Fig. 1

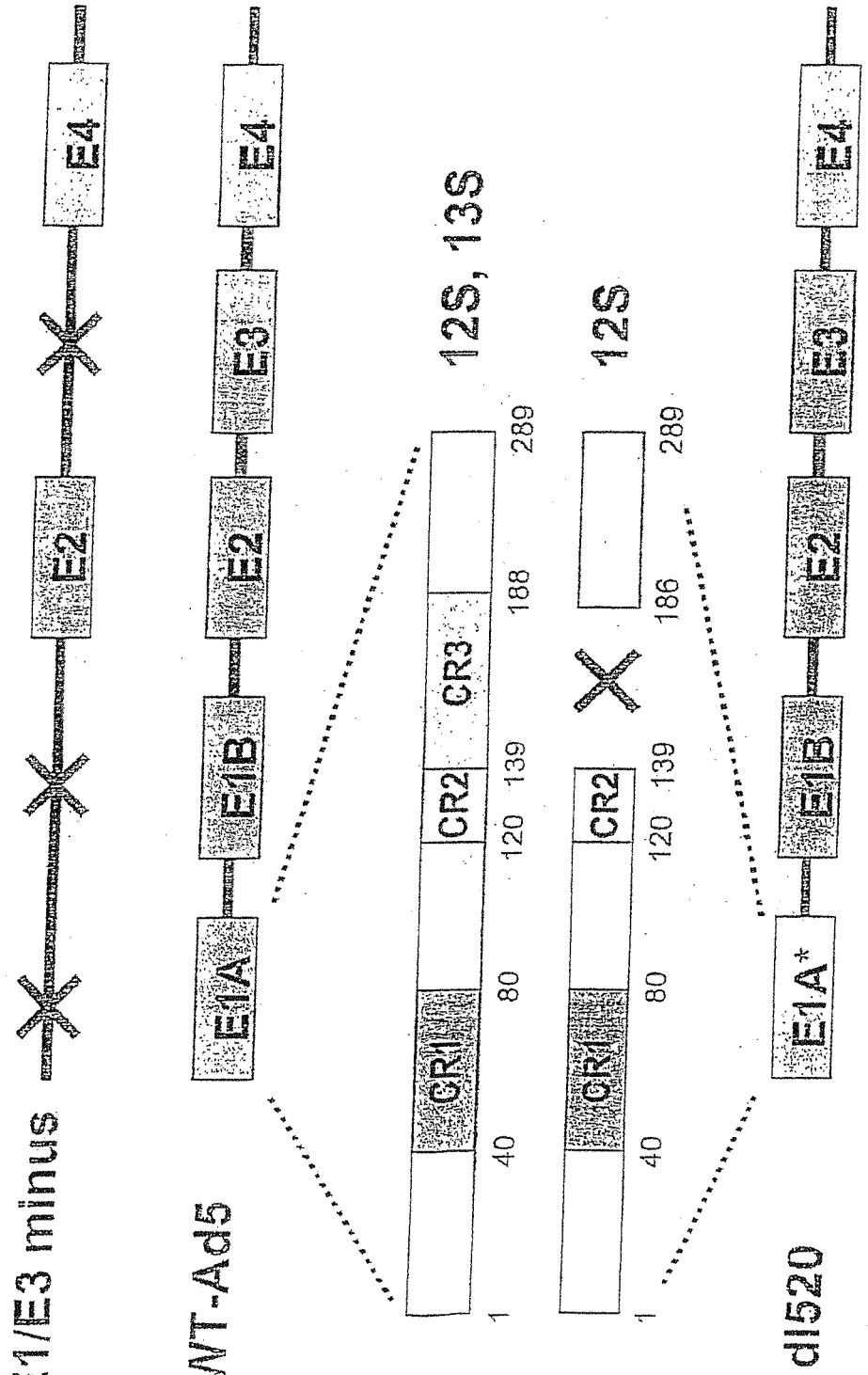

E1/E3 minus
E1A
E1B
E2
E4
WT-Ad5
E1A
E1B
E2
E3
E4
12S, 13S
CR1
CR2
CR3
40
80
120
139
188
289
1
12S
CR1
CR2
40
80
120
139
186
289
1
dl520
E1A*
E1B
E2
E3
E4

Fig. 2

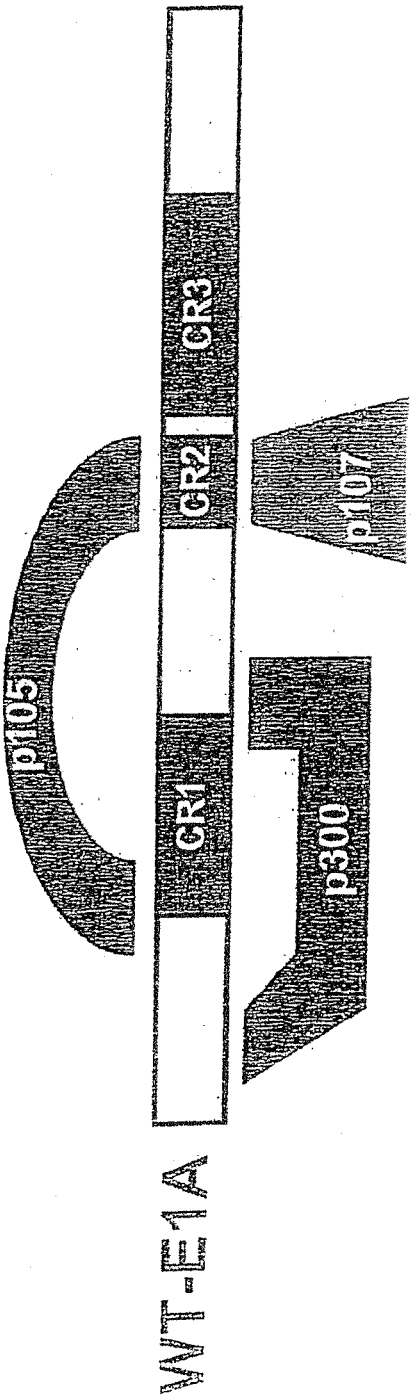


Fig. 3

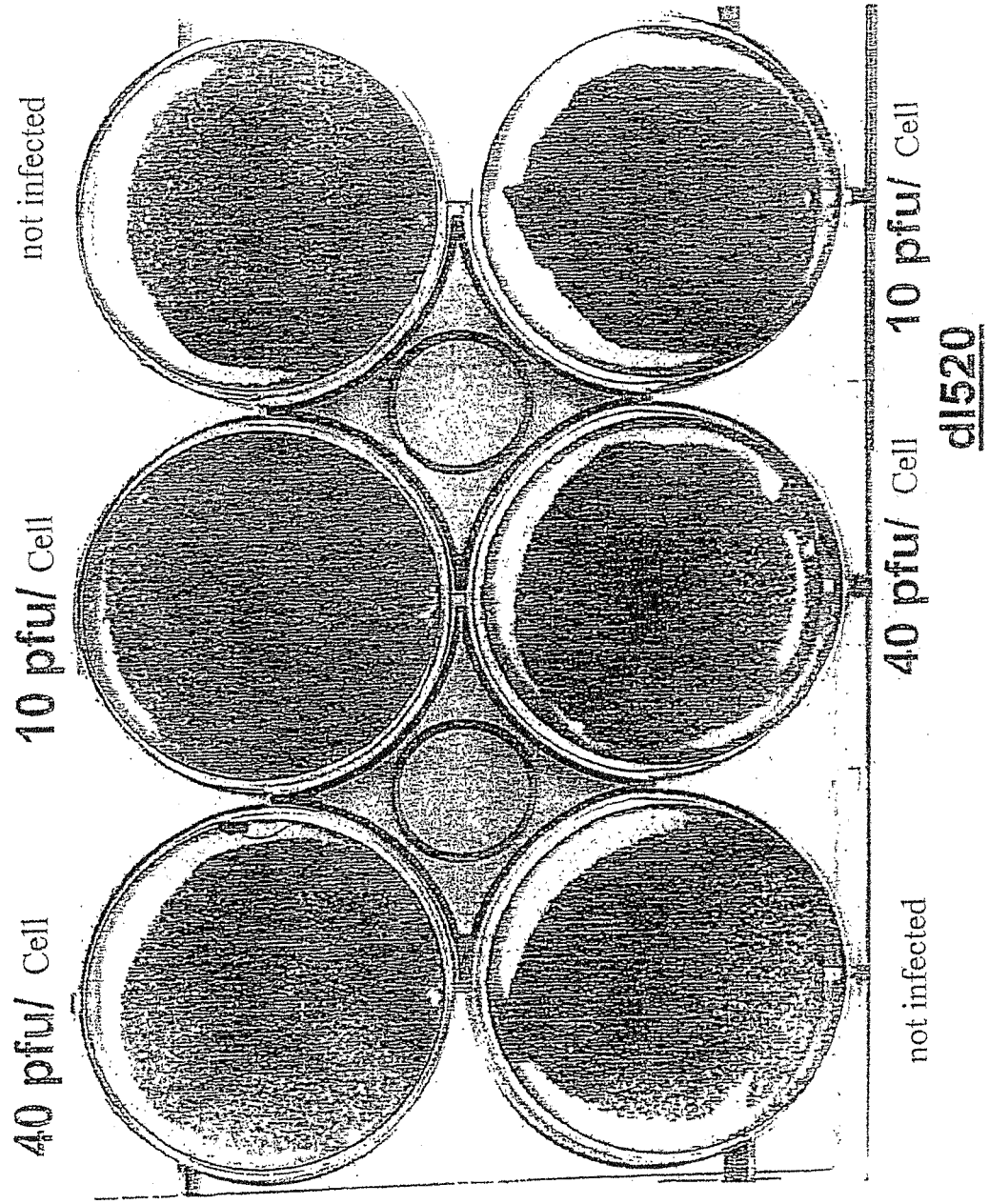

E1/E3-minus Ad5
40 pfu/ Cell
10 pfu/ Cell
not infected
not infected
40 pfu/ Cell
10 pfu/ Cell
dl520

Fig. 4

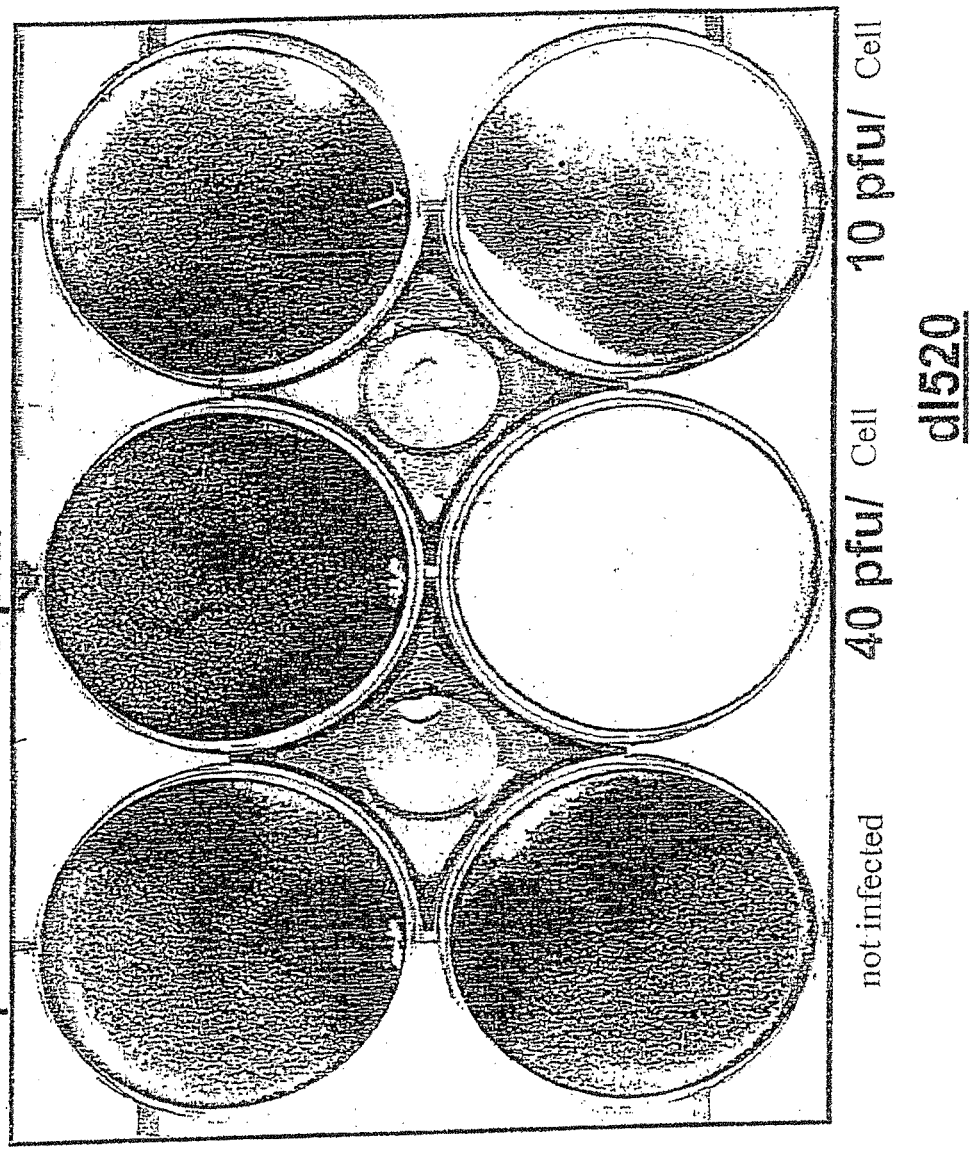

E1/E3-minus Ad5
40 pfu/ Cell
10 pfu/ Cell
not infected
not infected
40 pfu/ Cell
10 pfu/ Cell
dl520

