


R = OMe, spirotryprostatin A
R = H, demethoxyspirotryprostatin A

**Fig. 1**

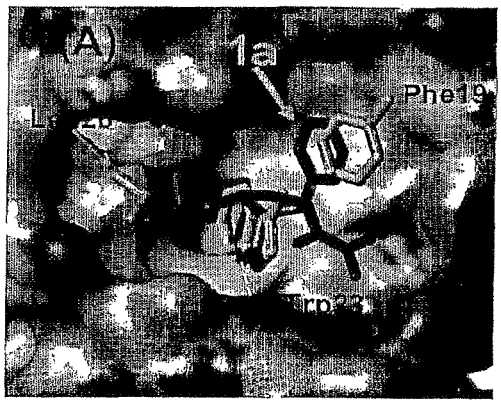



FIG. 2A

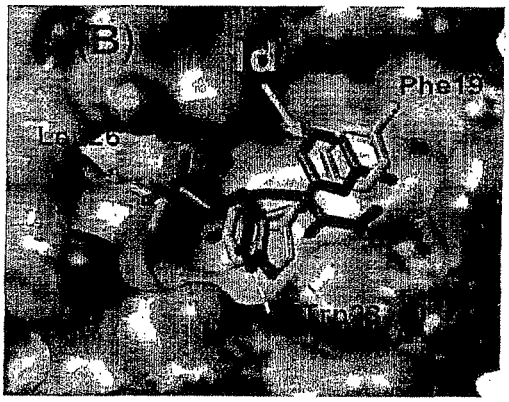



FIG. 2B

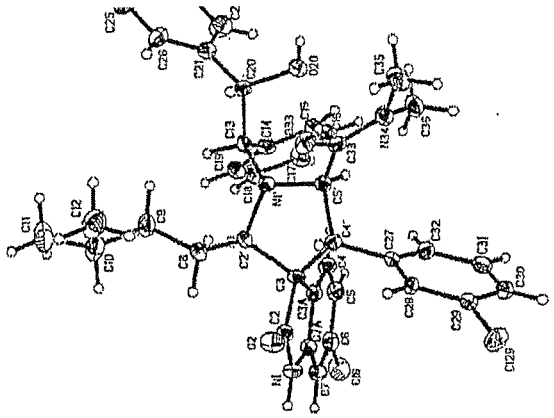


FIG. 3

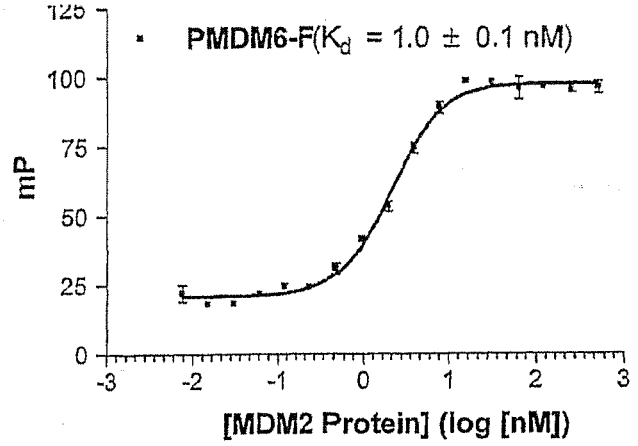



FIG. 4A

▲ p53 peptide (residues 13-29) ($K_i$ = 6.67 ± 1.24 μM)

■ PMDM6 ($K_i$ = 0.7 ± 0.1 nM)

