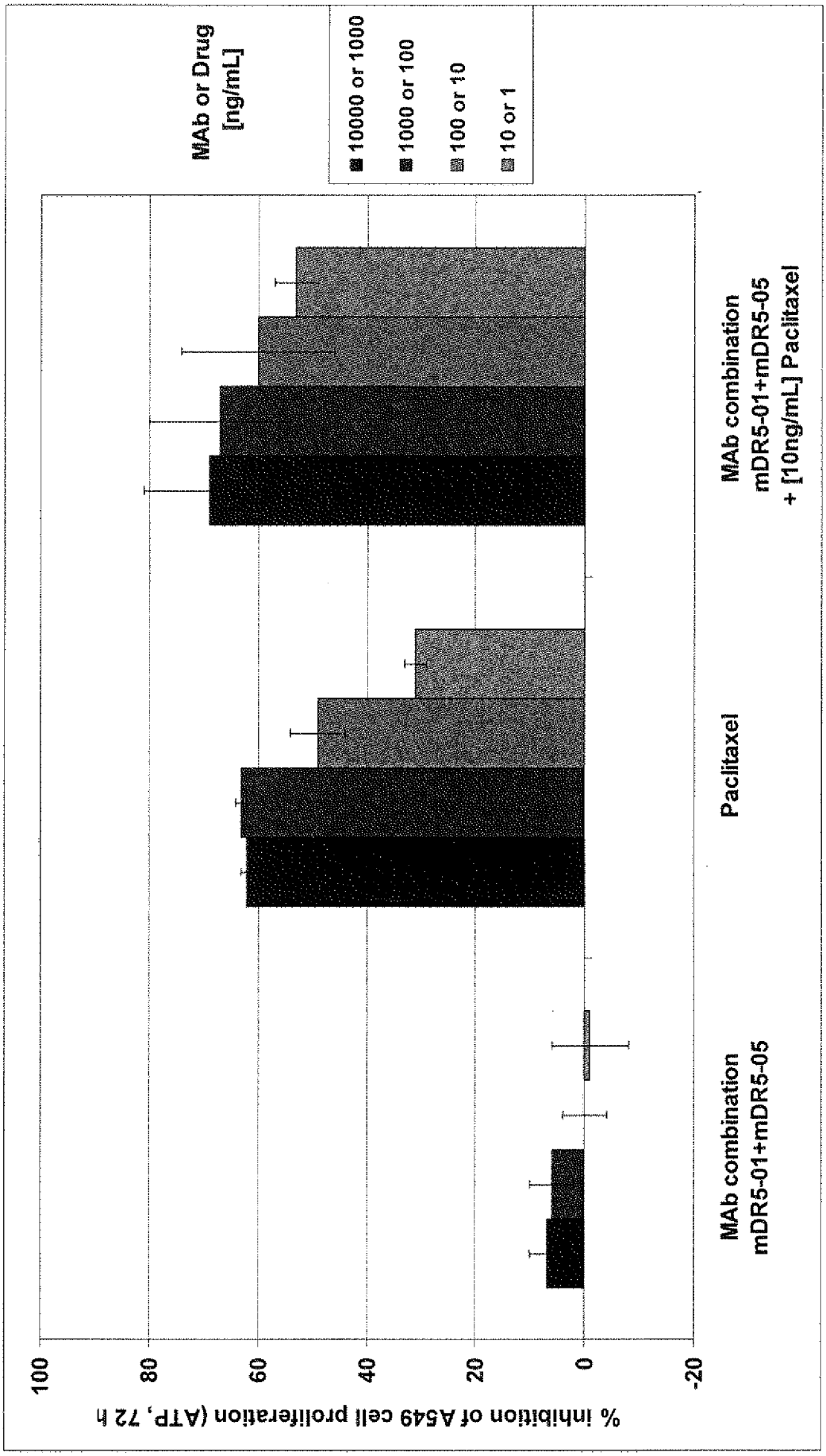

% inhibition of A549 cell proliferation (ATP, 72 h
100
80
60
40
20
0
-20
MAb or Drug [ng/mL]
10000 or 1000
1000 or 100
100 or 10
10 or 1
MAb combination mDR5-01+mDR5-05
Paclitaxel
MAb combination mDR5-01+mDR5-05 + [10ng/mL] Paclitaxel