Fig. 5

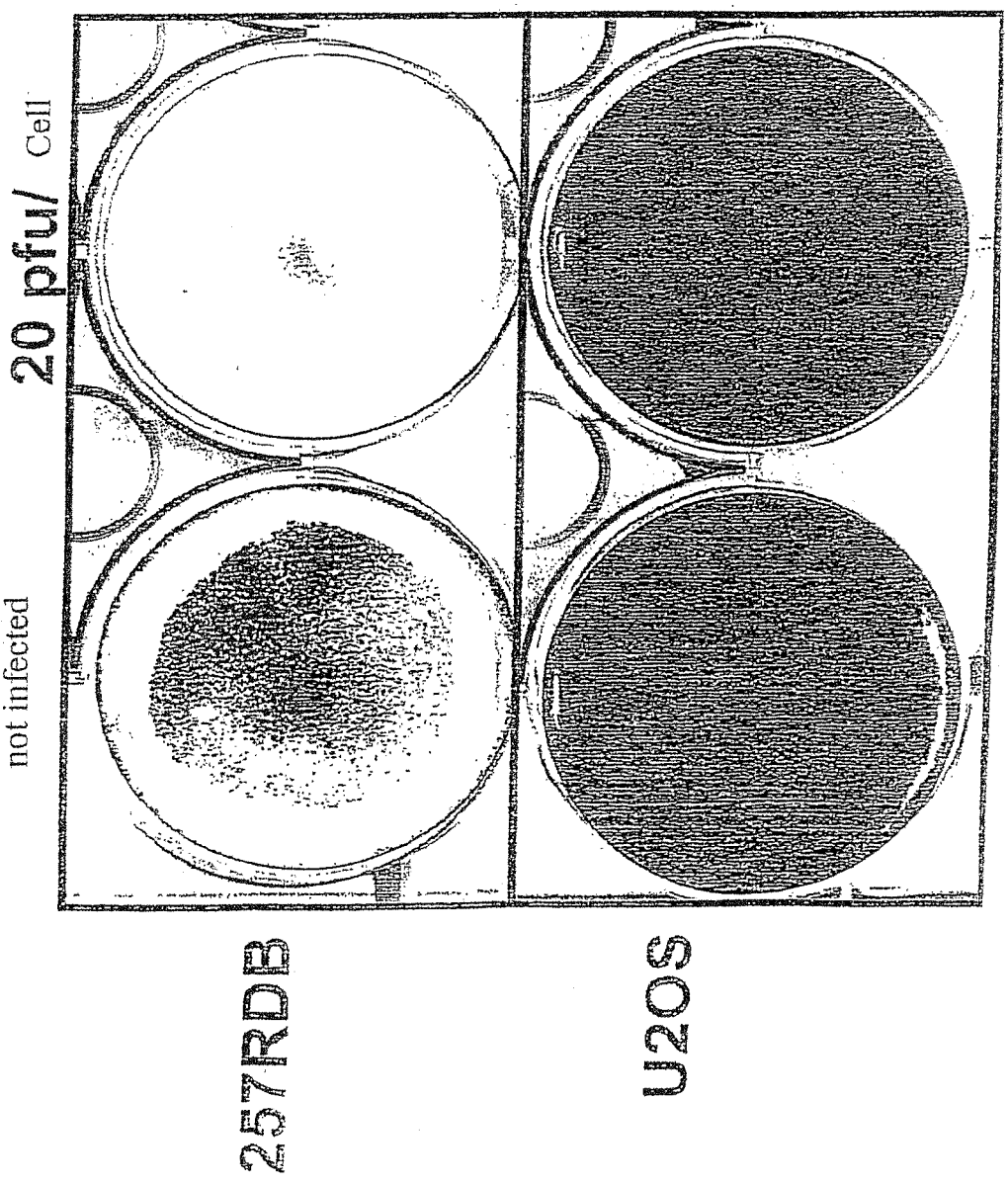


Fig. 6

Fig. 7

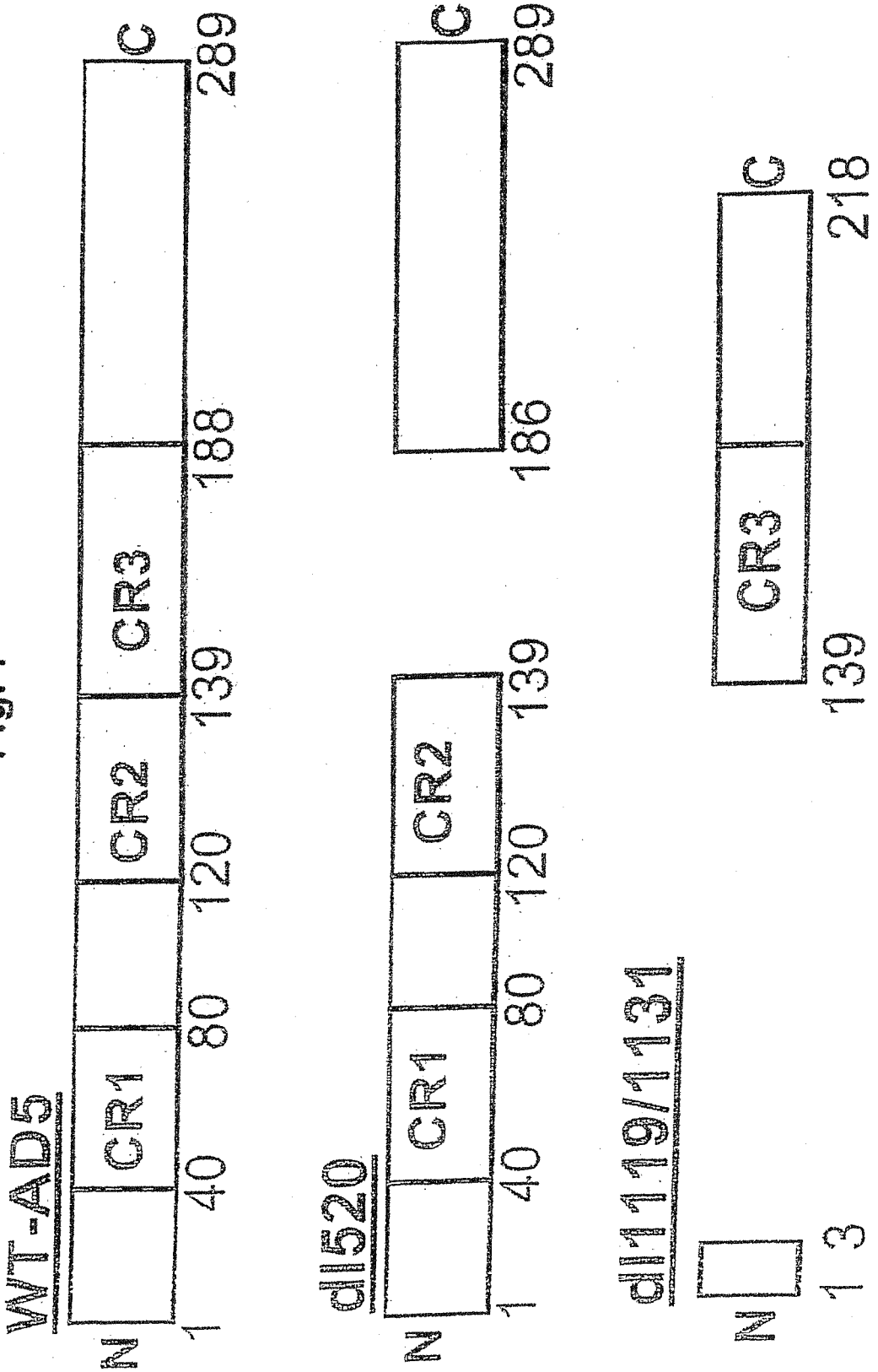

WT-AD5
N
C
CR1
CR2
CR3
1
40
80
120
139
188
289
dl520
N
C
CR1
CR2
1
40
80
120
139
186
289
dl1119/1131
N
C
CR3
1
3
139
218

Fig. 8

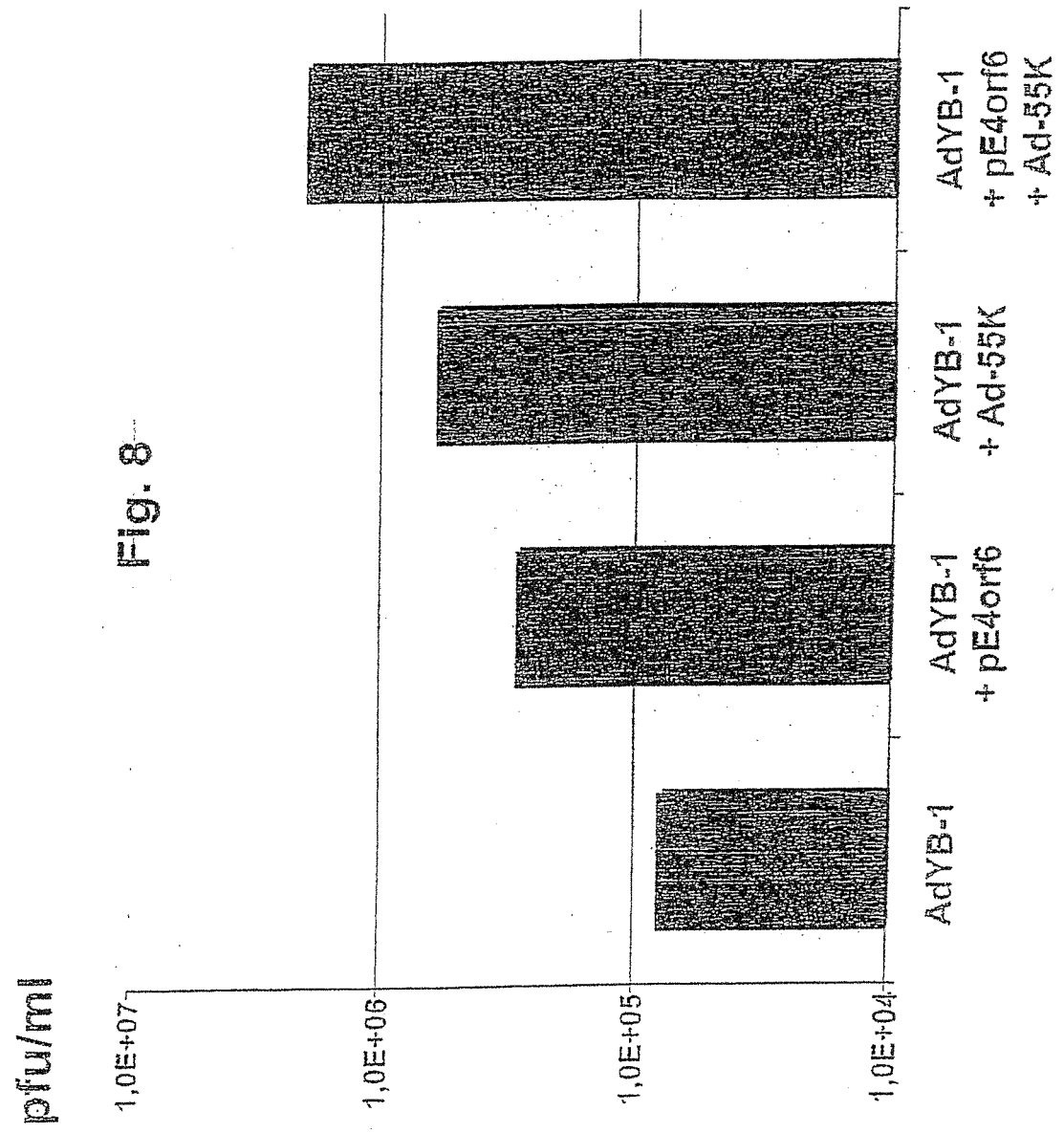

pfu/ml
1,0E+07
1,0E+06
1,0E+05
1,0E+04
AdYB-1
AdYB-1 + pE4orf6
AdYB-1 + Ad-55K
AdYB-1 + pE4orf6 + Ad-55K

Fig. 9

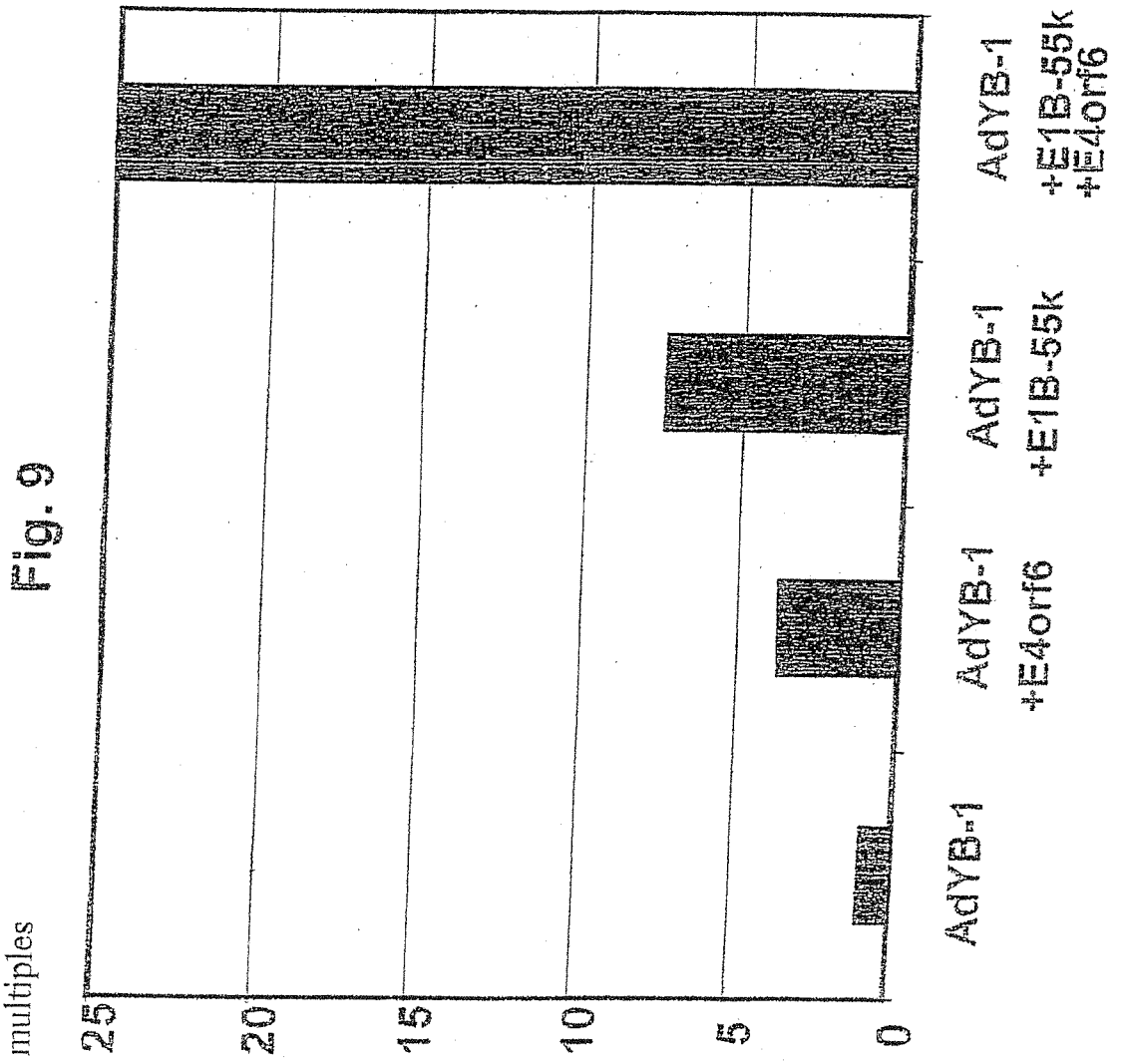

multiples
25
20
15
10
5
0
AdYB-1
AdYB-1 +E4orf6
AdYB-1 +E1B-55k
AdYB-1 +E1B-55k +E4orf6

Fig. 10

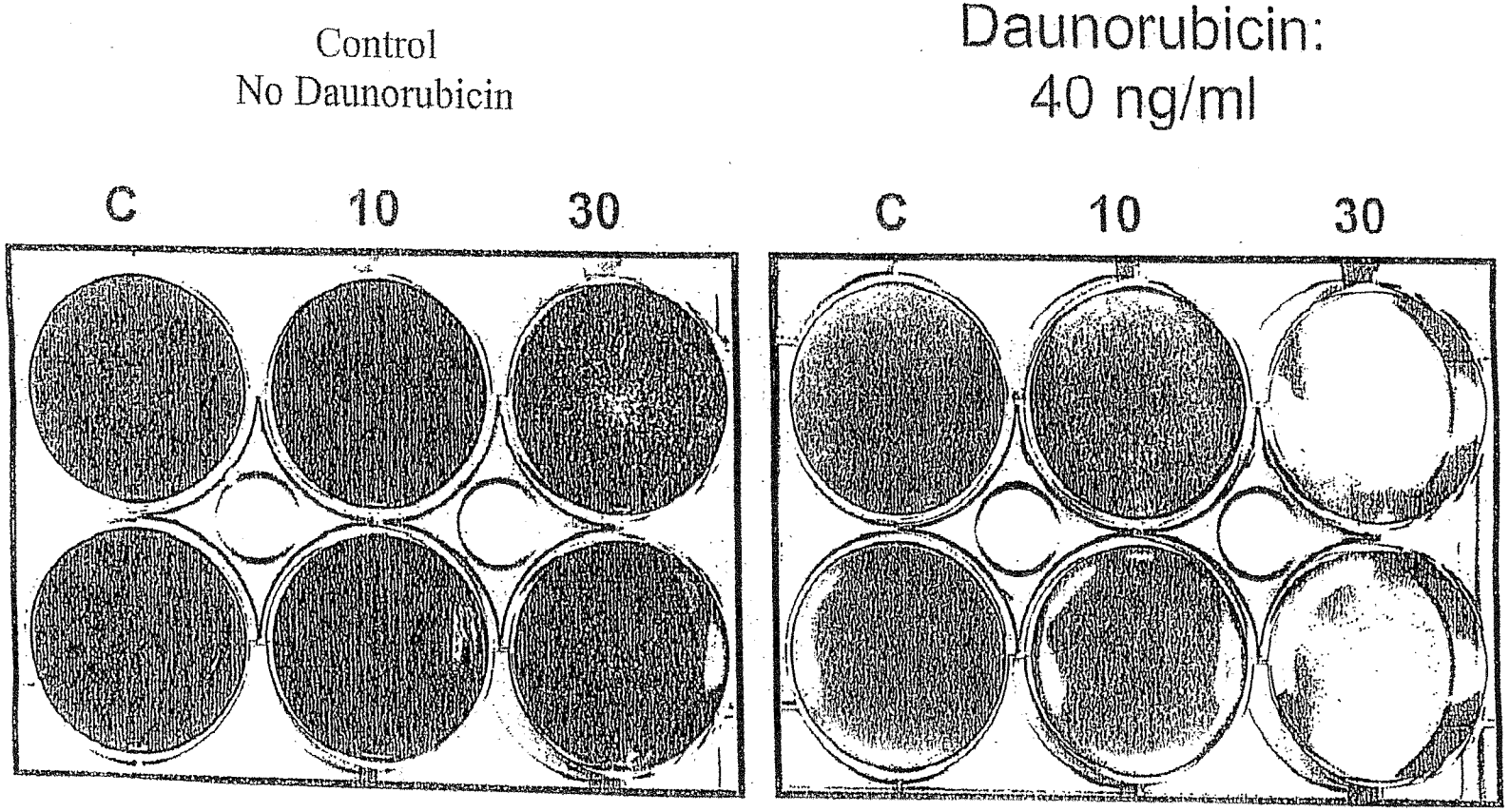
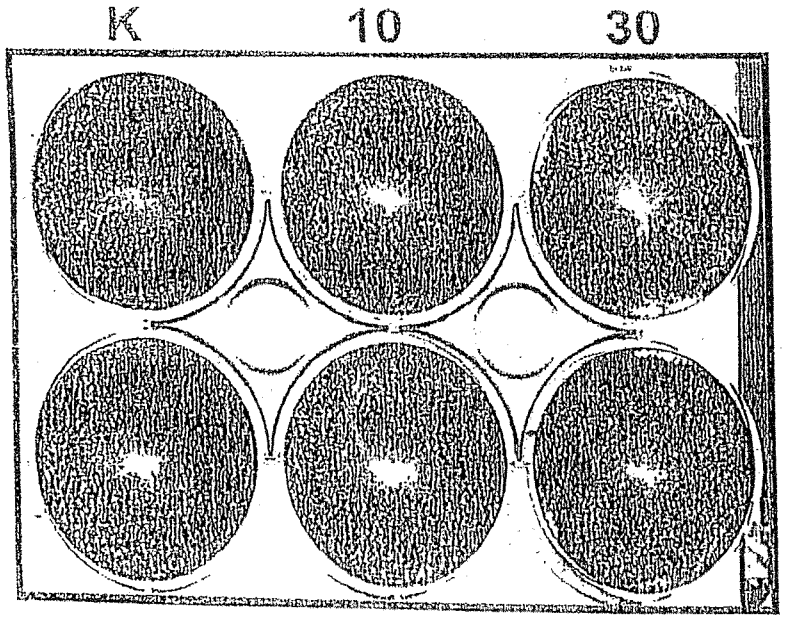


Fig. 11

Control
No Daunorubicin



Daunorubicin:
40 ng/ml

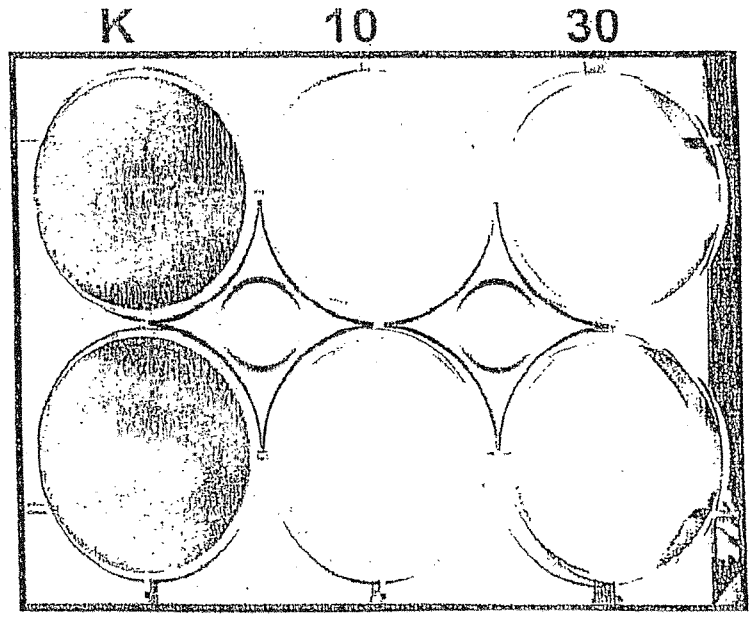
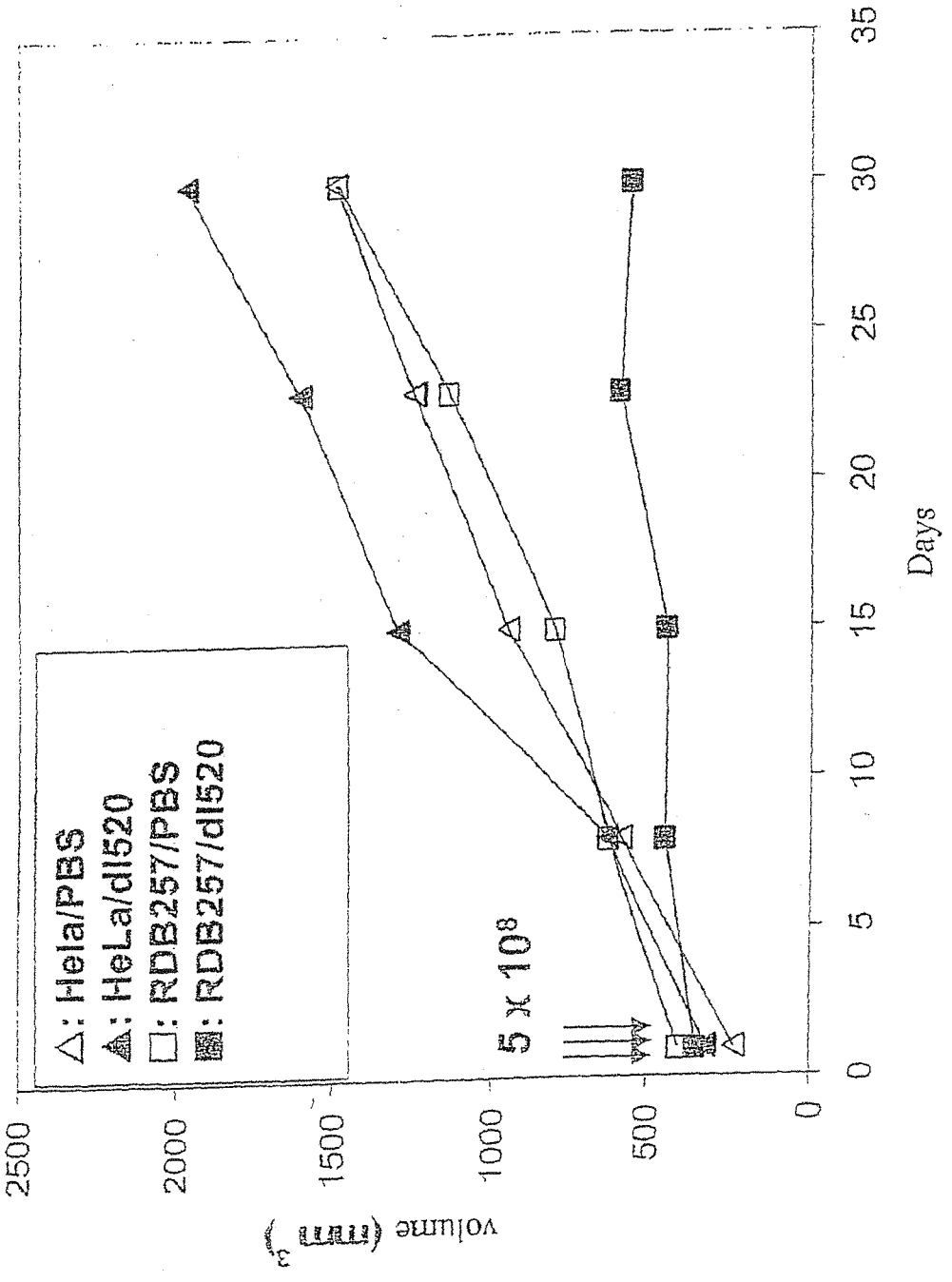
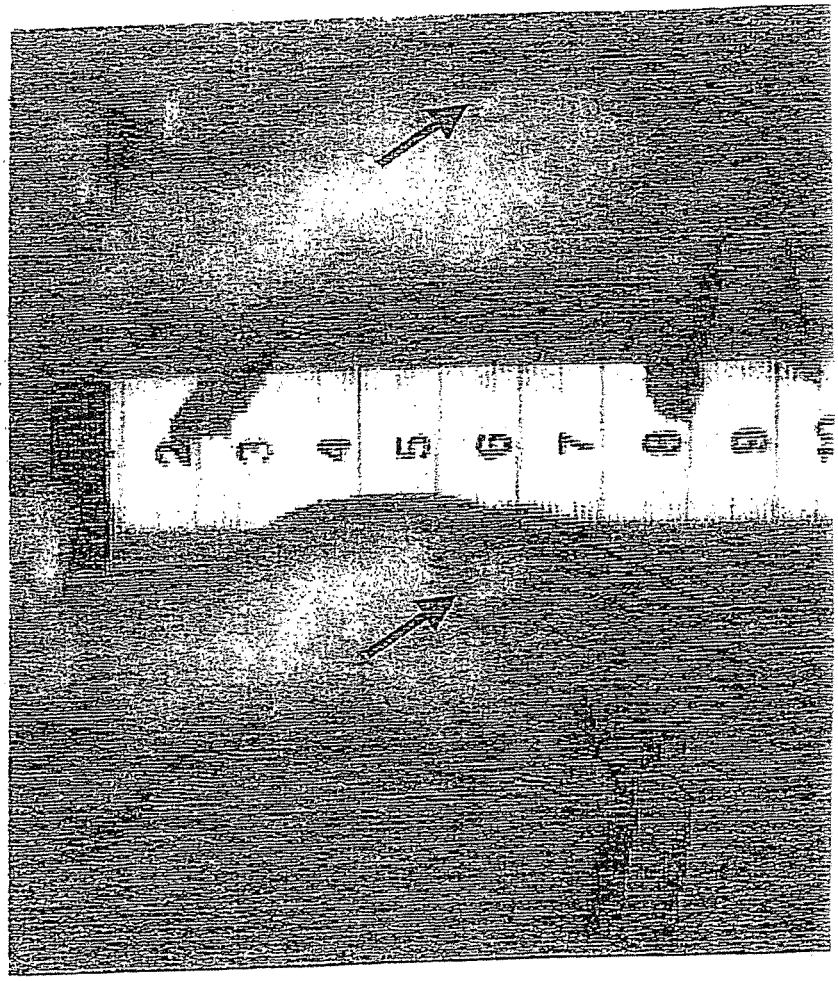