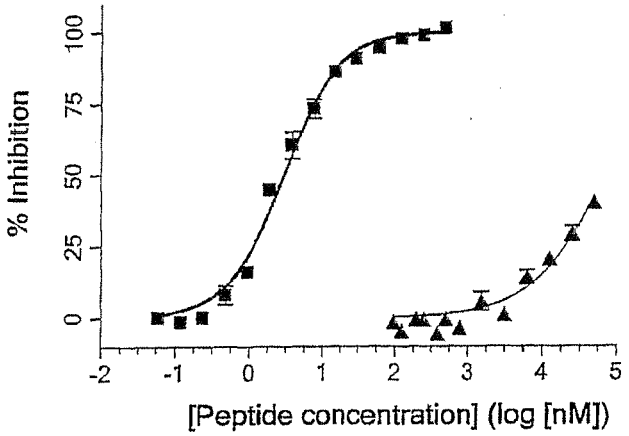
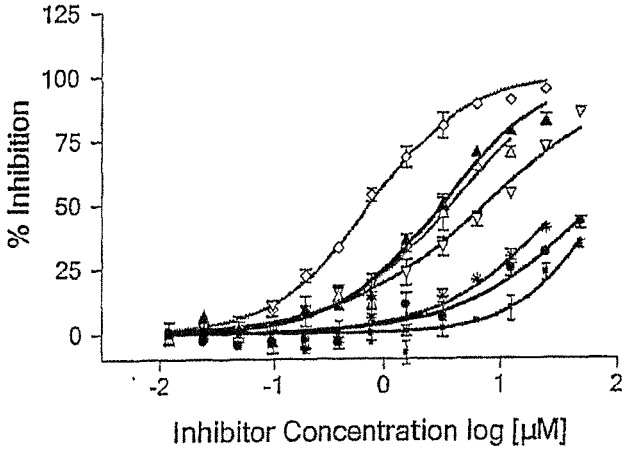



FIG. 4B




$K_i \pm SD$

- 1a (8.46 μM ± 1.44)
- 1b (0.30 μM ± 0.09)
- 1c (7.68 μM ± 1.68)
- 1d (0.086 μM ± 0.02)
- 1e (0.65 μM ± 0.14)
- 1f (0.39 μM ± 0.08)
- Native p53 peptide (6.67μM ± 1.24)

FIG. 5

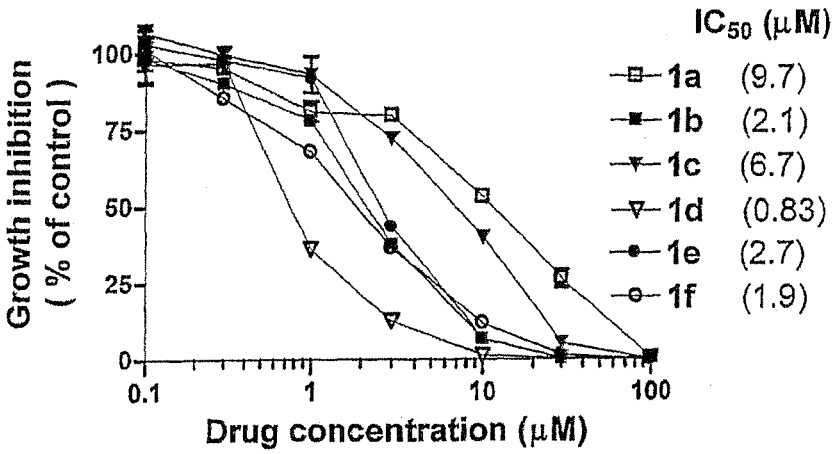

IC50 (μM)
1a (9.7)
1b (2.1)
1c (6.7)
1d (0.83)
1e (2.7)
1f (1.9)
Growth inhibition ( % of control )
100
75
50
25
0
0.1
1
10
100
Drug concentration (μM)

FIG. 6

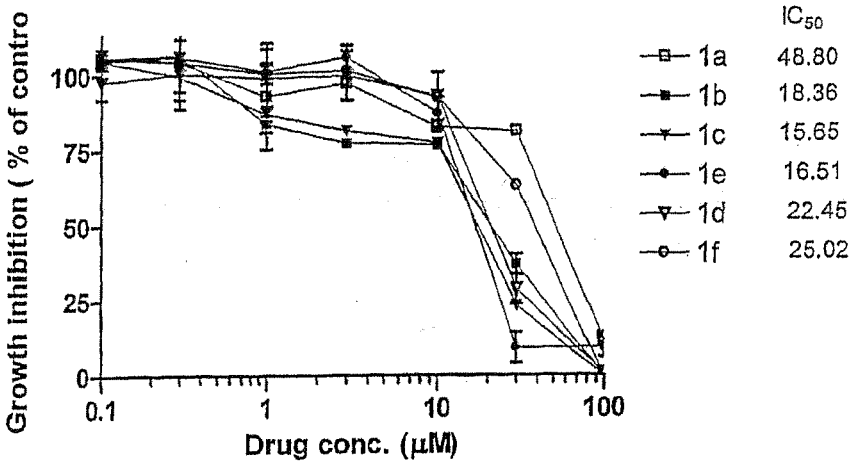

Growth inhibition ( % of contro
100
75
50
25
0
0.1
1
10
100
Drug conc. (μM)
IC50
1a 48.80
1b 18.36
1c 15.65
1e 16.51
1d 22.45
1f 25.02