Figure 21

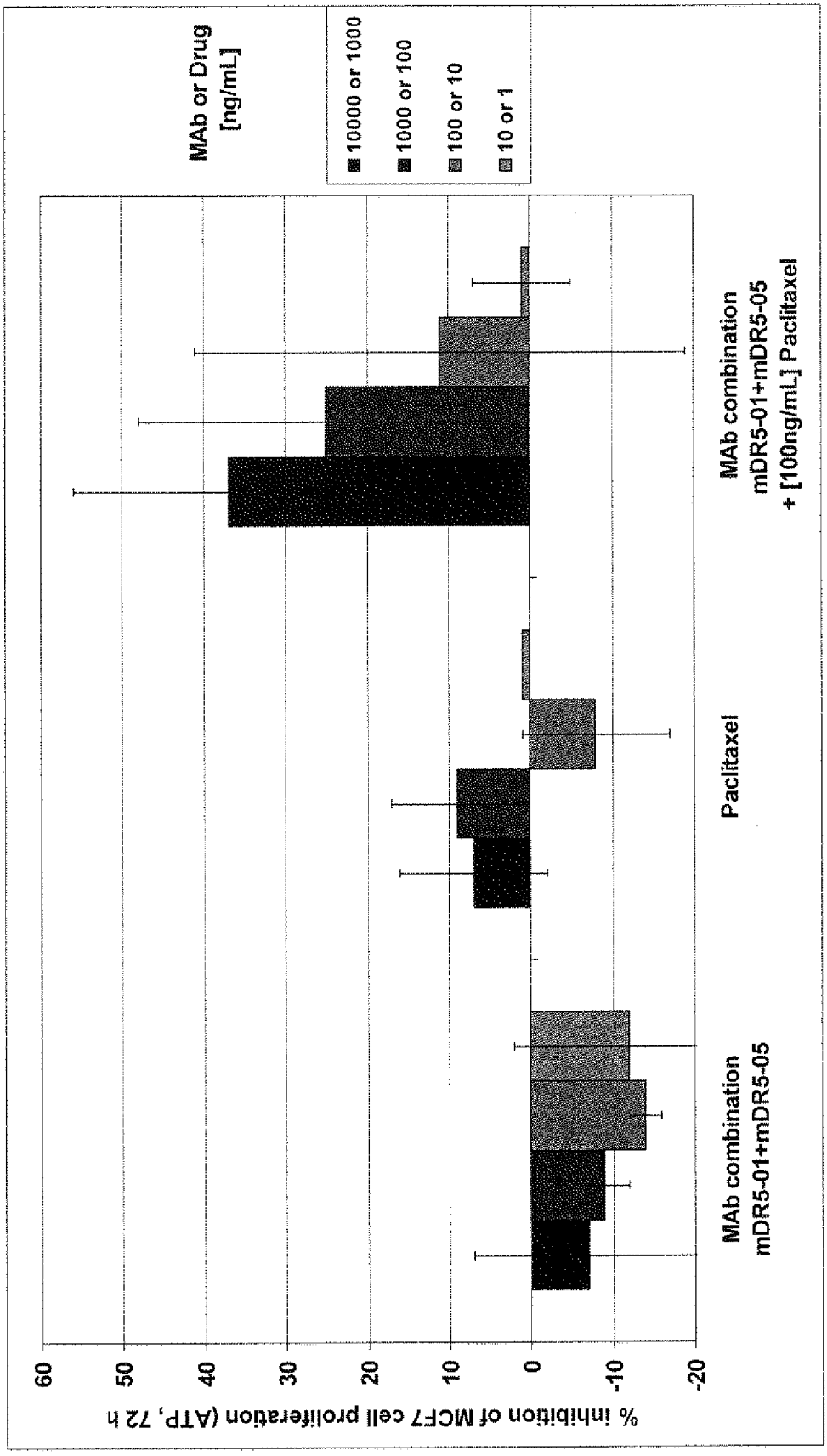

% inhibition of MCF7 cell proliferation (ATP, 72 h
60
50
40
30
20
10
0
-10
-20
MAb combination mDR5-01+mDR5-05
Paclitaxel
MAb combination mDR5-01+mDR5-05 + [100ng/mL] Paclitaxel
MAb or Drug [ng/mL]
10000 or 1000
1000 or 100
100 or 10
10 or 1