Fig. 12


△: Hela/PBS
▲: HeLa/dl520
□: RDB257/PBS
▩: RDB257/dl520
5 x 10⁸
volume (mm³)
Days
0
500
1000
1500
2000
2500
0
5
10
15
20
25
30
35



PBS 5 x 10^8 dl520

Fig. 13

Fig. 14

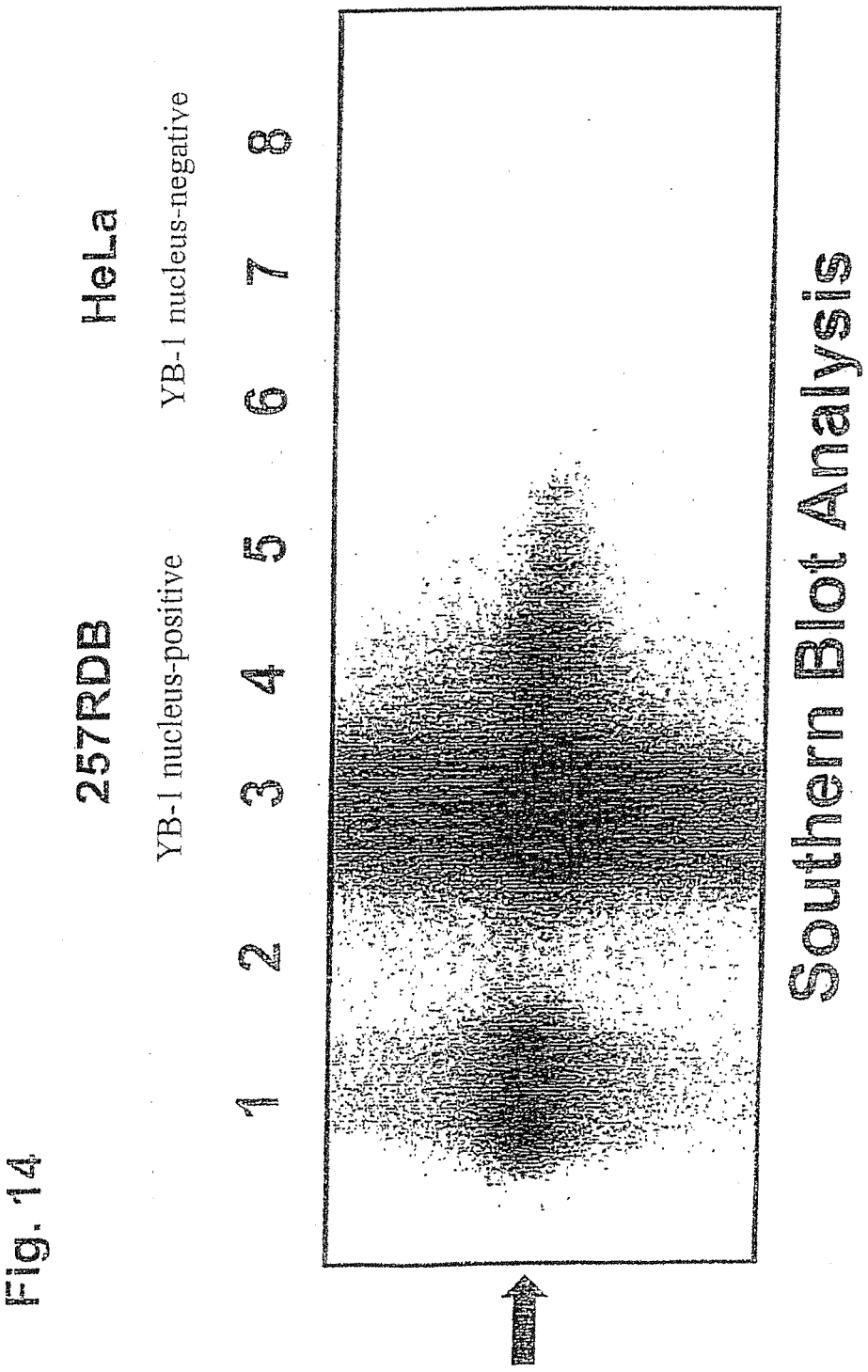

257RDB
HeLa
YB-1 nucleus-positive
YB-1 nucleus-negative
1 2 3 4 5 6 7 8
Southern Blot Analysis

Fig. 15

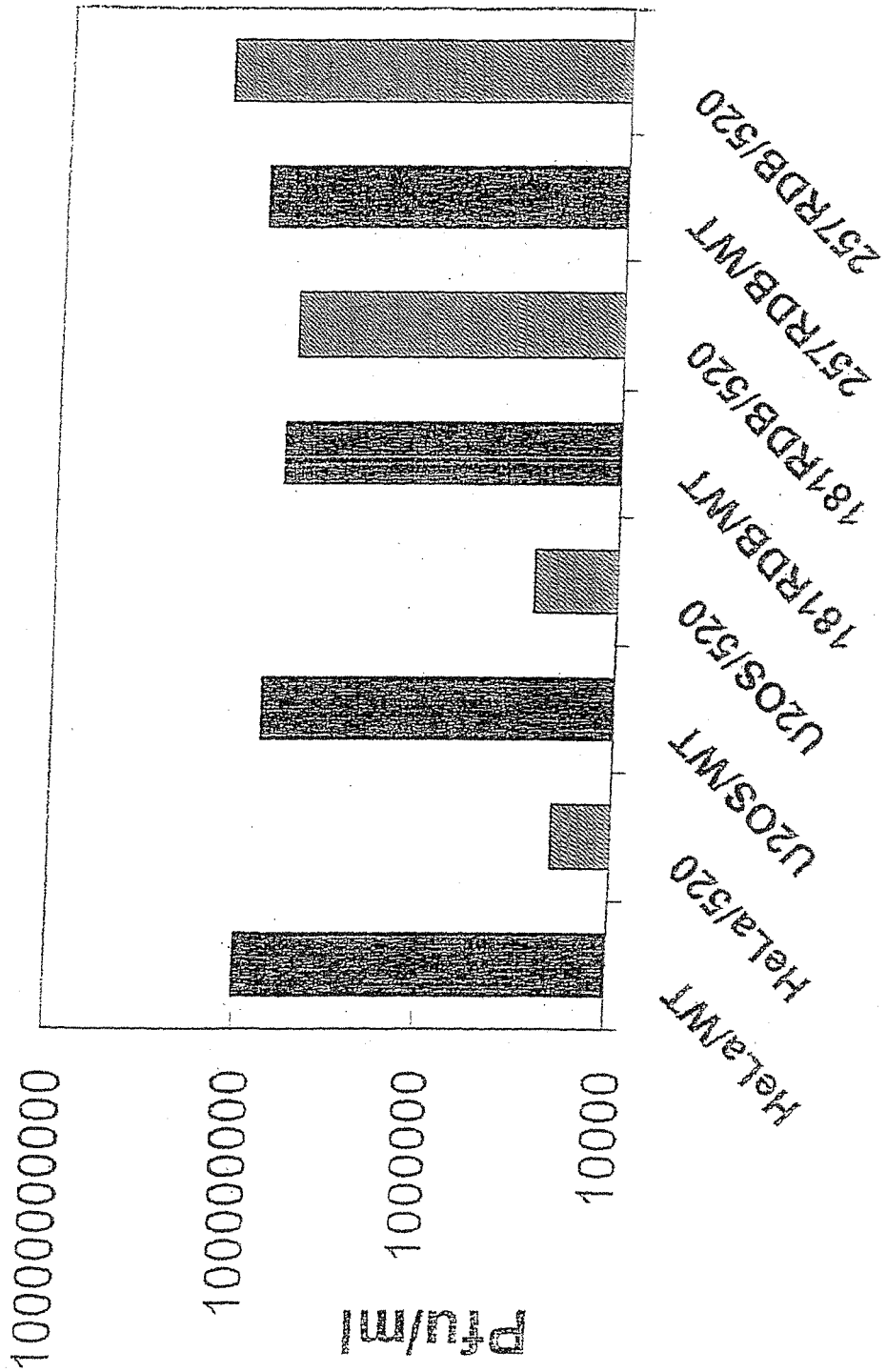
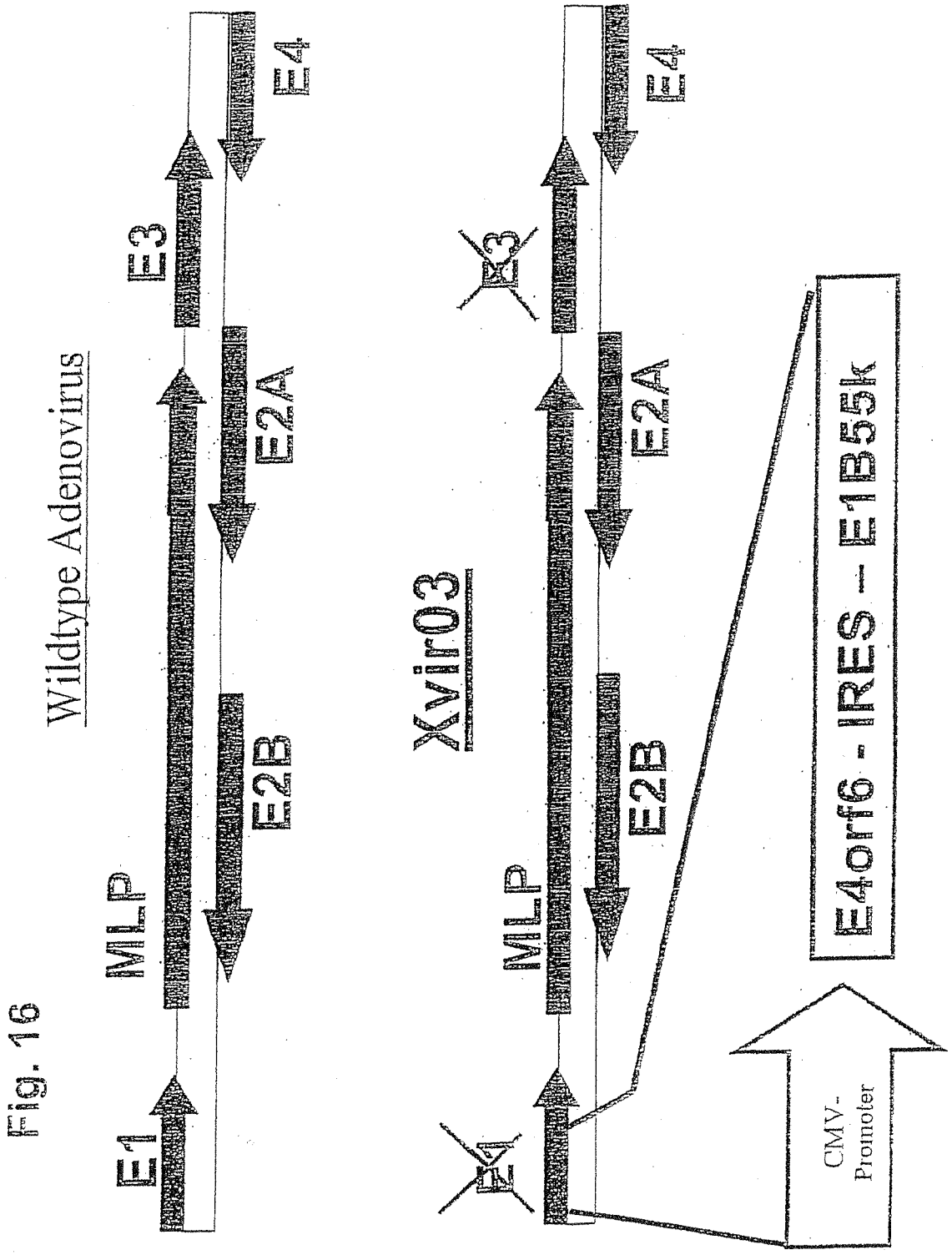

Pfu/ml
10000000000
1000000000
100000000
10000000
1000000
100000
10000
HeLa/MT
HeLa/520
U2OS/MT
U2OS/520
187RDB/MT
187RDB/520
257RDB/MT
257RDB/520

Fig. 16


Wildtype Adenovirus
E1
MLP
E2B
E2A
E3
E4
Xvir03
E1
MLP
E2B
E2A
E3
E4
E4orf6 - IRES - E1B55k
CMV-
Promoter