FIG. 7

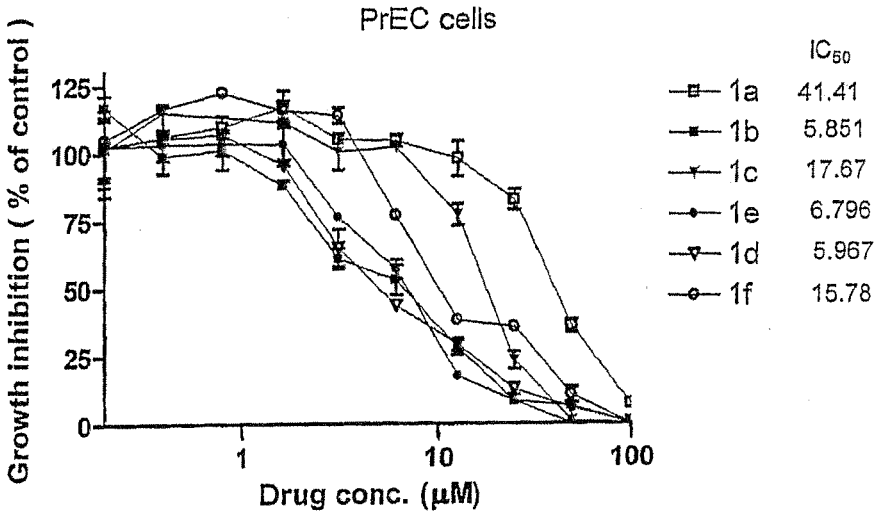

PrEC cells
Growth inhibition ( % of control )
125
100
75
50
25
0
1
10
100
Drug conc. (μM)
IC50
1a 41.41
1b 5.851
1c 17.67
1e 6.796
1d 5.967
1f 15.78

FIG. 8

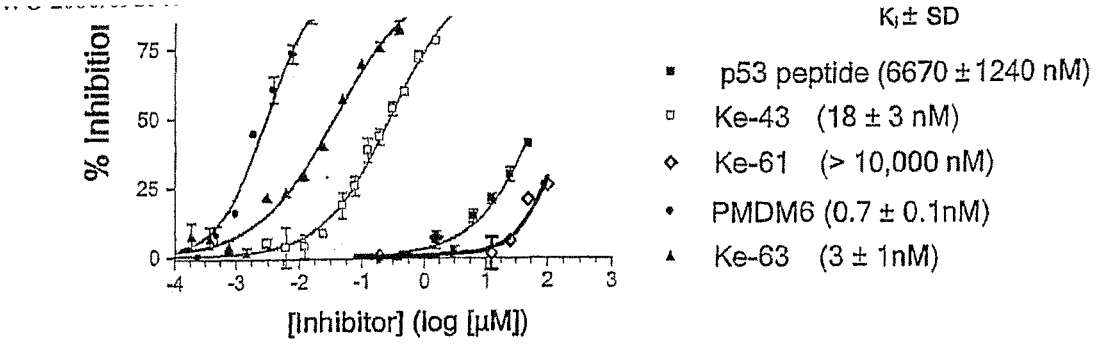

% Inhibitio
75
50
25
0
-4
-3
-2
-1
0
1
2
3
[Inhibitor] (log [µM])
Ki ± SD
p53 peptide (6670 ± 1240 nM)
Ke-43 (18 ± 3 nM)
Ke-61 (> 10,000 nM)
PMDM6 (0.7 ± 0.1nM)
Ke-63 (3 ± 1nM)