Figure 22

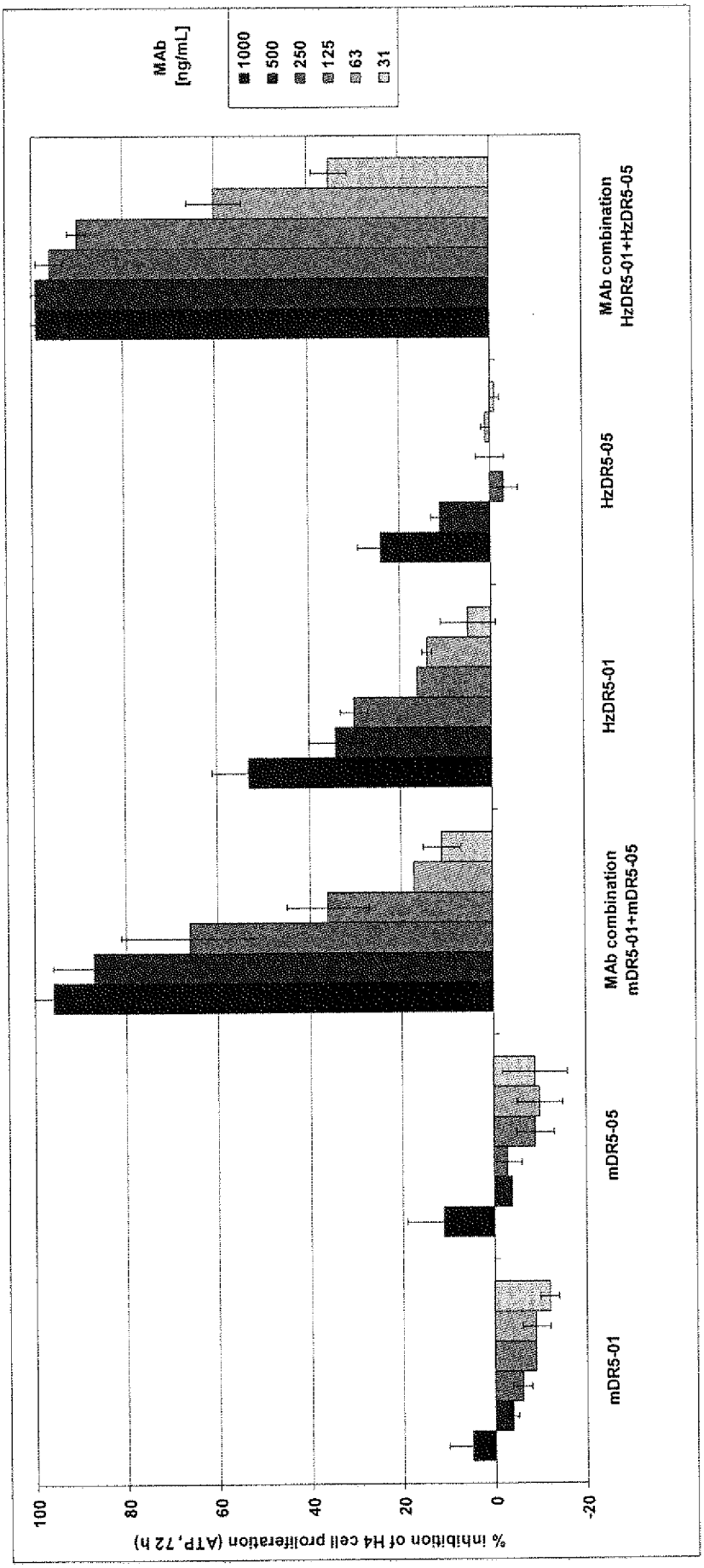

% inhibition of H4 cell proliferation (ATP, 72 h)
100
80
60
40
20
0
-20
MAb [ng/mL]
1000
500
250
125
63
31
mDR5-01
mDR5-05
MAb combination mDR5-01+mDR5-05
HzDR5-01
HzDR5-05
MAb combination HzDR5-01+HzDR5-05