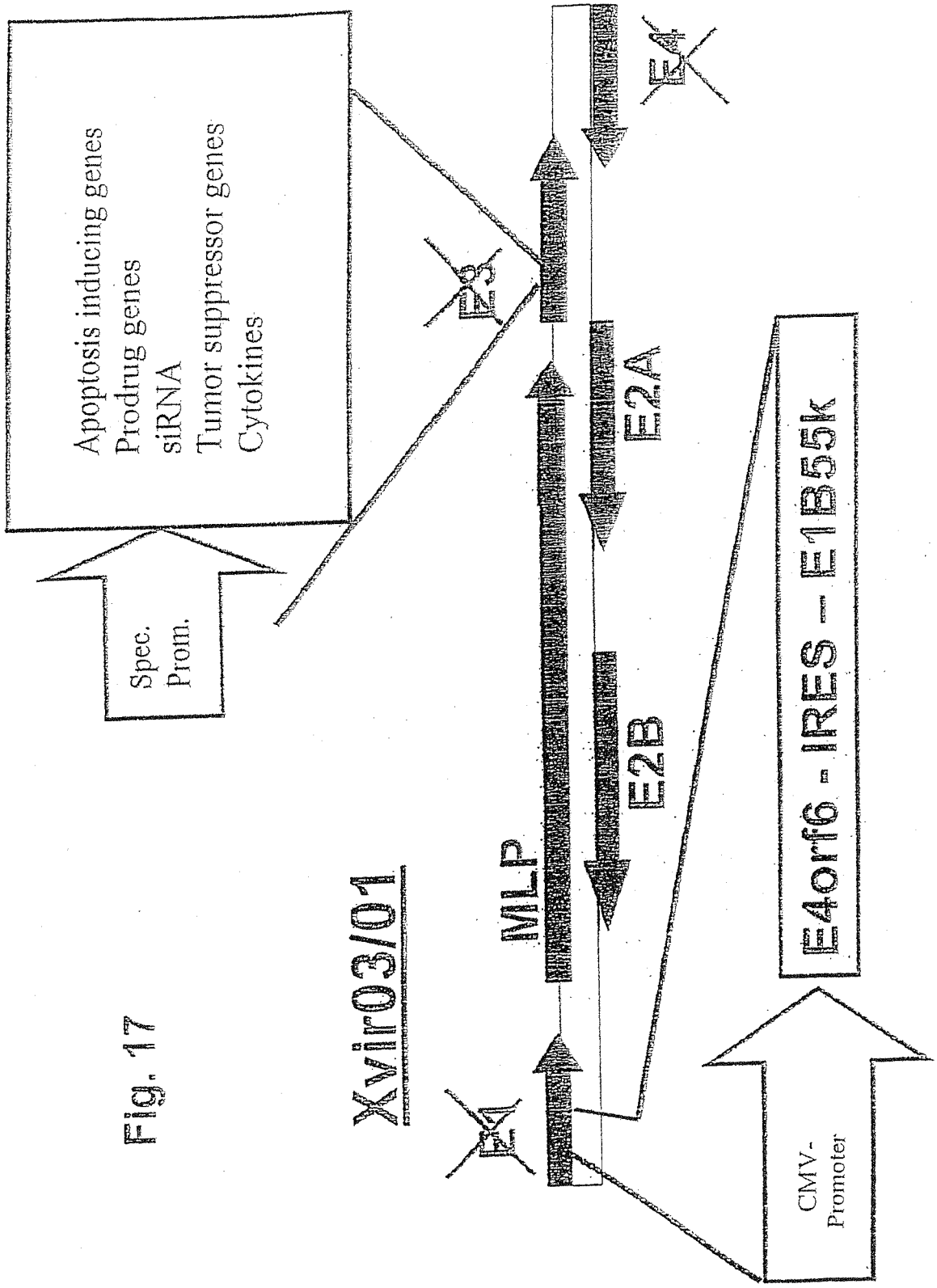


Fig. 17

XviIr03/01

Fig. 18A

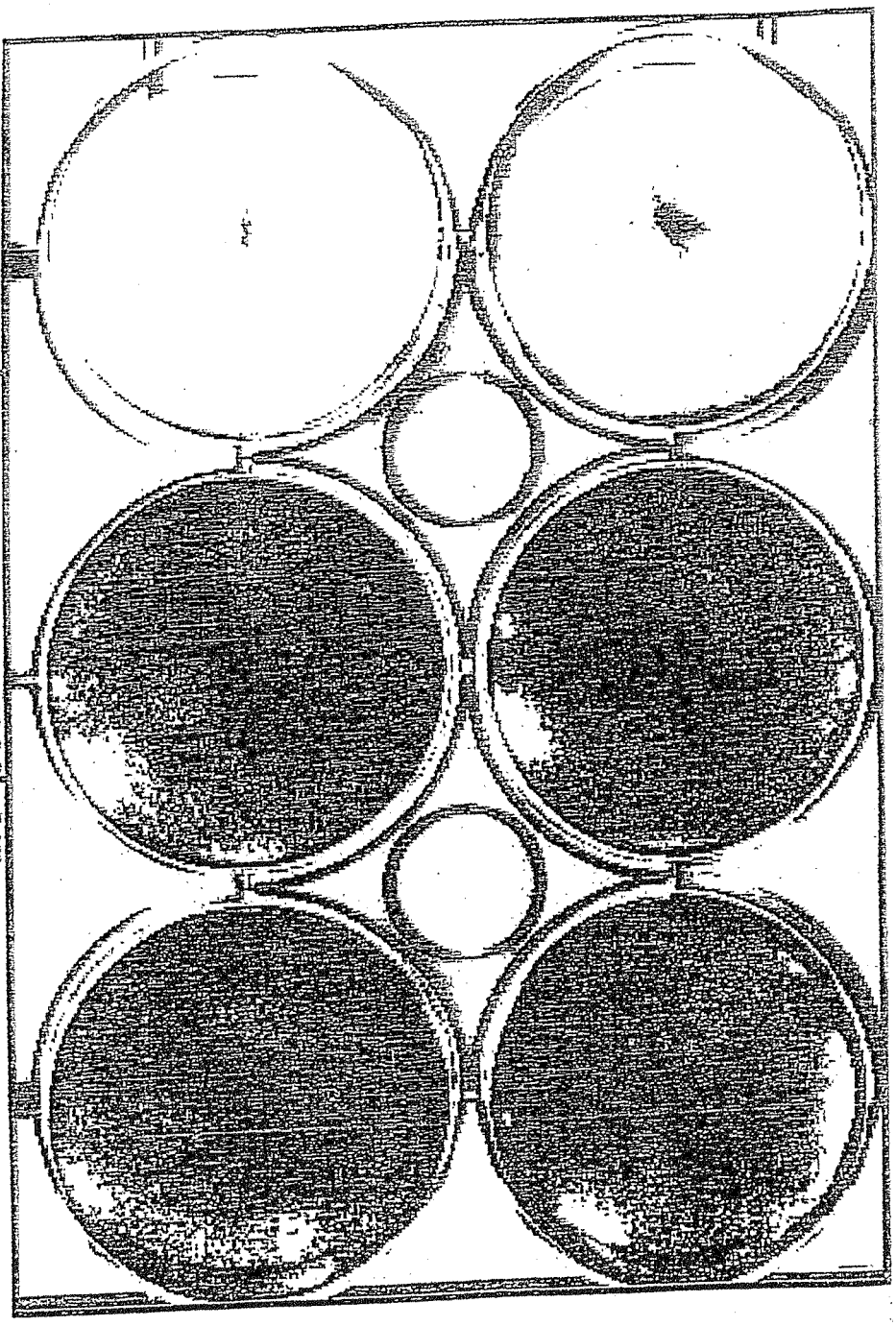


Fig. 18B

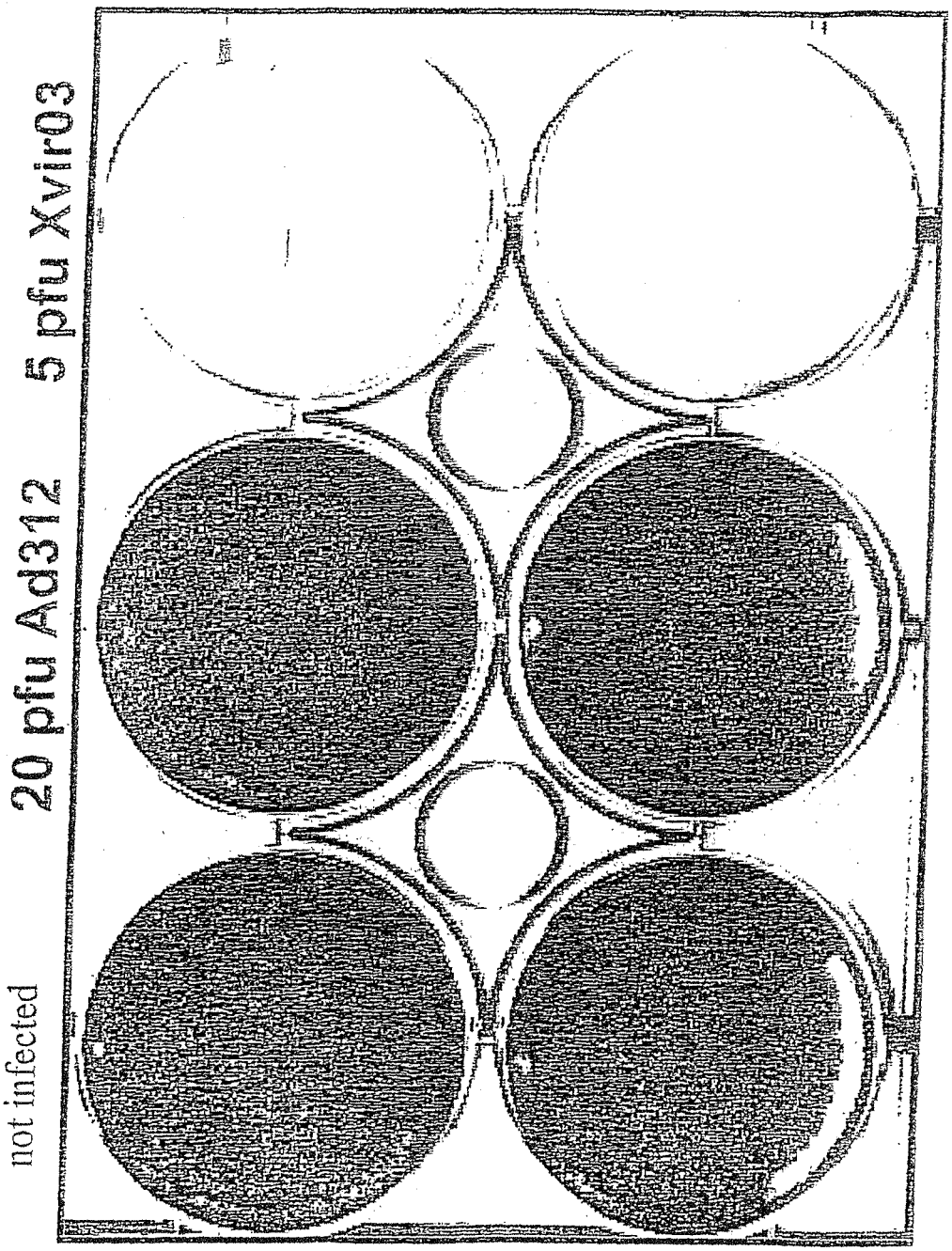
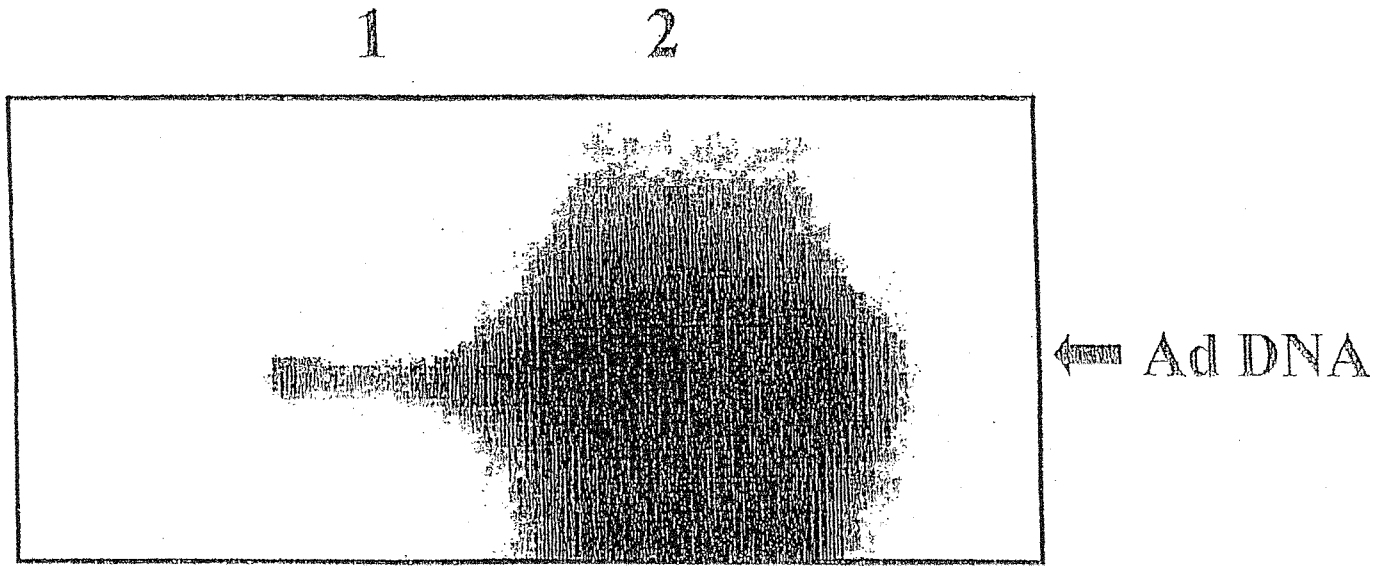


Fig. 19

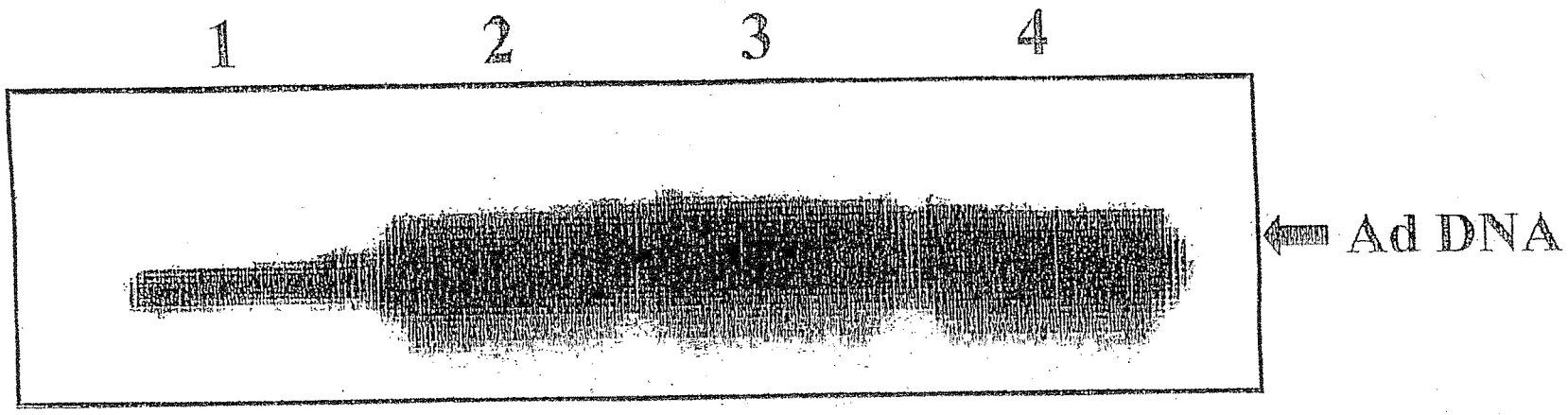
U373 cells infected with 10 pfu/cell
dl520 after 24 h of incubation
with 5µM Irinotecan



Southern Blot Analysis

Fig. 20

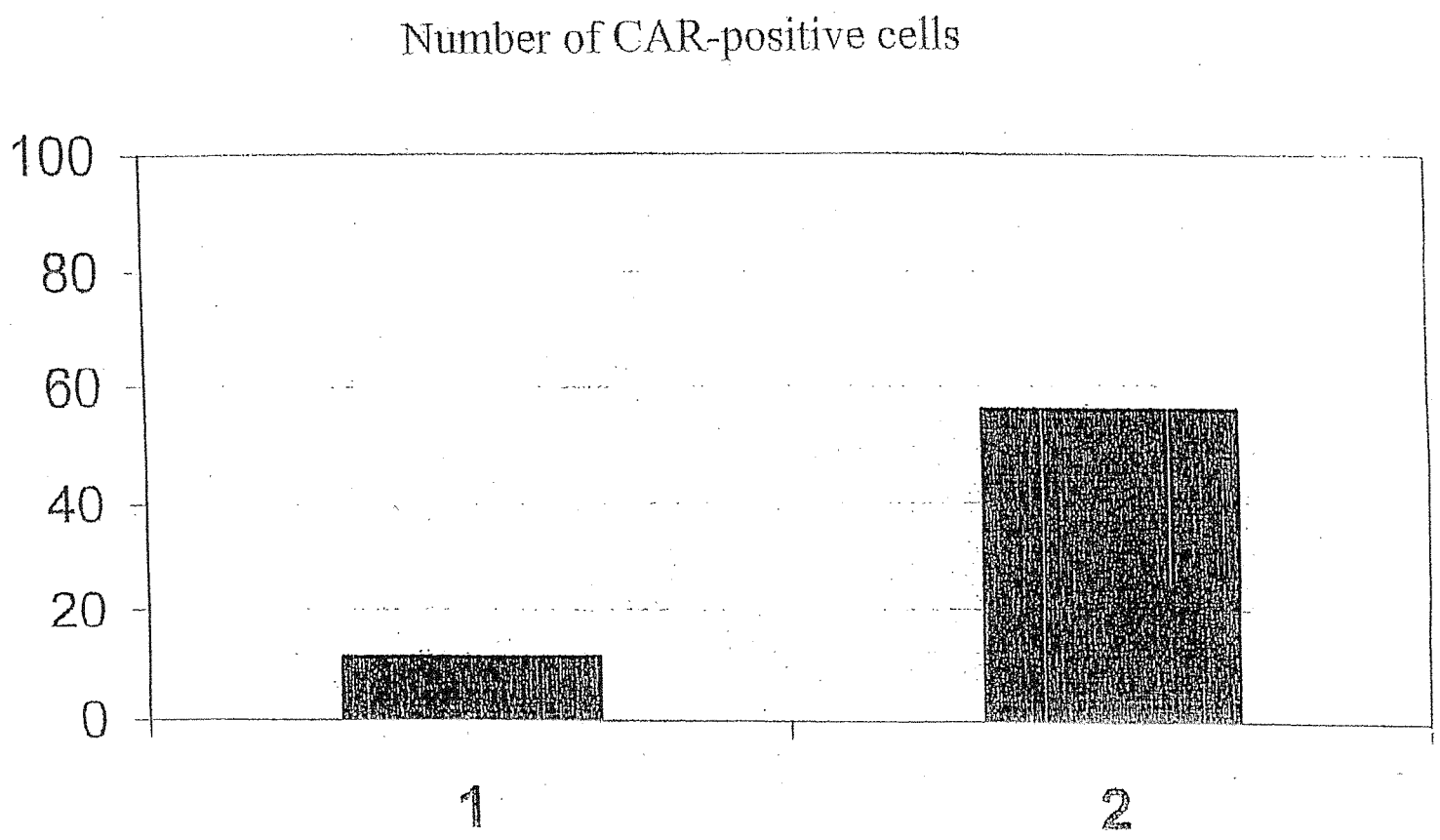
U373 cells infected with 10 pfu/cell dl520 after 24 h of incubation with increasing concentration of Trichostatin



Southern Blot Analysis

Fig. 21

FACS-Analysis: Car-Expression of U373 cells after 24 h of incubation with Trichostatin



Oncolytic Effect of dl520 in U373 cells in combination with Irinotecan and Trichostatin

Fig. 22

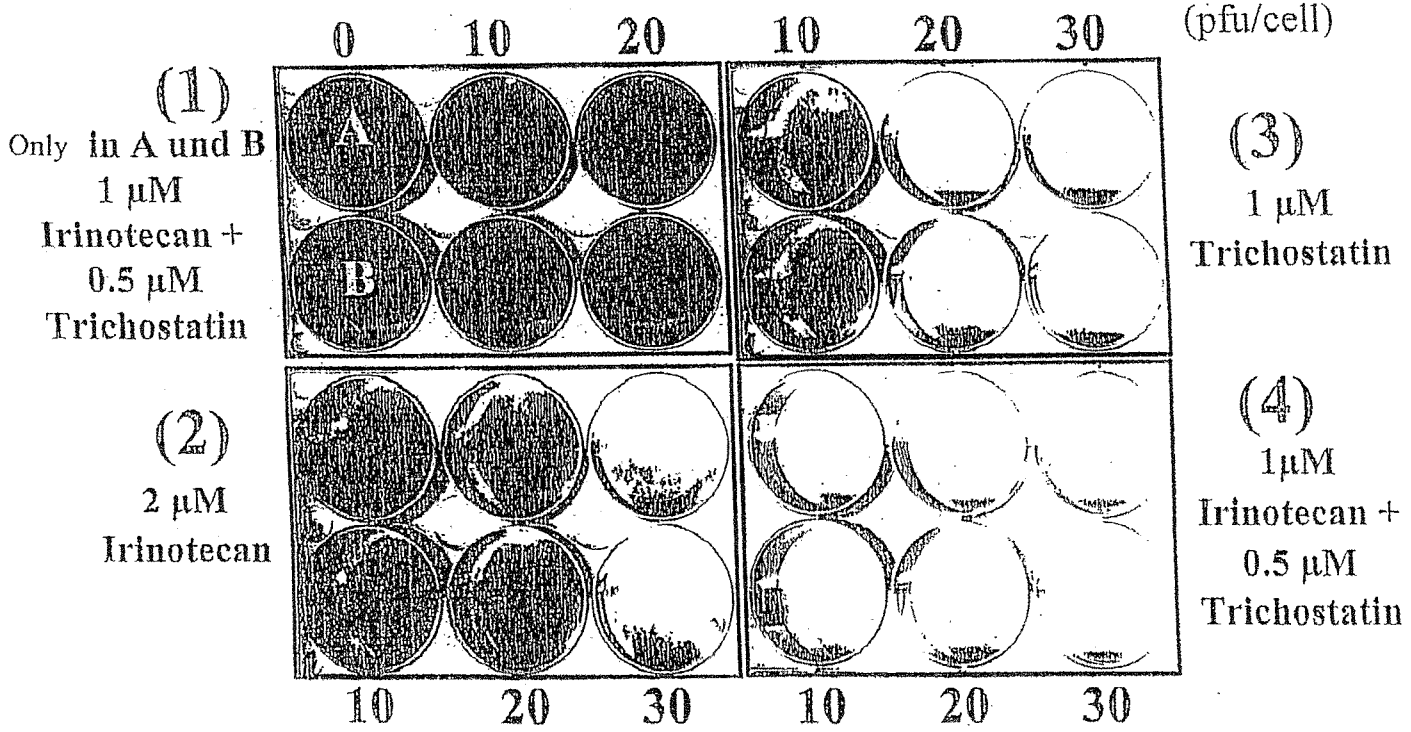


Fig. 23

E1B55k region:
ORF = 2019 – 3506 bp
***Bfr*I cleavage site = 3534bp**
3'UTR = 3506 – 4147 bp

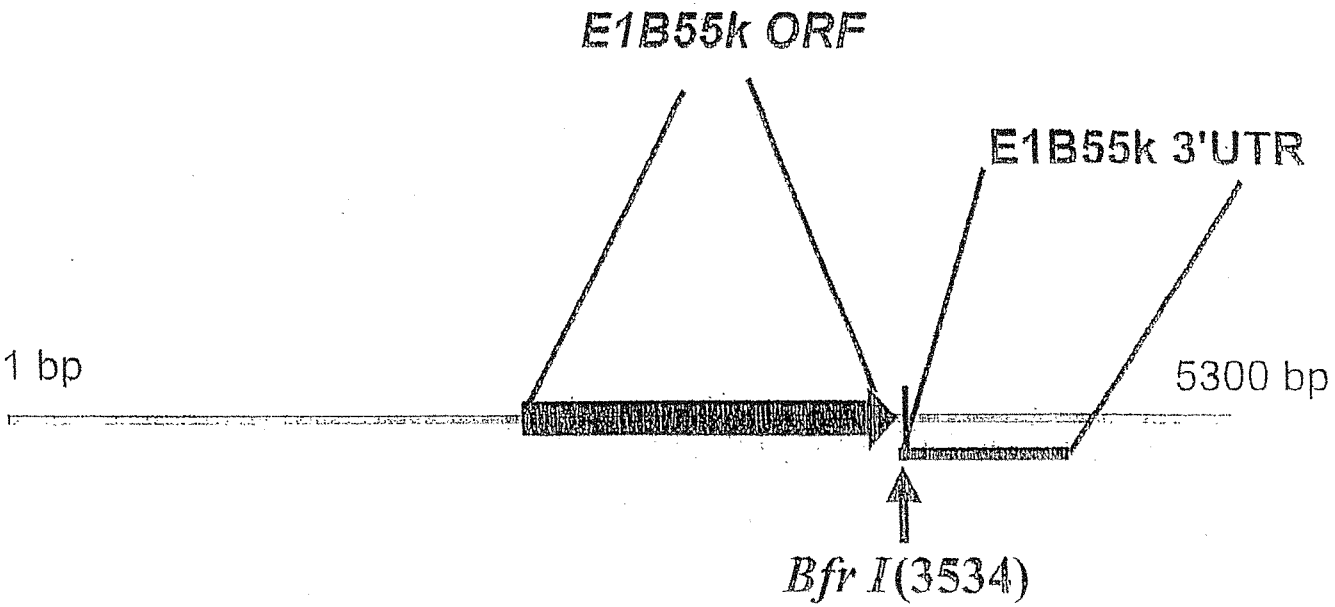


Fig. 24

The sequence of the E1B55k 3'-UTR is shown from position 3507 to 4107 bp

5'tgaggtactgaaatgtgtgggcgtggcttaagggtgggaaagaatatataaggtggg
ggtcttatgtagttttgtatctgttttgcagcagccgccgccgccatgagcaccaactcgttt
gatggaagcattgtgagctcatatttgacaacgcgcatgcccccatgggccggggtgc
gtcagaatgtgatgggctccagcattgatggtcgccccgtcctgcccgcaaactctacta
ccttgacctacgagaccgtgtctggaacgccgttggagactgcagcctccgccgccgc
ttcagccgctgcagccaccgcccgcgggattgtgactgactttgctttcctgagcccgctt
gcaagcagtgcagcttcccgttcatccgcccgcgatgacaagttgacggctcttttggca
caattggattctttgacccgggaacttaatgtcgtttctcagcagctgttggatctgcgcca
gcaggtttctgccctgaaggcttcctcccctcccaatgcggtttaaaacataaataaaaa
accagactctgtttggatttggatcaagcaagtgtcttgctgtctttatttaggggttttgc

Fig. 25

Northern blot Anlaysis of the E2 gene expression
Expression in Ad312 infected cells

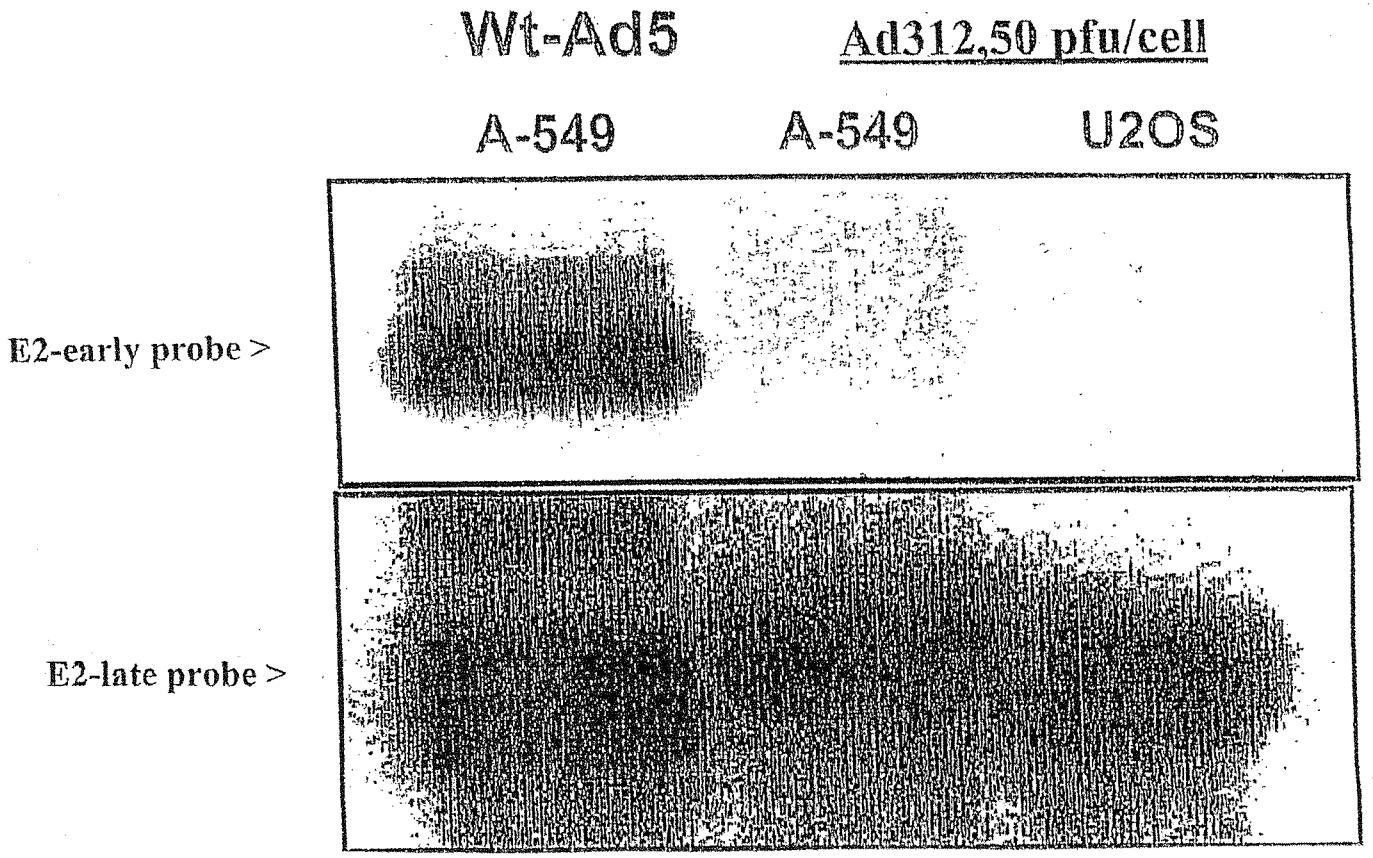


Fig. 26

Northern blot Analysis of the E2 gene expression in infected cells

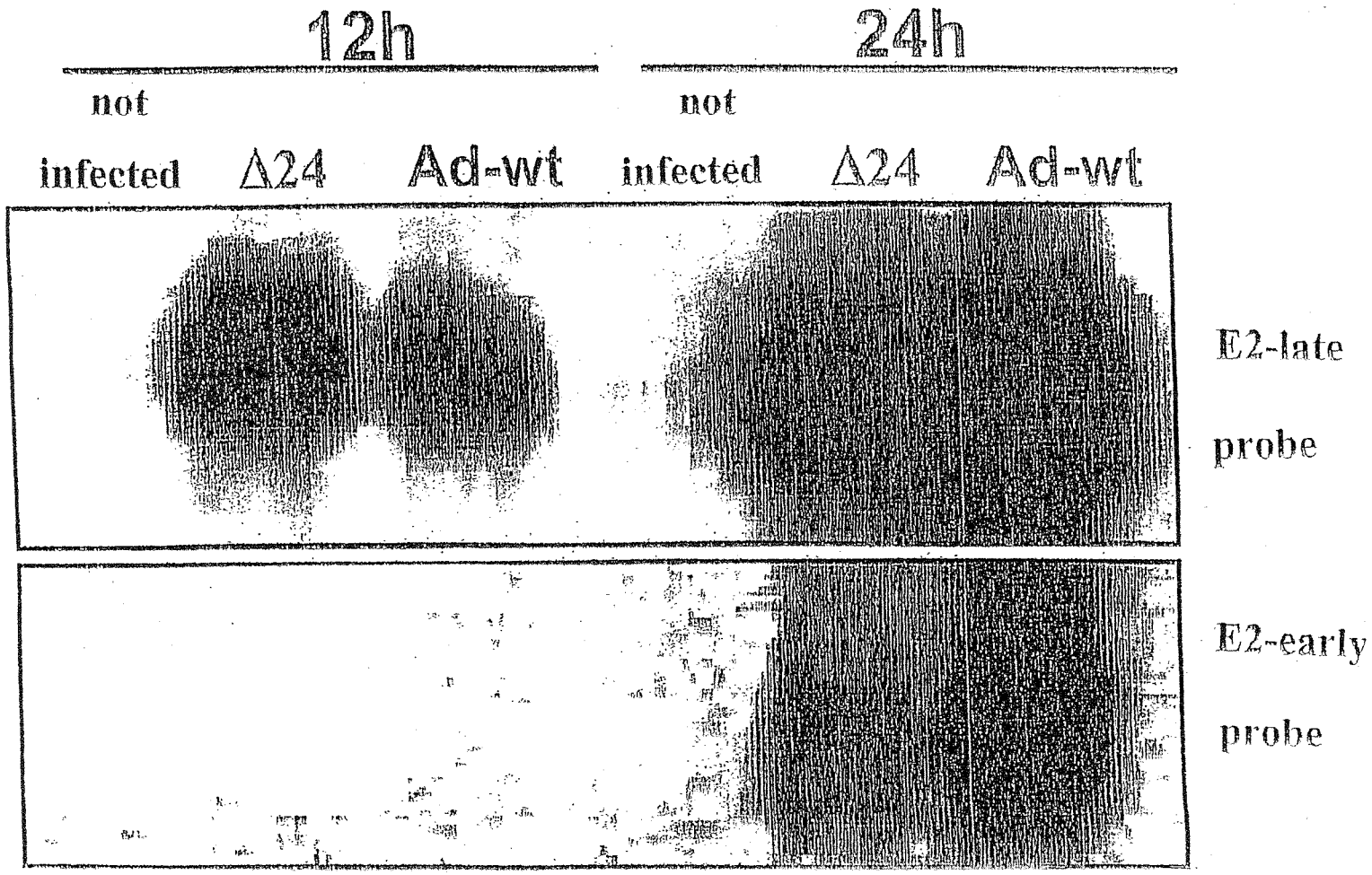
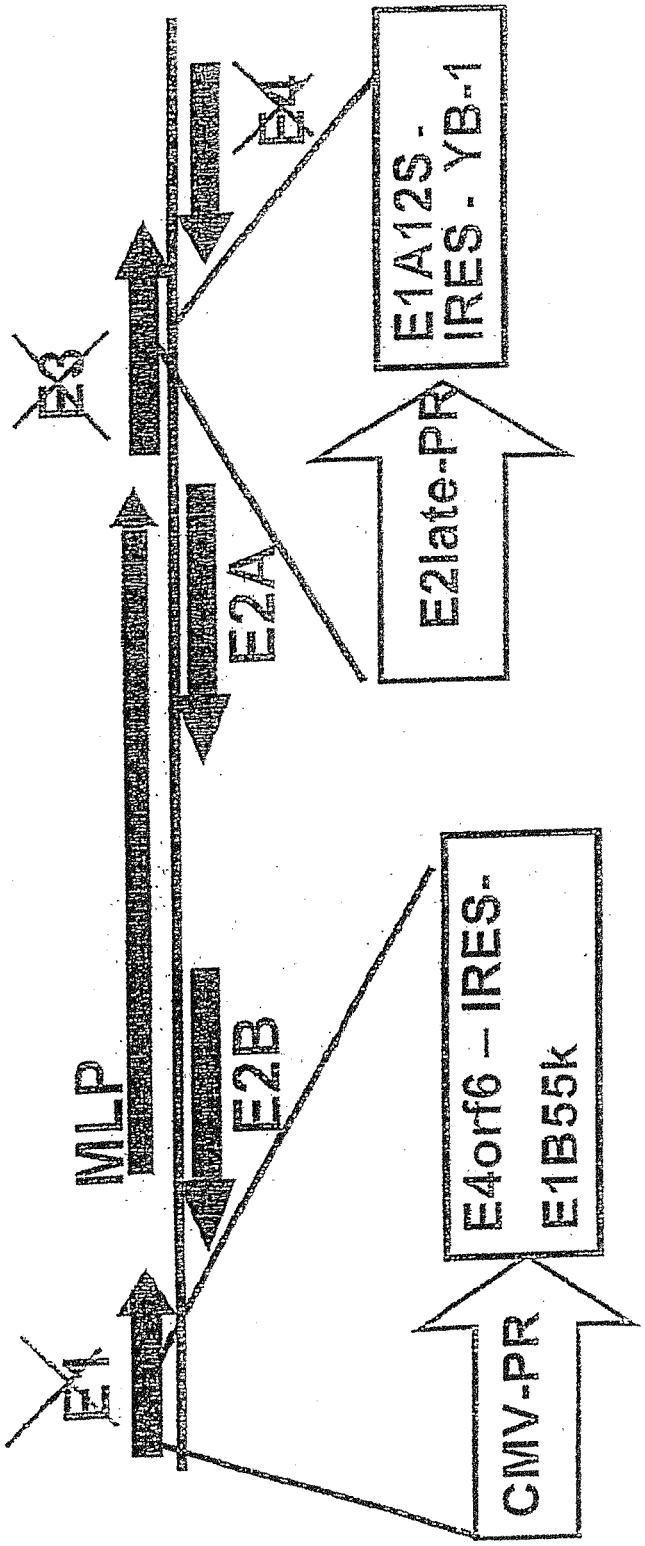