Figure 23

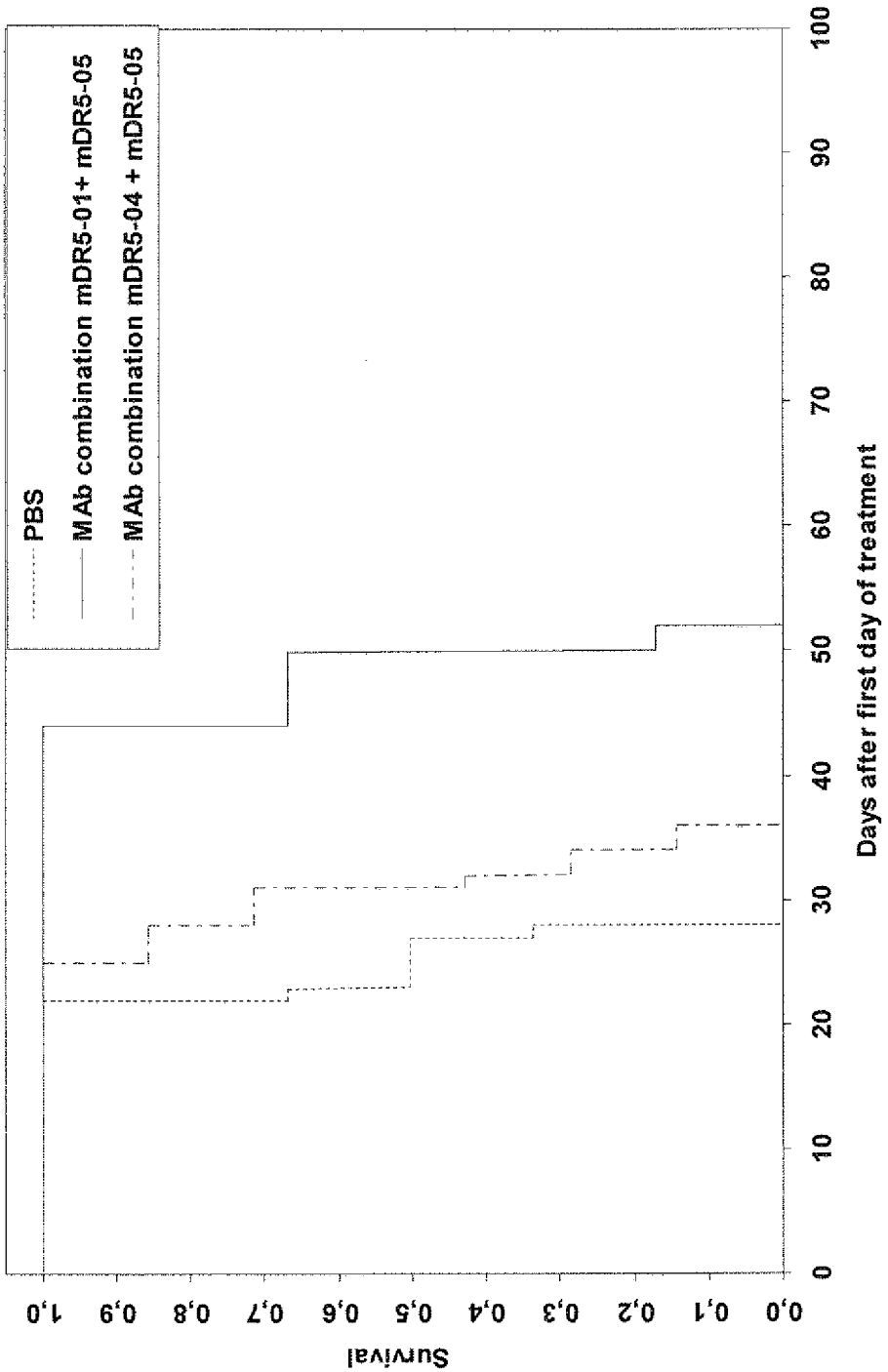

PBS
MAb combination mDR5-01+ mDR5-05
MAb combination mDR5-04 + mDR5-05
Survival
0,0
0,1
0,2
0,3
0,4
0,5
0,6
0,7
0,8
0,9
1,0
0
10
20
30
40
50
60
70
80
90
100
Days after first day of treatment