Fig. 27

XvirPSJL1



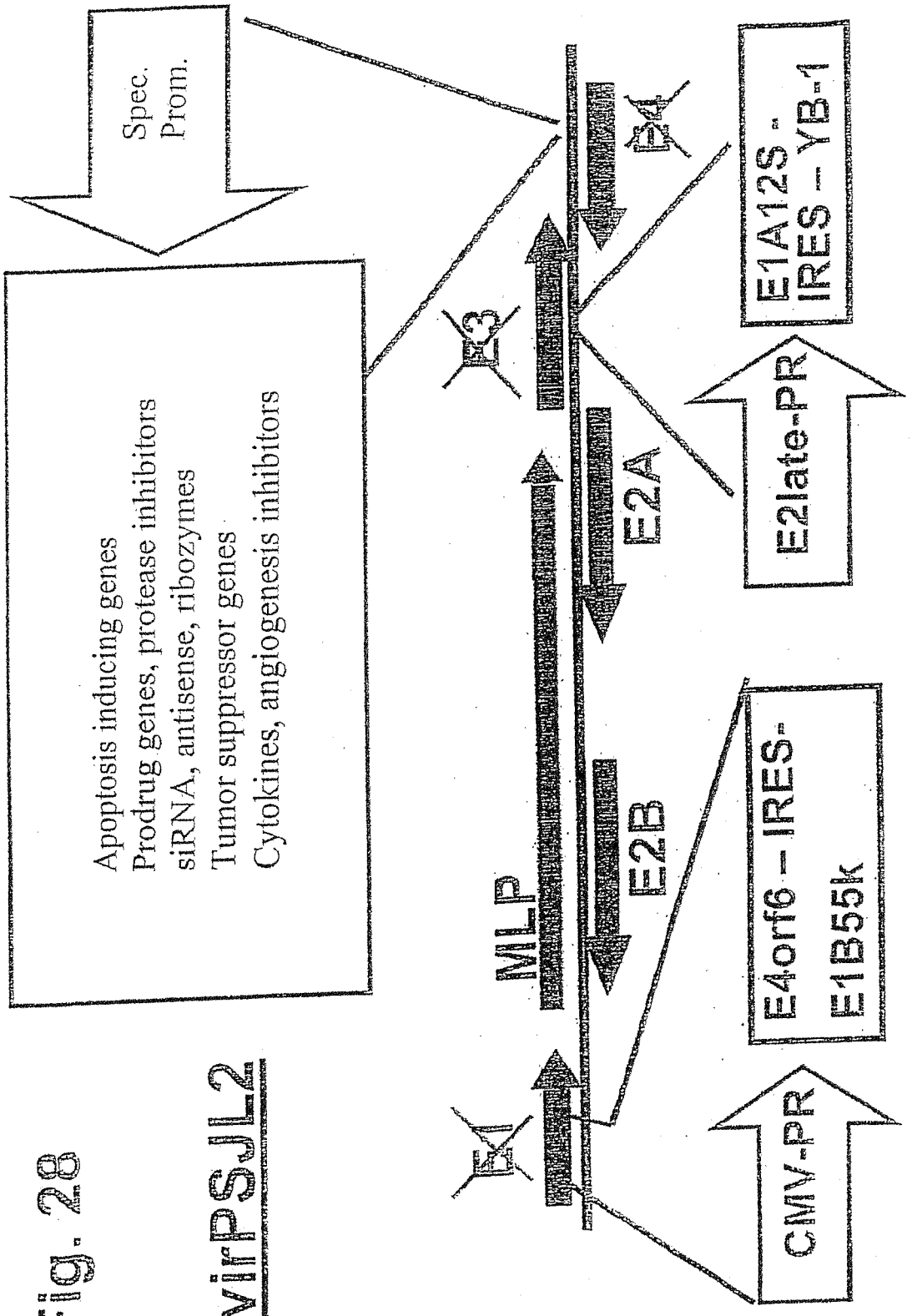


Fig. 28

XviPSJL2

HeLa cells infected with dl520
at different MOI

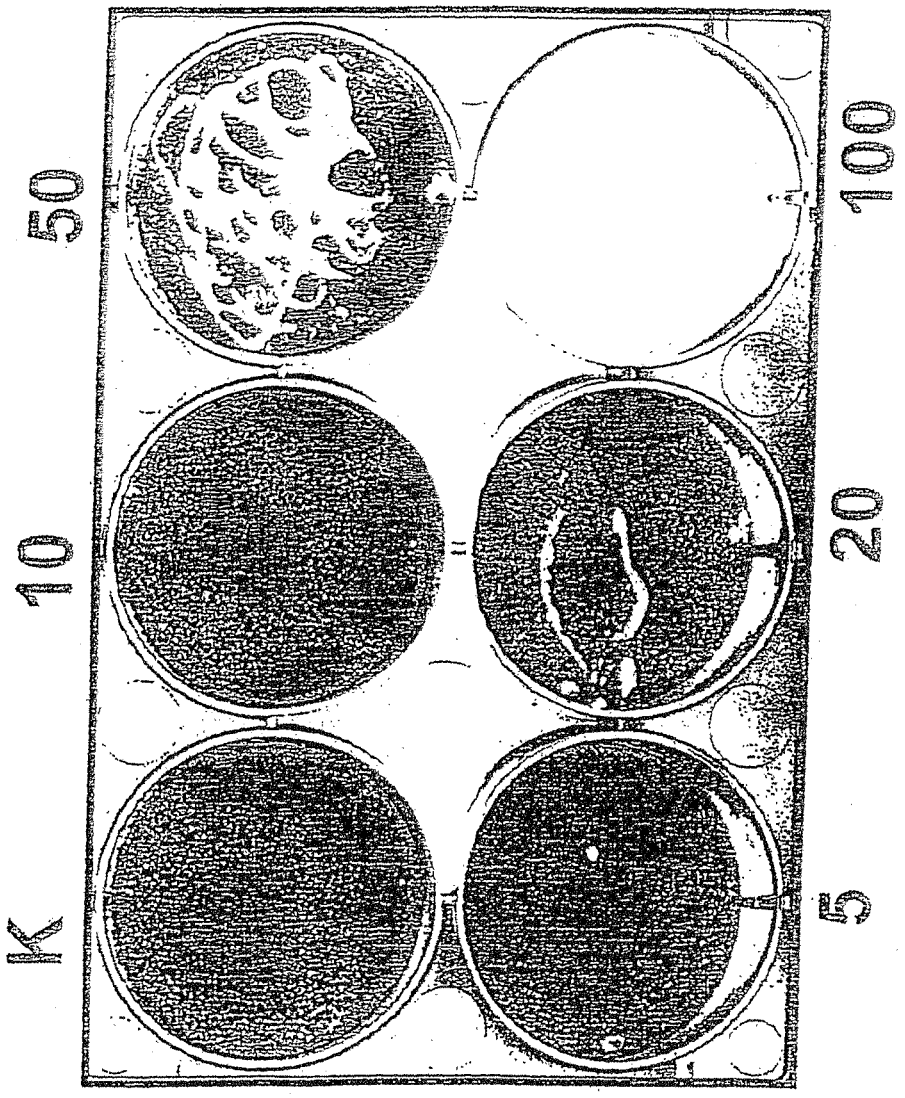


Fig. 29

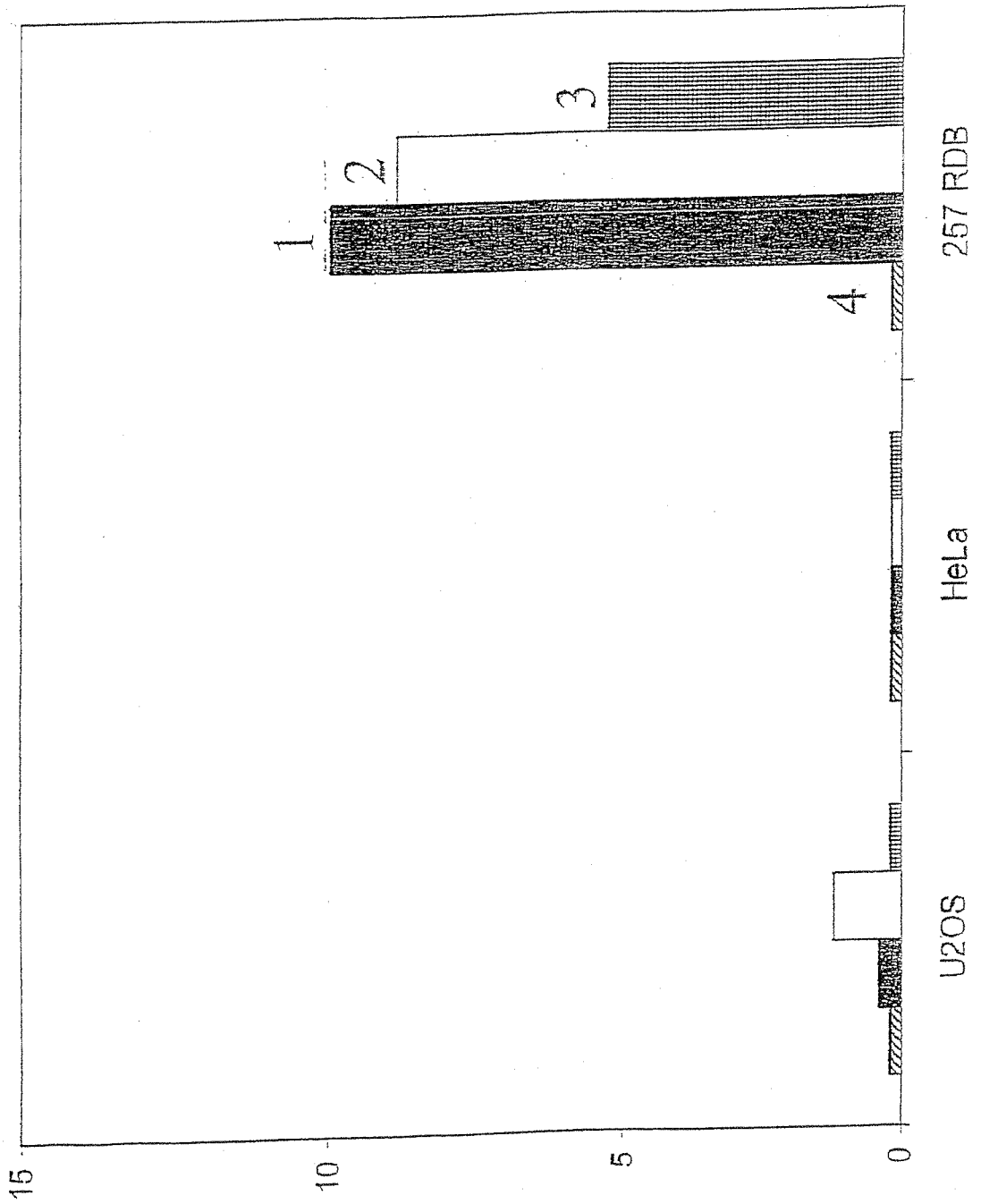


Fig. 30

Fig. 31

Release of viral particles by AdYB-1 compared to Ad312

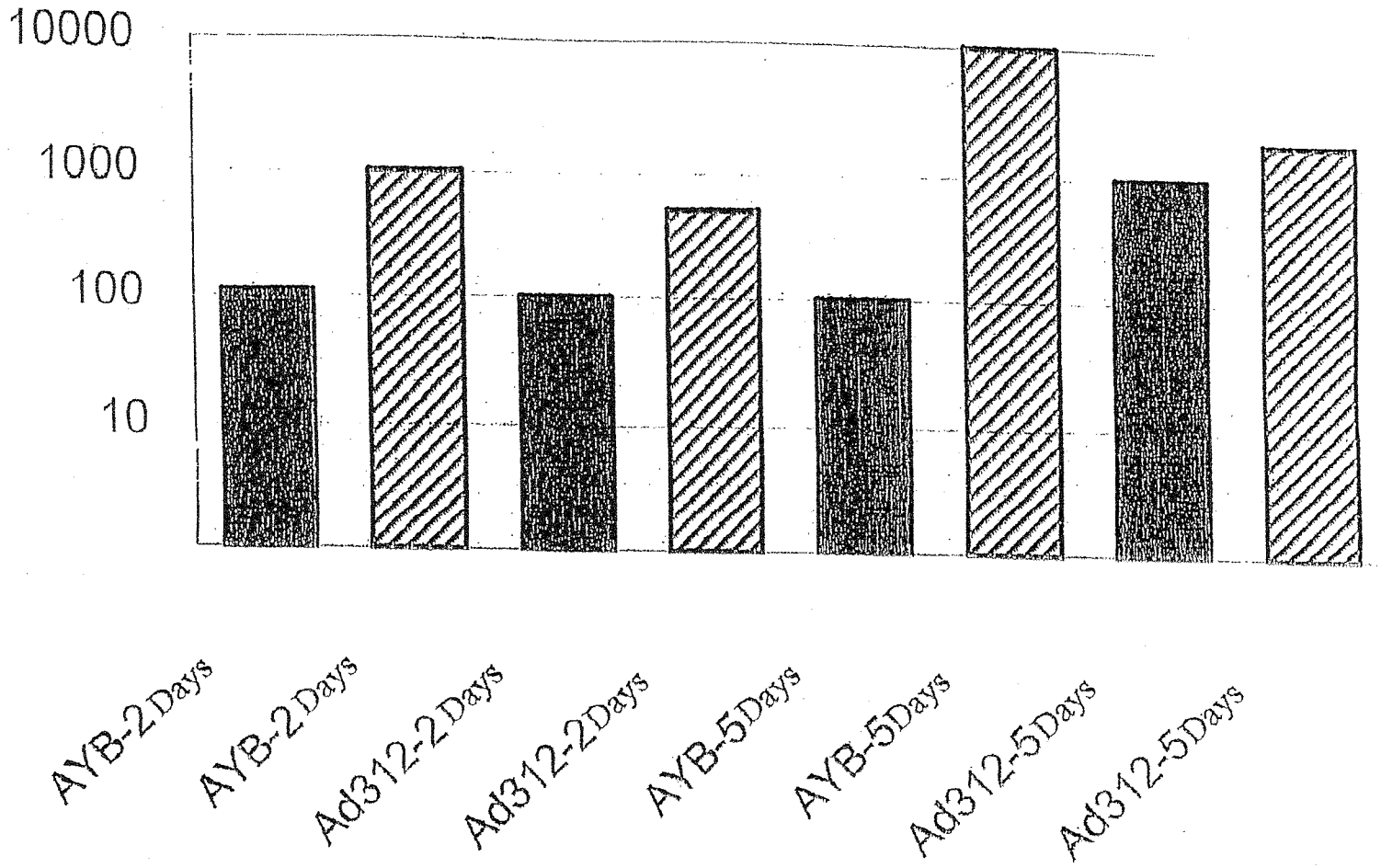
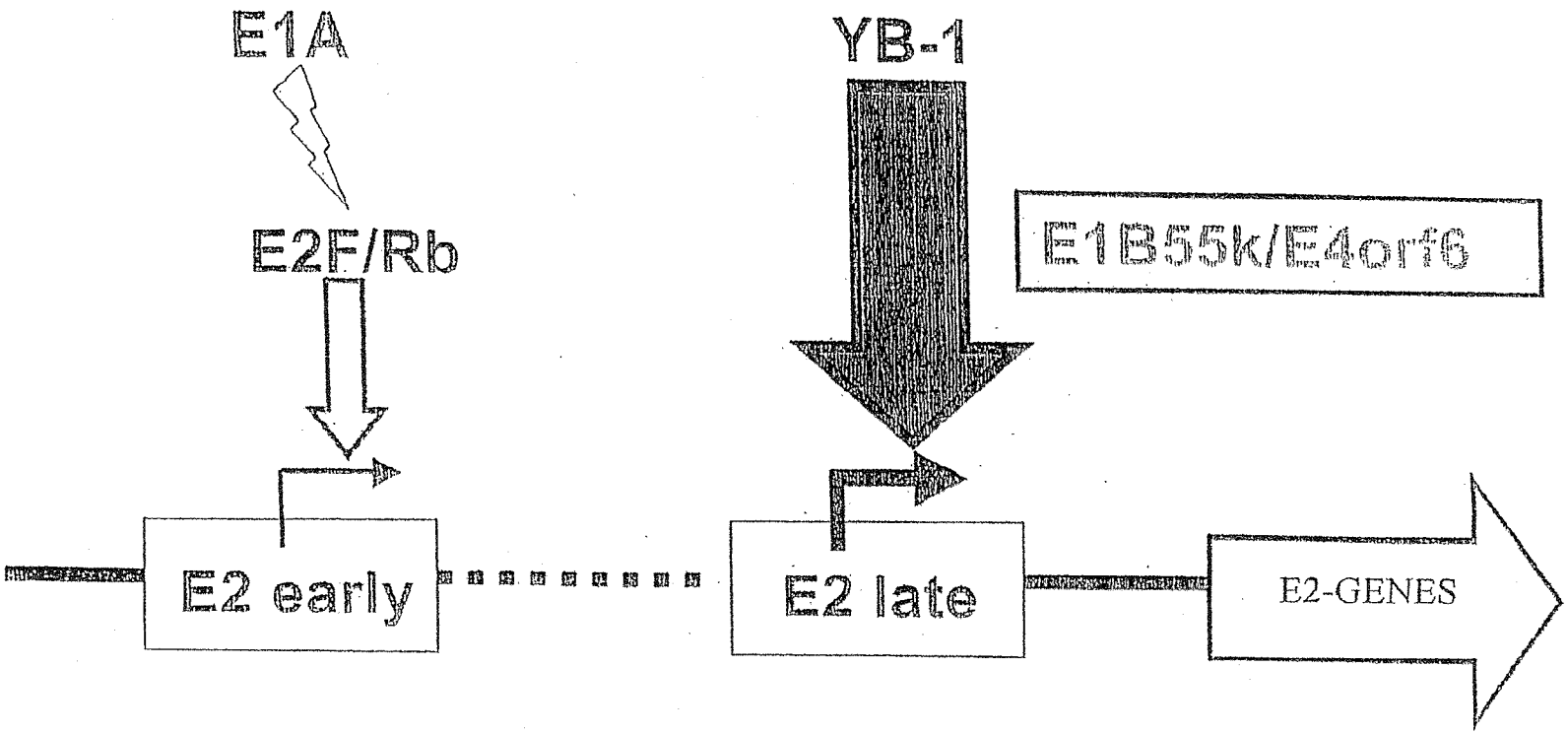


Fig. 32



1. E2-early promoter is E2F-dependent

2. E2-late promoter is YB-1-dependent

Fig. 33

Wildtype Adenovirus

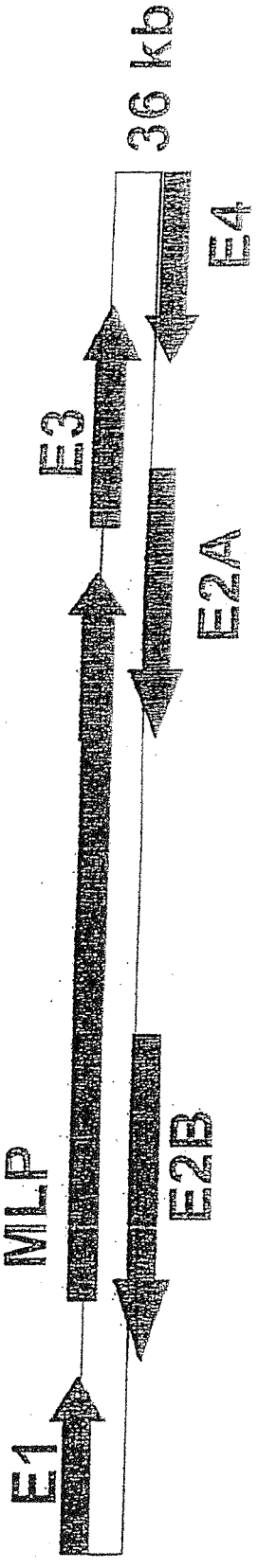


Fig. 34 Xvir05/Promoter

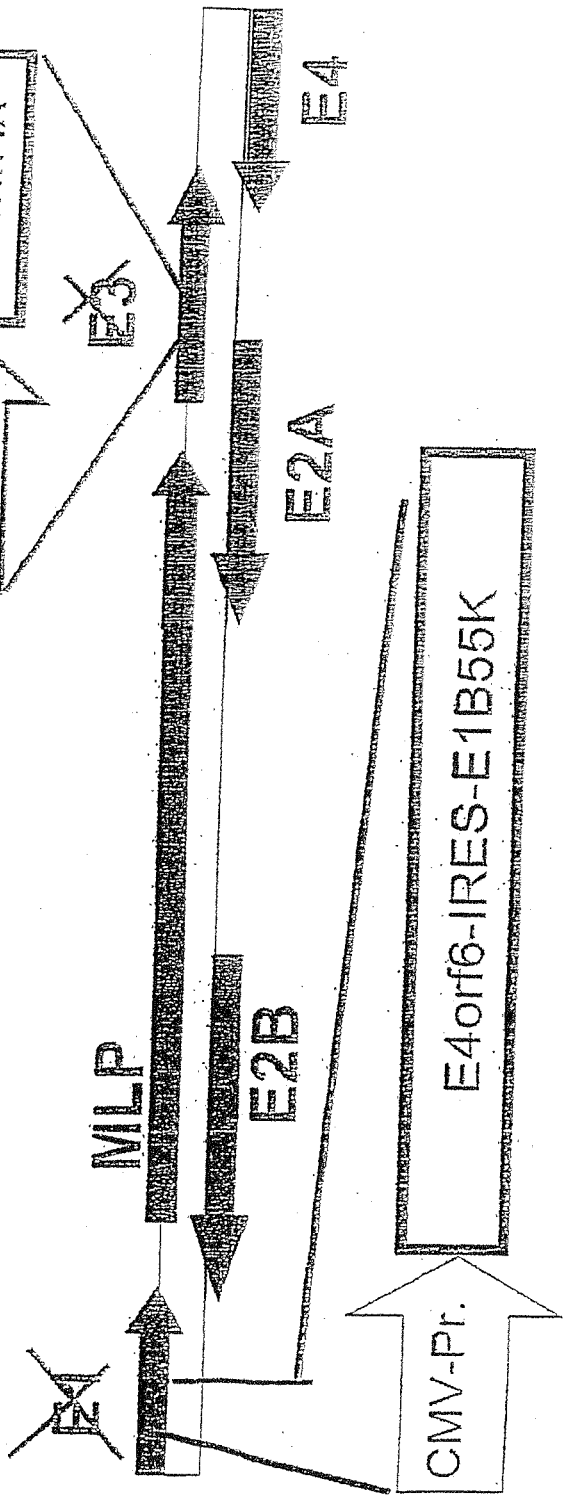


Fig. 35 XVir05/E1A12S

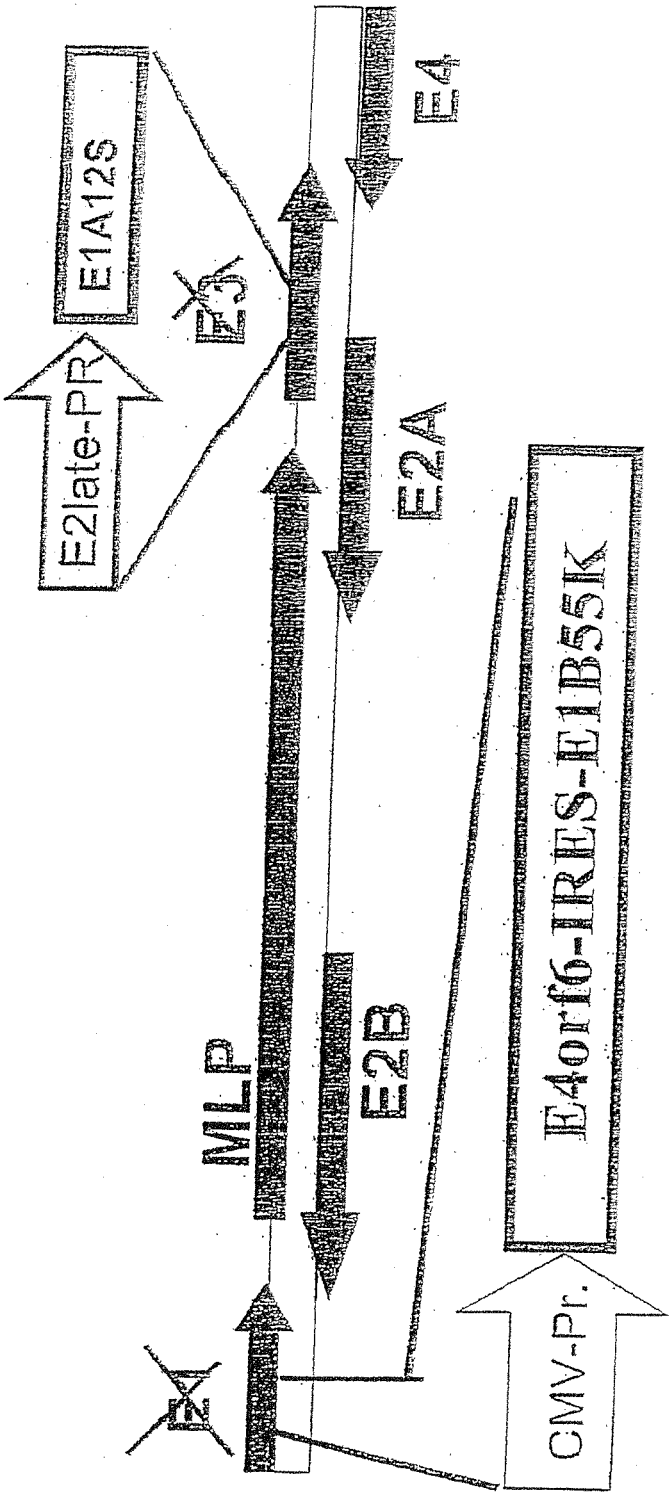


Fig. 36

XVir05/E1B19K

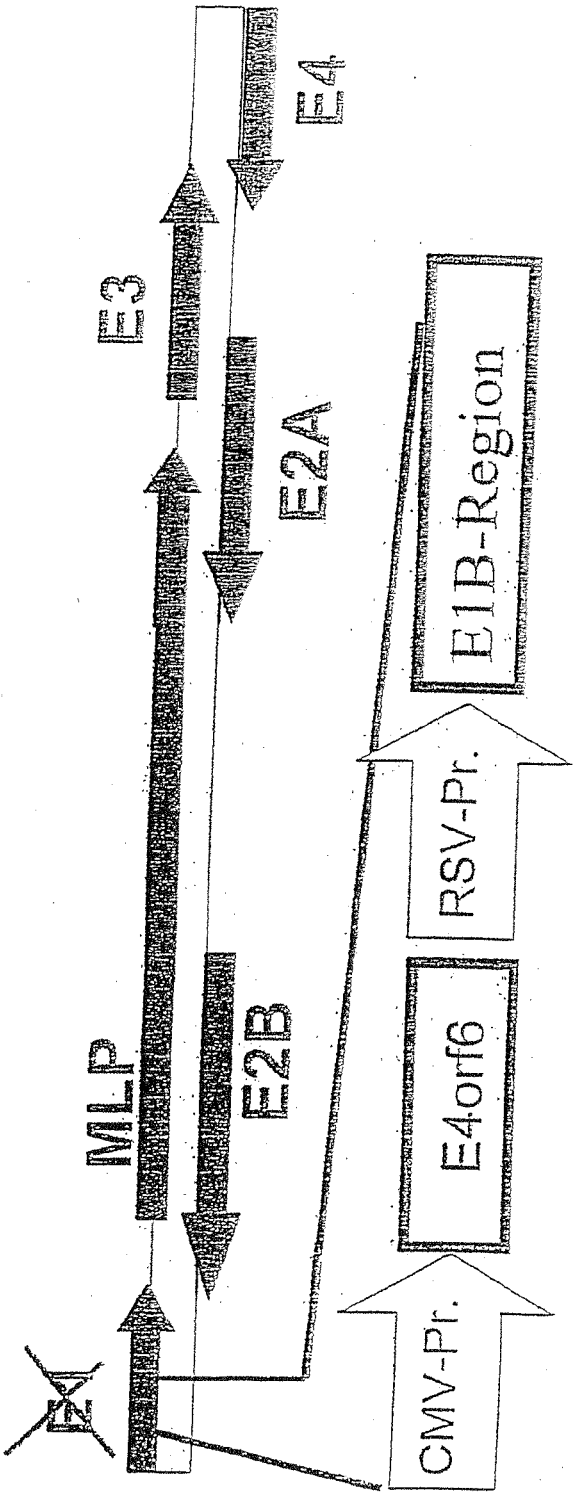


Fig. 37

XviroS/E3-IX

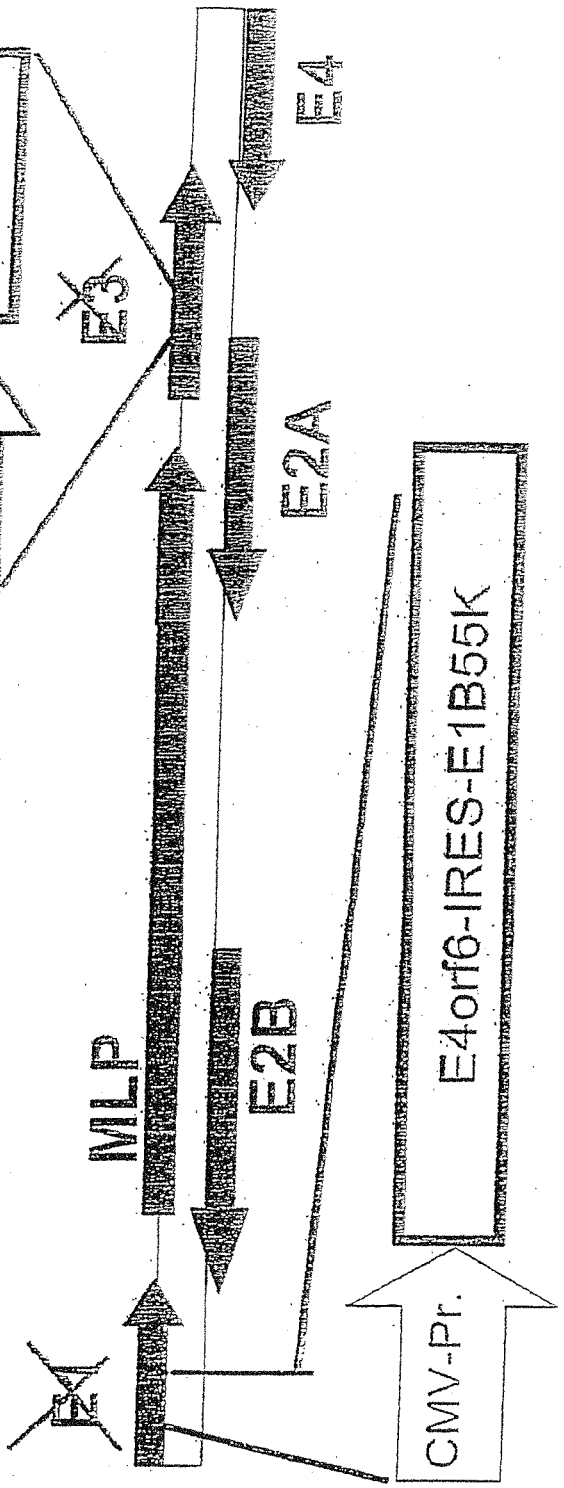


Fig. 3B

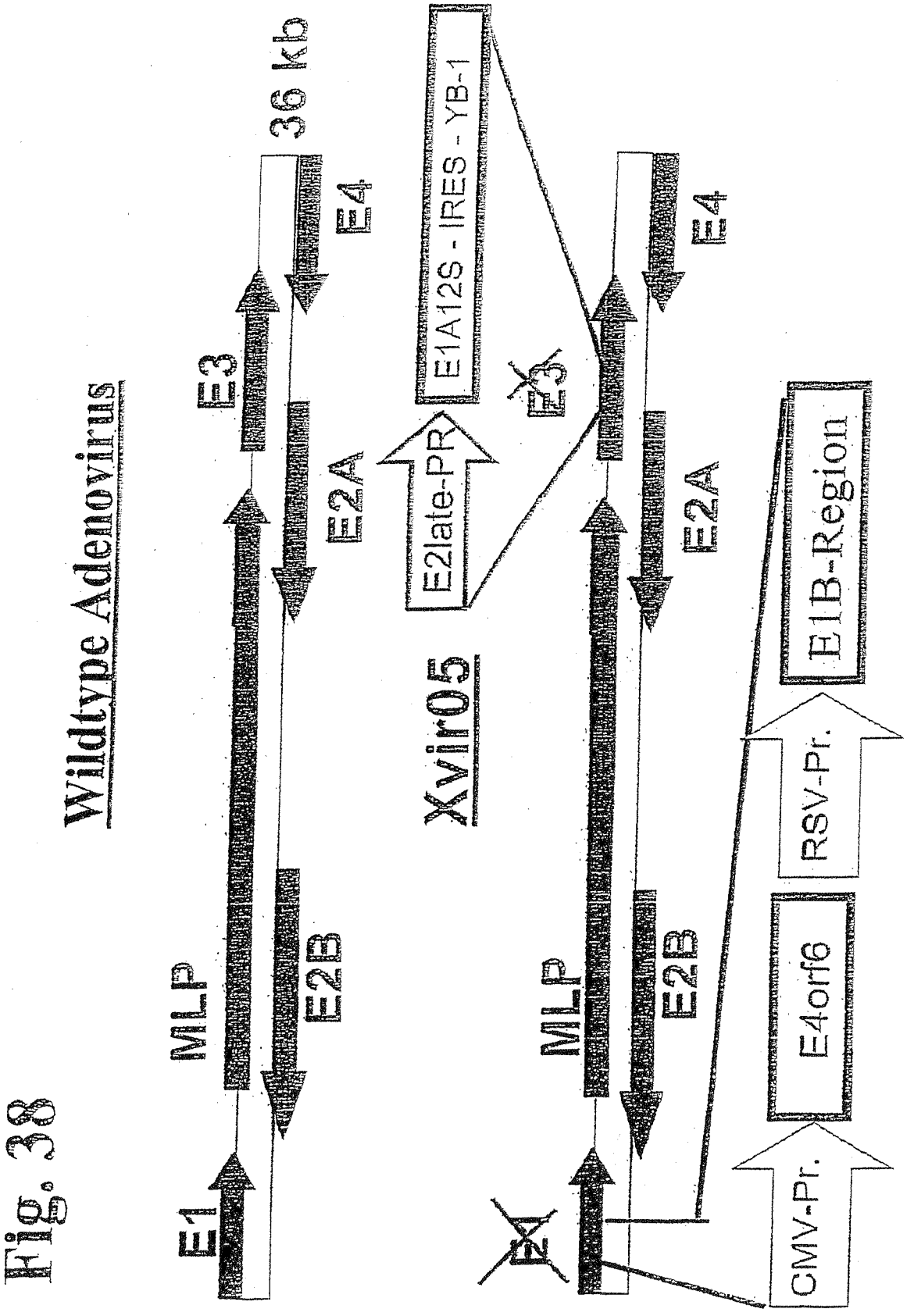
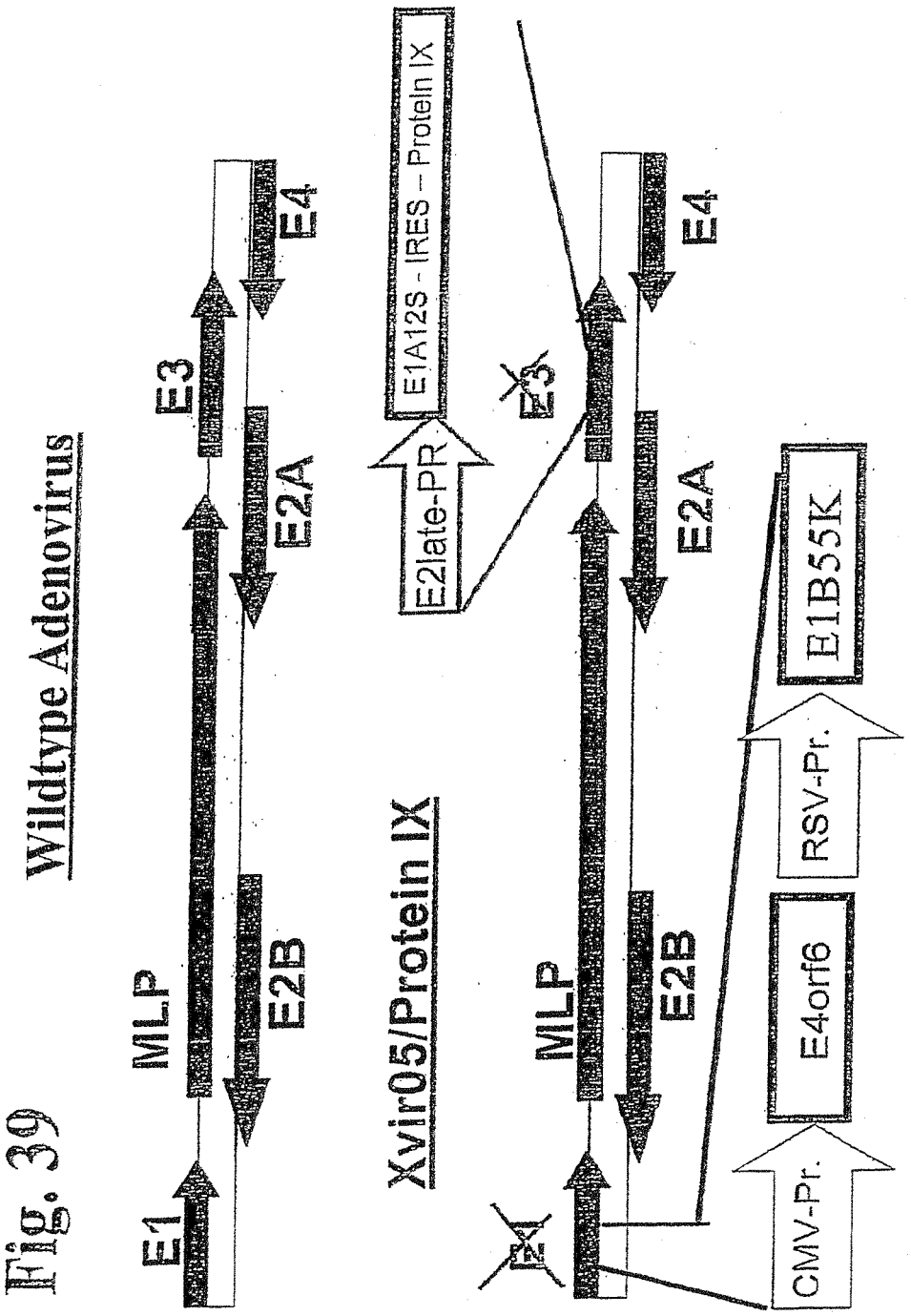

Wildtype Adenovirus
E1
MLP
E2B
E2A
E3
E4
36 kb
Xvir05
E2late-PR
E1A12S - IRES - YB-1
E3
E4
E2A
MLP
E2B
E1B-Region
RSV-Pr.
E4orf6
CMV-Pr.

Fig. 39


Wildtype Adenovirus
E1
MLP
E2B
E2A
E3
E4
Xvir05/Protein IX
E1A12S - IRES – Protein IX
E2late-PR
E3
E4
E2A
MLP
E2B
E1
CMV-Pr.
E4orf6
RSV-Pr.
E1B55K

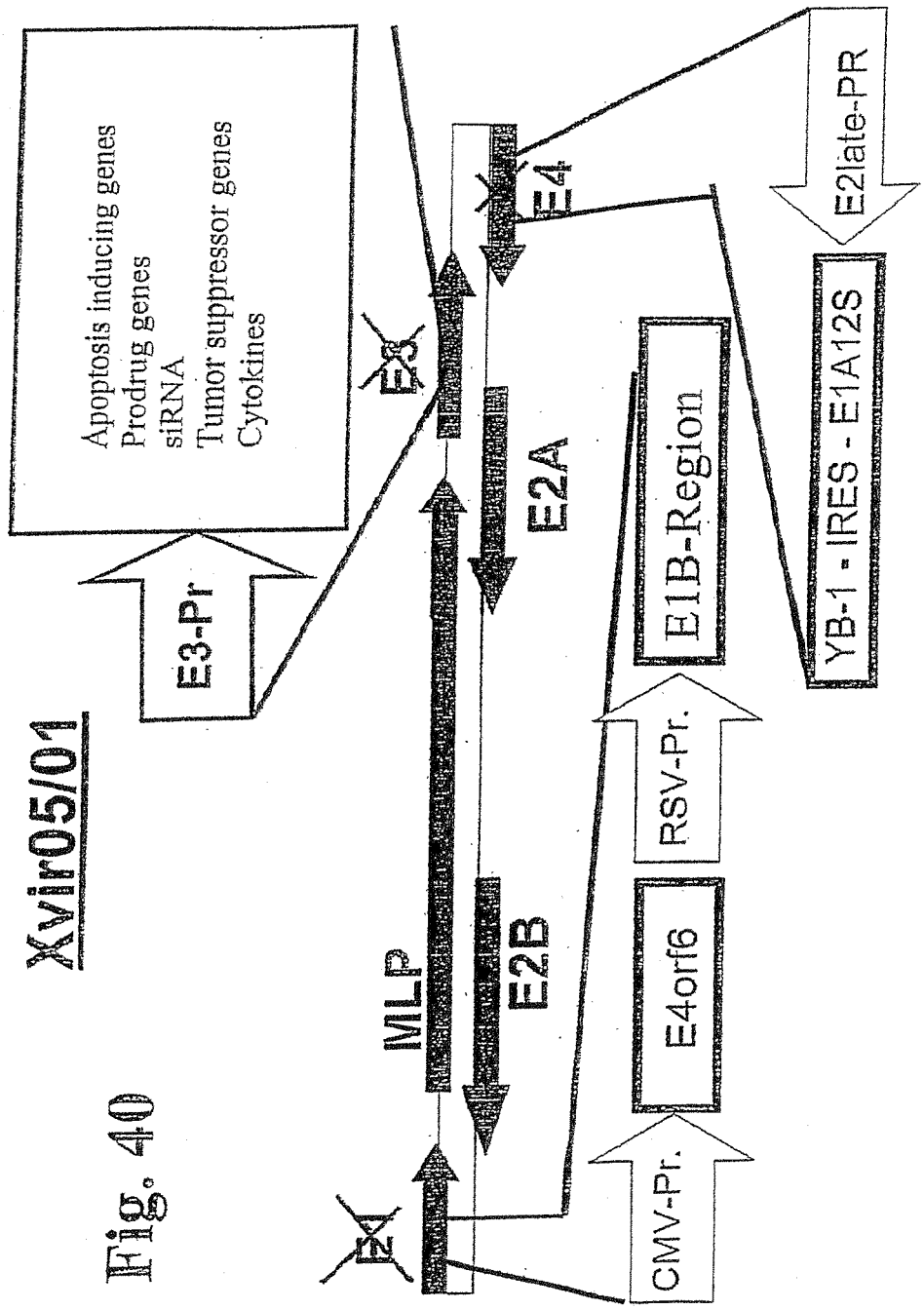

Xvir05/01
Apoptosis inducing genes
Prodrug genes
siRNA
Tumor suppressor genes
Cytokines
E3-Pr
E3
E4
E2late-PR
YB-1 - IRES - E1A12S
E1B-Region
E2A
MLP
E2B
E4orf6
RSV-Pr.
CMV-Pr.
E1

Fig. 40

Fig. 41

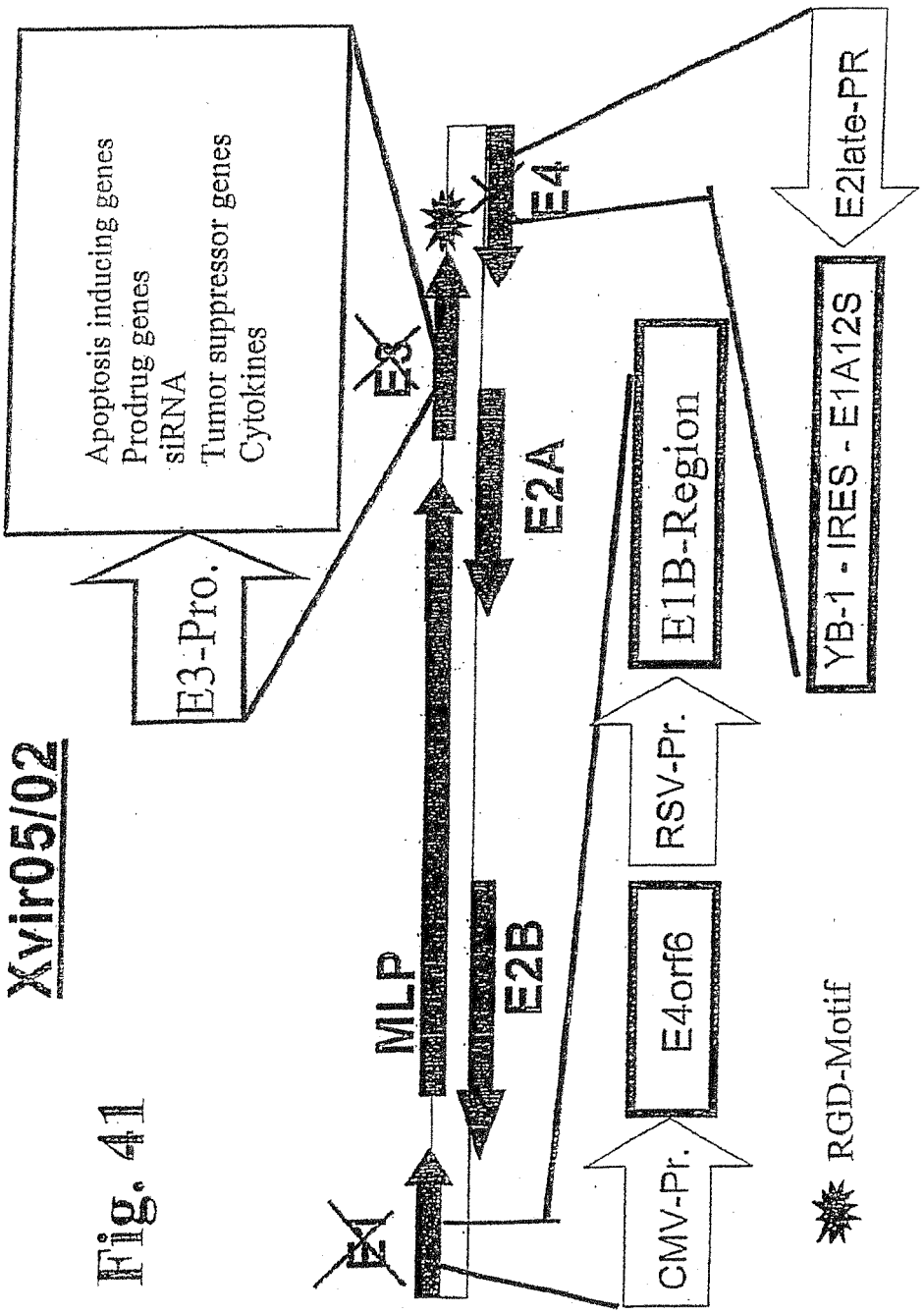
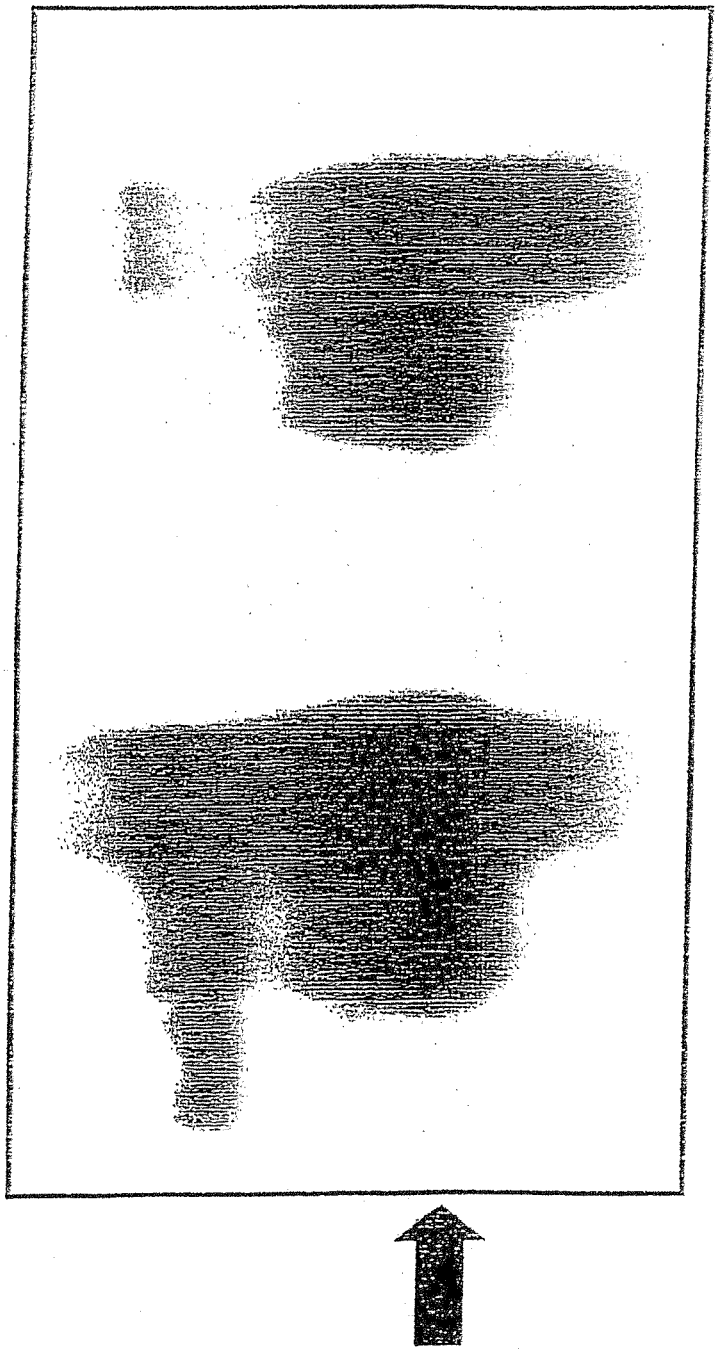
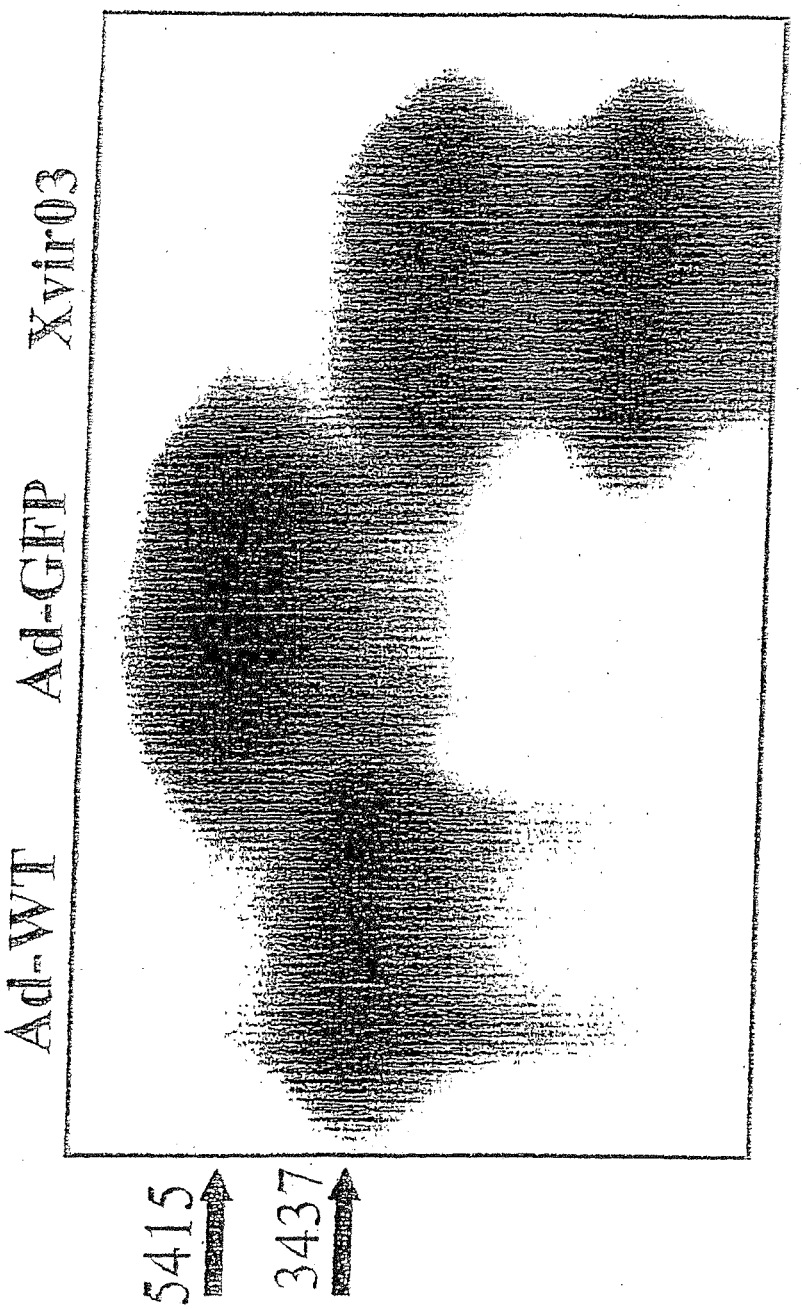