Figure 24

H-FR1-IMGT
H-CDR1-IMGT
H-FR2-IMGT
H-CDR2-IMGT
H-FR3-IMGT
H-CDR3-IMGT

Figure 25

```
<---------------------------------- L-FR1-IMGT ----------------------------------
GAG ATT GTT ATG ACA CAG TCC CCT GCT ACA TTG AGT GTT AGT CCA GGC GAA AGA GCT ACA CTG
  E   I   V   M   T   Q   S   P   A   T   L   S   V   S   P   G   E   R   A   T   L

----------------------> _____ L-CDR1-IMGT _____ <---------------------- L-FR2-IMGT ----------
TCA TGT AGG GCC TCT CAG TCT ATT AGC AAT AAC CTG CAC TGG TAT CAG CAA AAG CCA GGT CAA
  S   C   R   A   S   Q   S   I   S   N   N   L   H   W   Y   Q   Q   K   P   G   Q

----------------------> L-CDR2-IMGT <----------------------------------------------
GCC CCC AGG CTG CTG ATT AAG TTT GCA TCT CAA AGT ATT ACA GGA ATC CCT GCT CGG TTC AGC
  A   P   R   L   L   I   K   F   A   S   Q   S   I   T   G   I   P   A   R   F   S

---------------------------------------------------- L-FR3-IMGT ----------------------
GGC TCC GGG AGT GGA ACC GAG TTT ACA CTC ACA ATC TCA AGC CTC CAG TCC GAA GAC TTC GCC
  G   S   G   S   G   T   E   F   T   L   T   I   S   S   L   Q   S   E   D   F   A

----------------------> _____ L-CDR3-IMGT _____ <----------
GTA TAT TAC TGT CAG CAG GGC AAC TCT TGG CCC TAC ACC TTC GGT CAG GGA ACC AAG CTG GAG
  V   Y   Y   C   Q   Q   G   N   S   W   P   Y   T   F   G   Q   G   T   K   L   E

ATC AAG
  I   K
```