Xvir05/02
Apoptosis inducing genes
Prodrug genes
siRNA
Tumor suppressor genes
Cytokines
E3-Pro.
E3
E4
E2late-PR
E2A
E1B-Region
YB-1 - IRES - E1A12S
MLP
E2B
RSV-Pr.
E4orf6
CMV-Pr.
RGD-Motif

Fig. 42



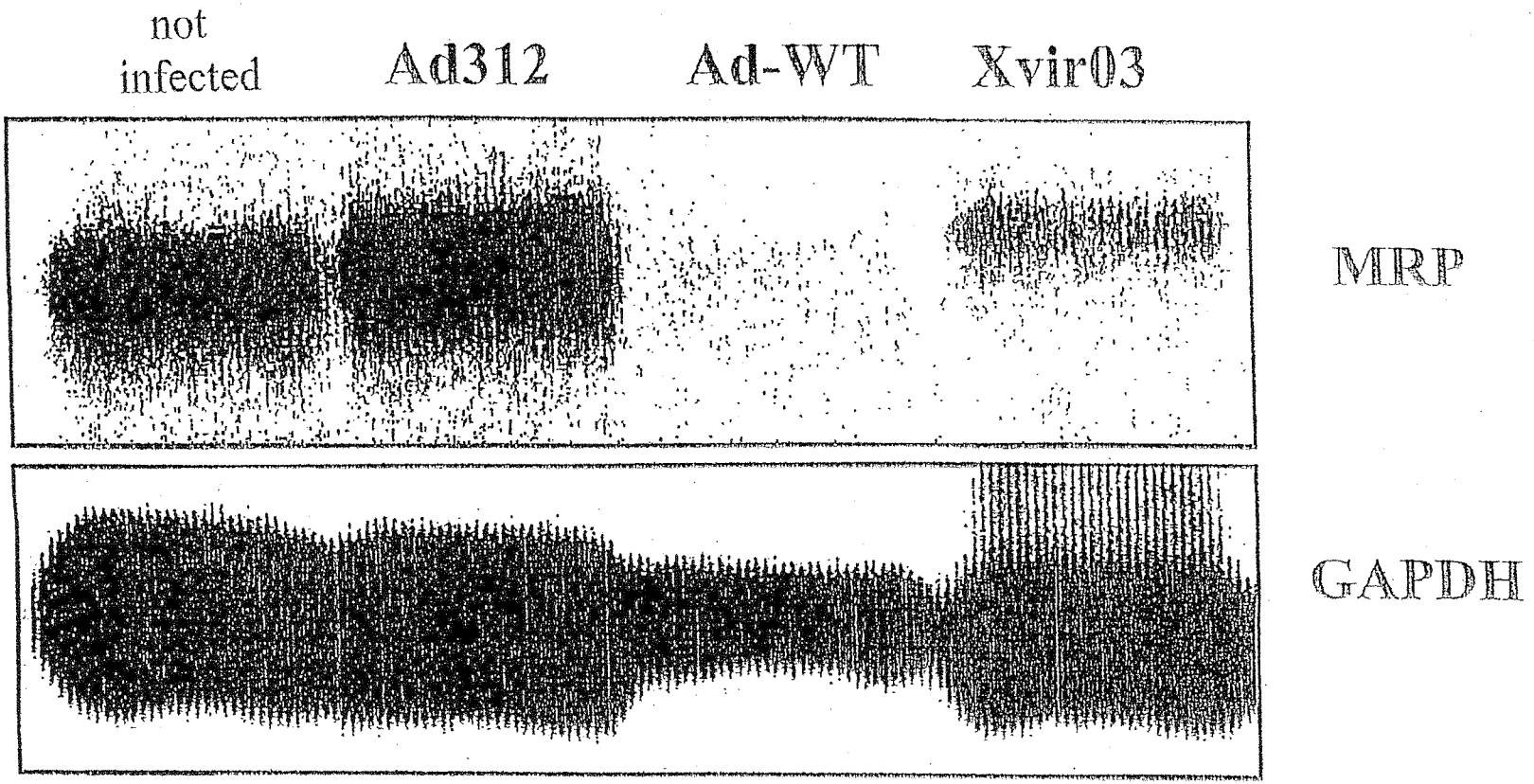
Northern Blot Analysis

Fig. 43



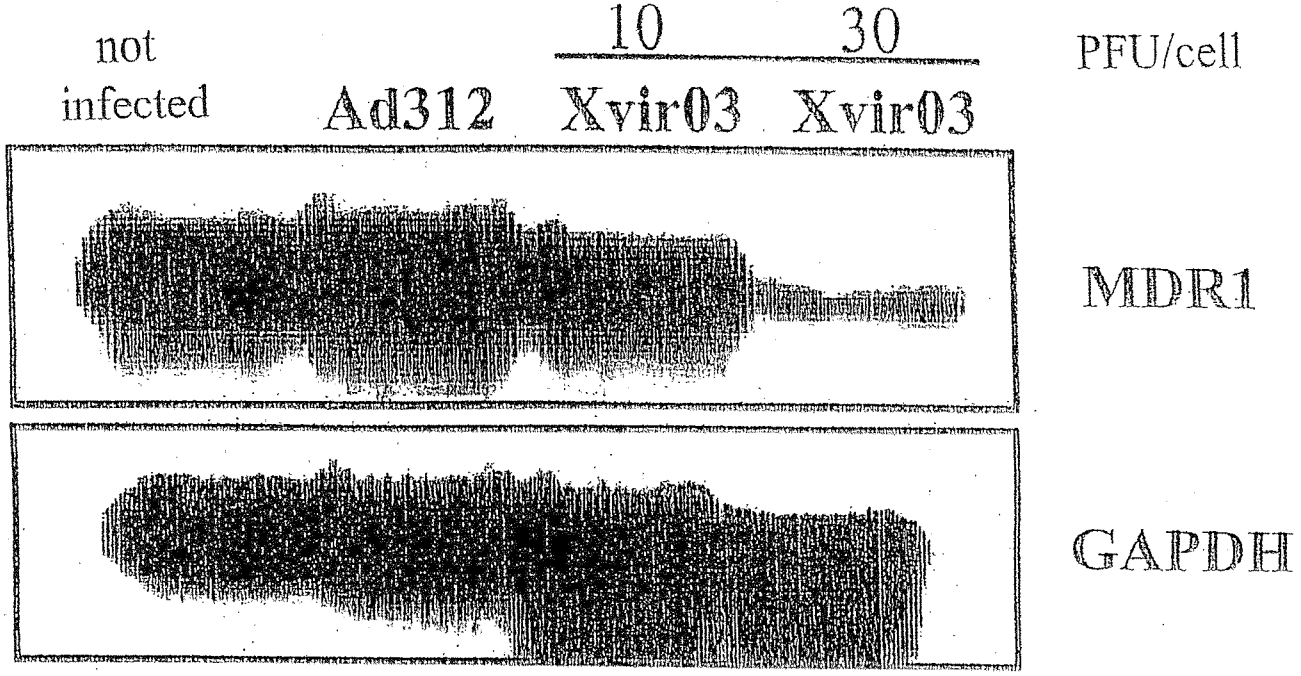
Northern Blot Analysis

Fig. 44



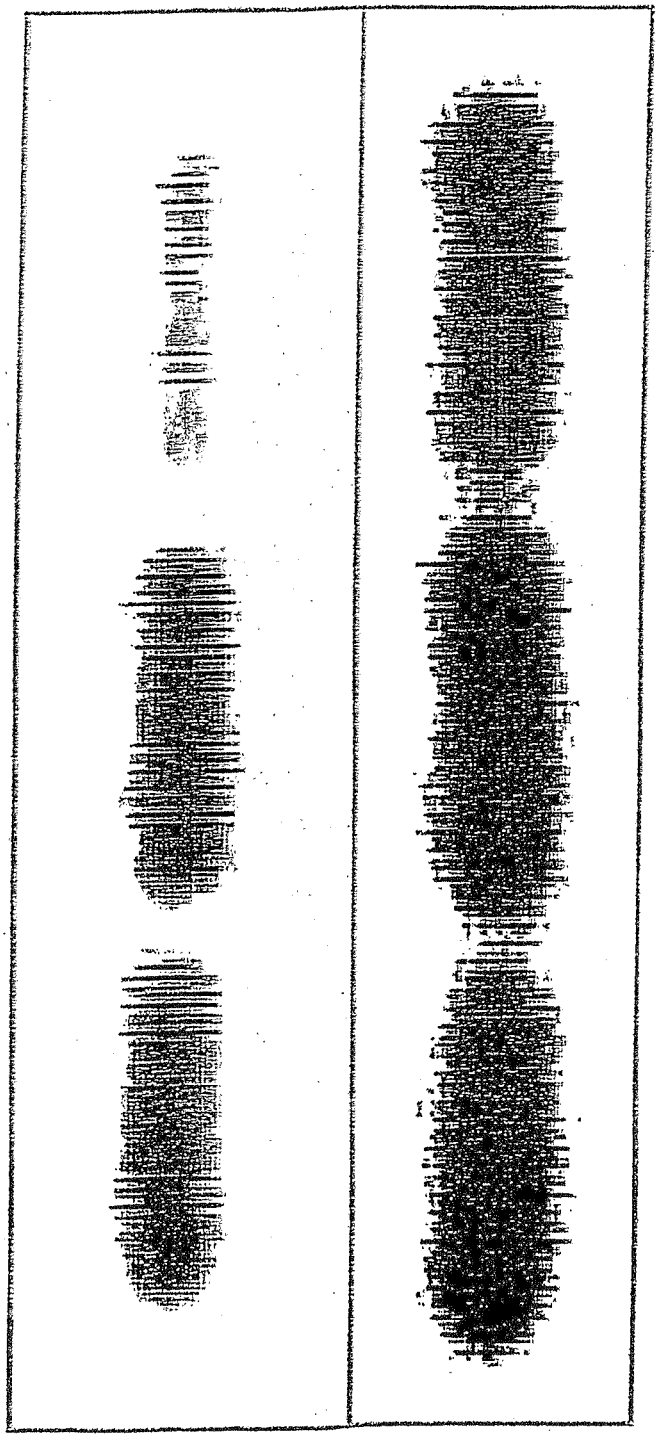
Northern Blot Analysis

Fig. 45



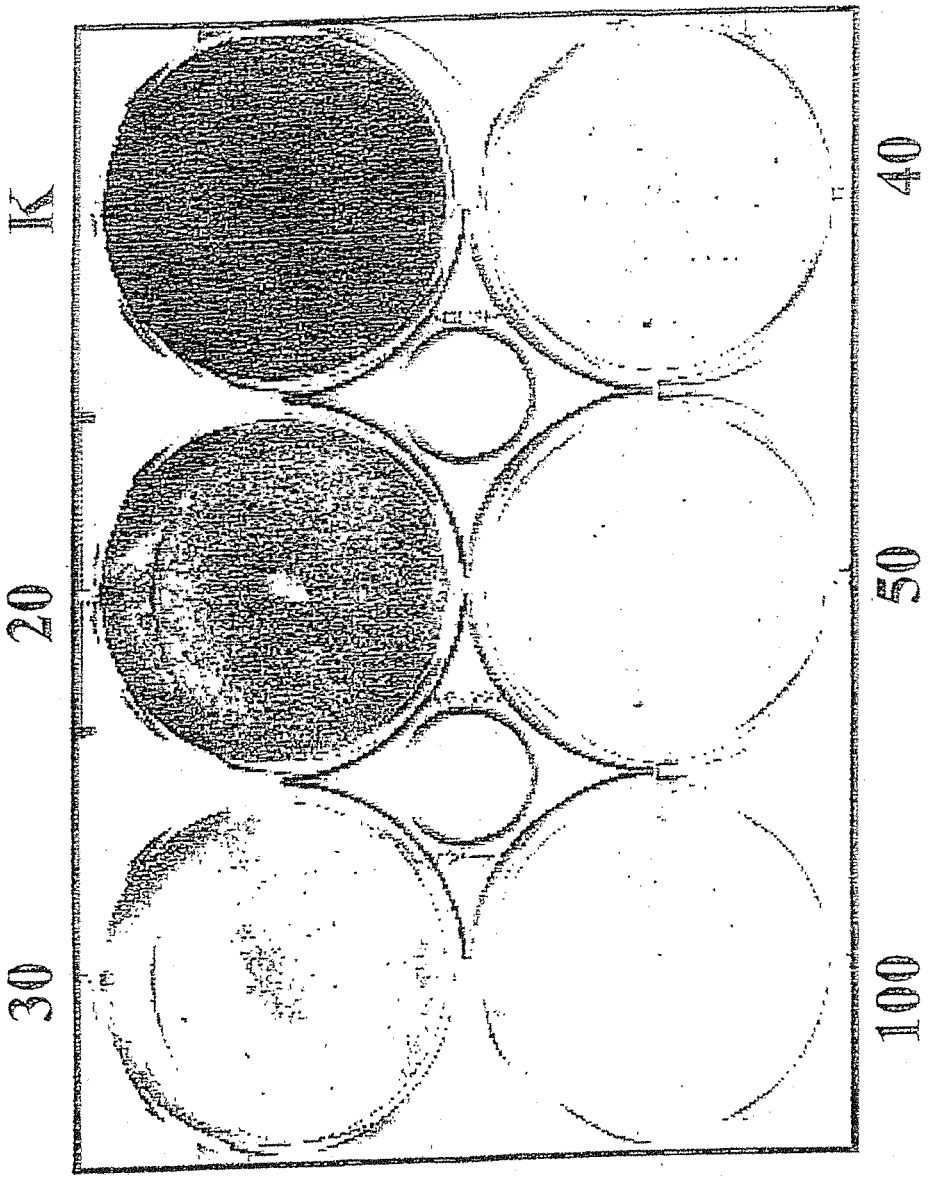
Northern Blot Analysis

Fig. 46



Northern Blot Analysis

Fig. 47



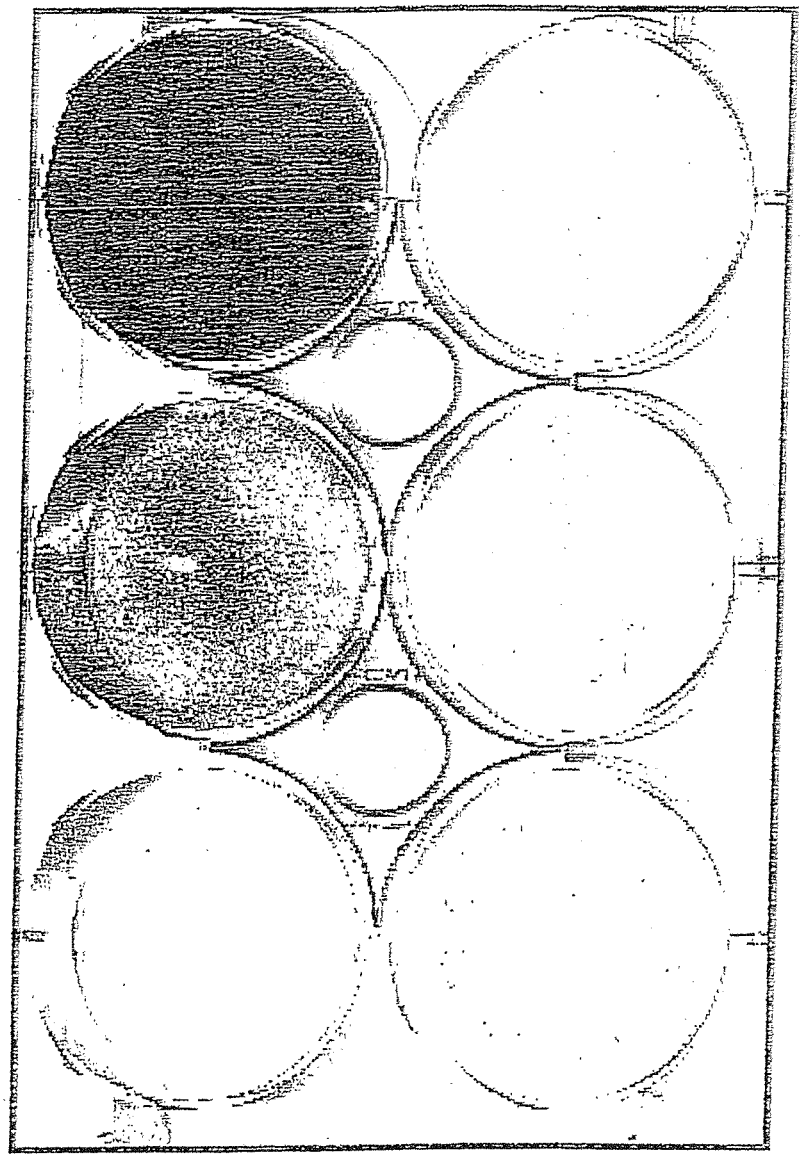


Fig. 48

Fig. 49

not
infected

30 ng/ml
Daunorubicin

15pfu/cellXvir03

15pfu/cellXvir03 +
30ng/ml
Daunorubicin

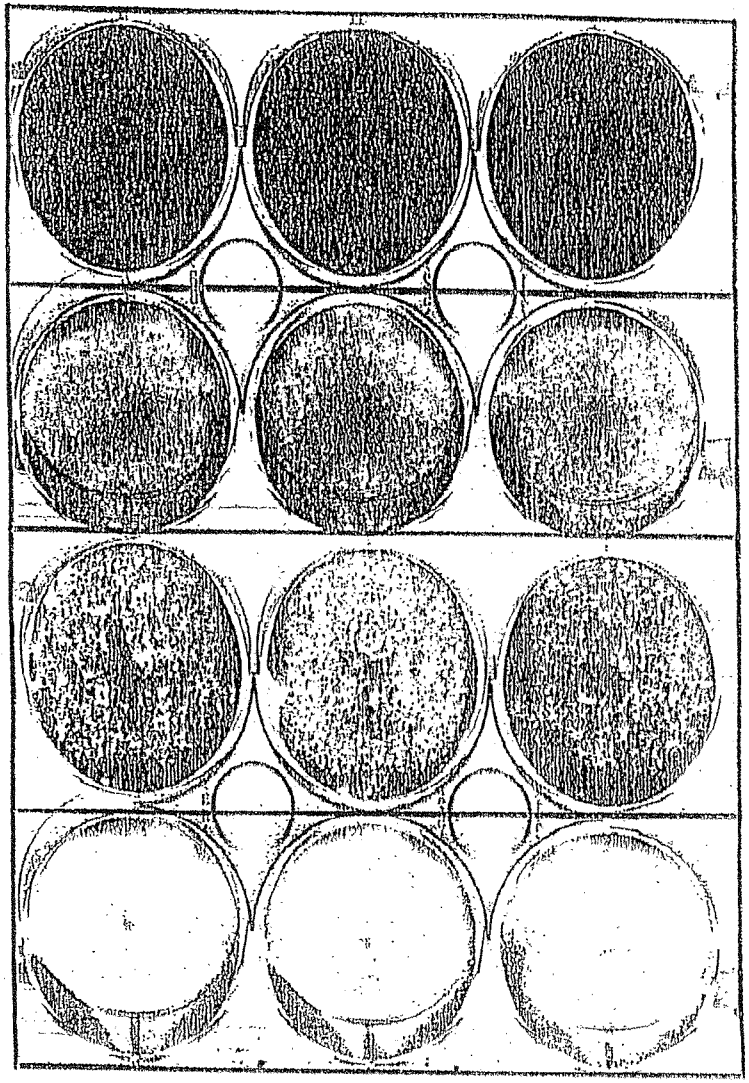


Fig. 5D