Figure 26

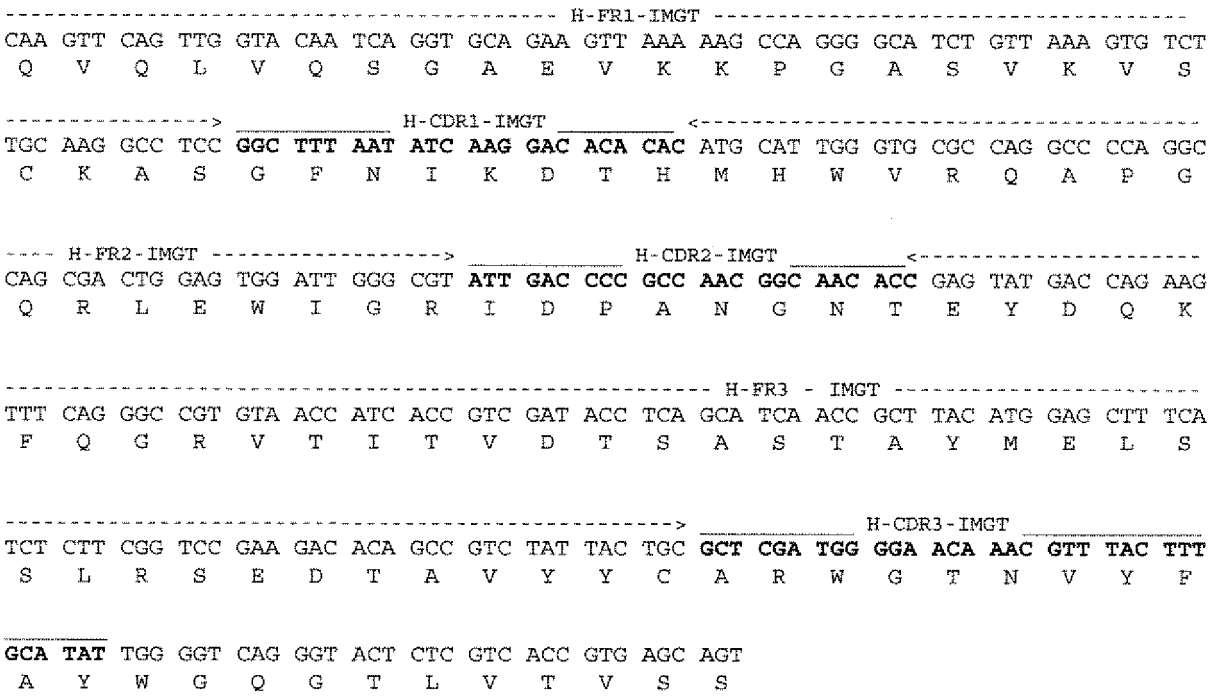

H-FR1-IMGT
CAA GTT CAG TTG GTA CAA TCA GGT GCA GAA GTT AAA AAG CCA GGG GCA TCT GTT AAA GTG TCT
Q V Q L V Q S G A E V K K P G A S V K V S
H-CDR1-IMGT
TGC AAG GCC TCC GGC TTT AAT ATC AAG GAC ACA CAC ATG CAT TGG GTG CGC CAG GCC CCA GGC
C K A S G F N I K D T H M H W V R Q A P G
H-FR2-IMGT
H-CDR2-IMGT
CAG CGA CTG GAG TGG ATT GGG CGT ATT GAC CCC GCC AAC GGC AAC ACC GAG TAT GAC CAG AAG
Q R L E W I G R I D P A N G N T E Y D Q K
H-FR3 - IMGT
TTT CAG GGC CGT GTA ACC ATC ACC GTC GAT ACC TCA GCA TCA ACC GCT TAC ATG GAG CTT TCA
F Q G R V T I T V D T S A S T A Y M E L S
H-CDR3-IMGT
TCT CTT CGG TCC GAA GAC ACA GCC GTC TAT TAC TGC GCT CGA TGG GGA ACA AAC GTT TAC TTT
S L R S E D T A V Y Y C A R W G T N V Y F
GCA TAT TGG GGT CAG GGT ACT CTC GTC ACC GTG AGC AGT
A Y W G Q G T L V T V S S

Figure 27

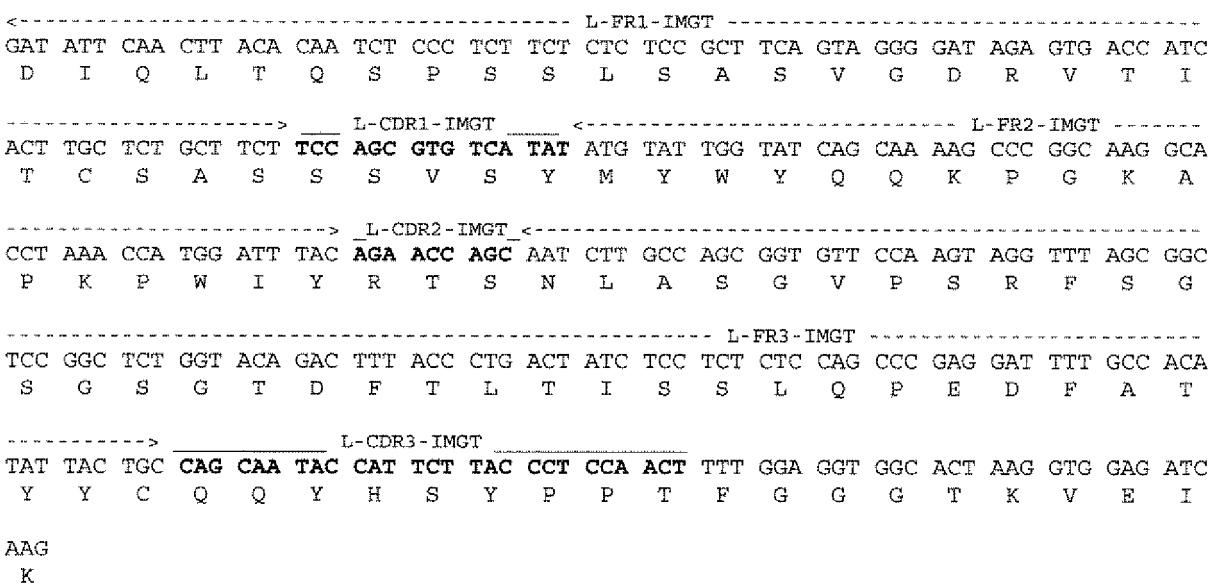

L-FR1-IMGT
GAT ATT CAA CTT ACA CAA TCT CCC TCT TCT CTC TCC GCT TCA GTA GGG GAT AGA GTG ACC ATC
D I Q L T Q S P S S L S A S V G D R V T I
L-CDR1-IMGT
L-FR2-IMGT
ACT TGC TCT GCT TCT TCC AGC GTG TCA TAT ATG TAT TGG TAT CAG CAA AAG CCC GGC AAG GCA
T C S A S S S V S Y M Y W Y Q Q K P G K A
L-CDR2-IMGT
CCT AAA CCA TGG ATT TAC AGA ACC AGC AAT CTT GCC AGC GGT GTT CCA AGT AGG TTT AGC GGC
P K P W I Y R T S N L A S G V P S R F S G
L-FR3-IMGT
TCC GGC TCT GGT ACA GAC TTT ACC CTG ACT ATC TCC TCT CTC CAG CCC GAG GAT TTT GCC ACA
S G S G T D F T L T I S S L Q P E D F A T
L-CDR3-IMGT
TAT TAC TGC CAG CAA TAC CAT TCT TAC CCT CCA ACT TTT GGA GGT GGC ACT AAG GTG GAG ATC
Y Y C Q Q Y H S Y P P T F G G G T K V E I
AAG
K

Figure 28