FIG. 9

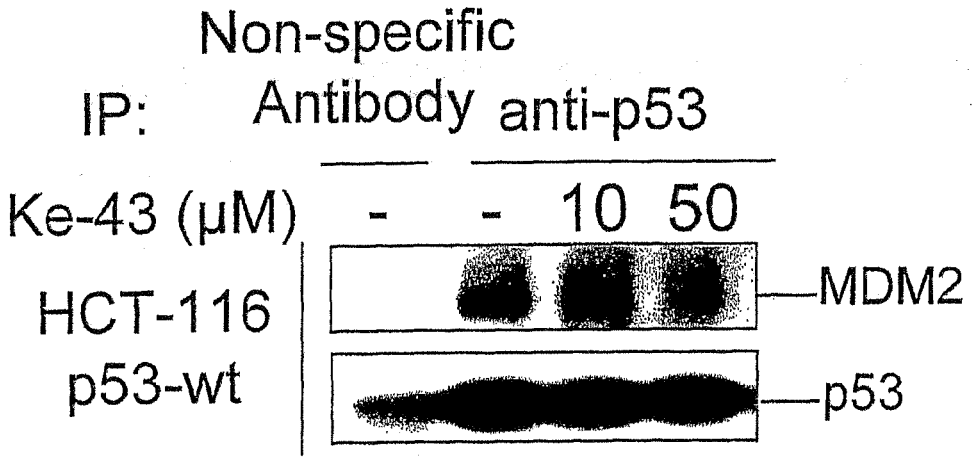

Non-specific
IP: Antibody anti-p53
Ke-43 (μM) - - 10 50
HCT-116
p53-wt
MDM2
p53

FIG. 10

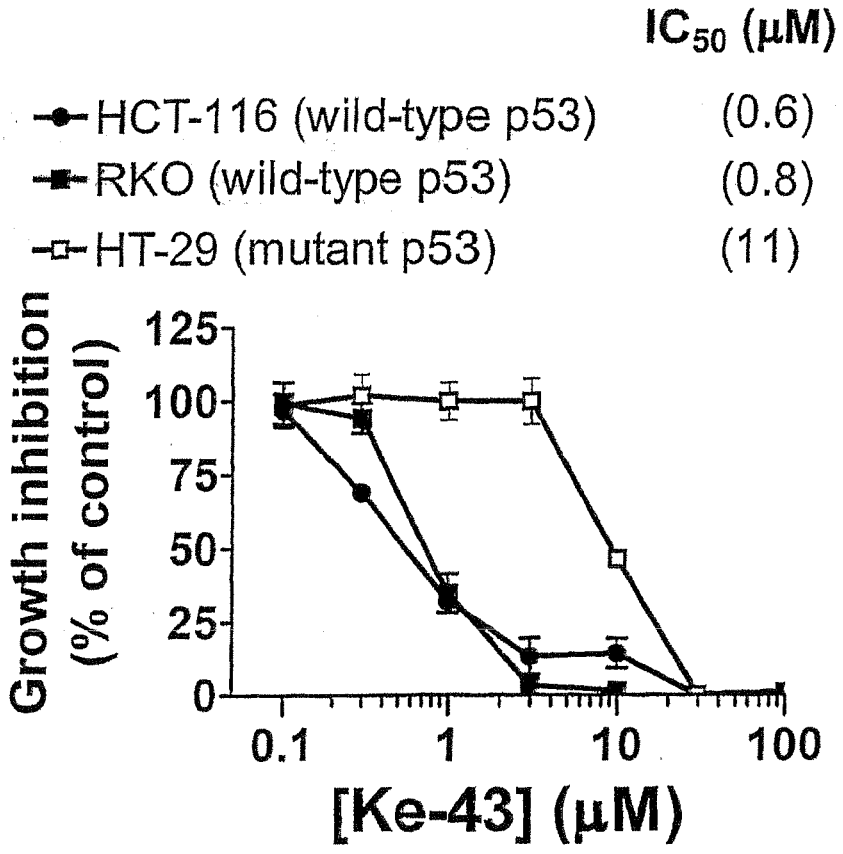

IC50 (μM)
HCT-116 (wild-type p53) (0.6)
RKO (wild-type p53) (0.8)
HT-29 (mutant p53) (11)
Growth inhibition (% of control)
125
100
75
50
25
0
0.1
1
10
100
[Ke-43] (μM)

FIG. 11

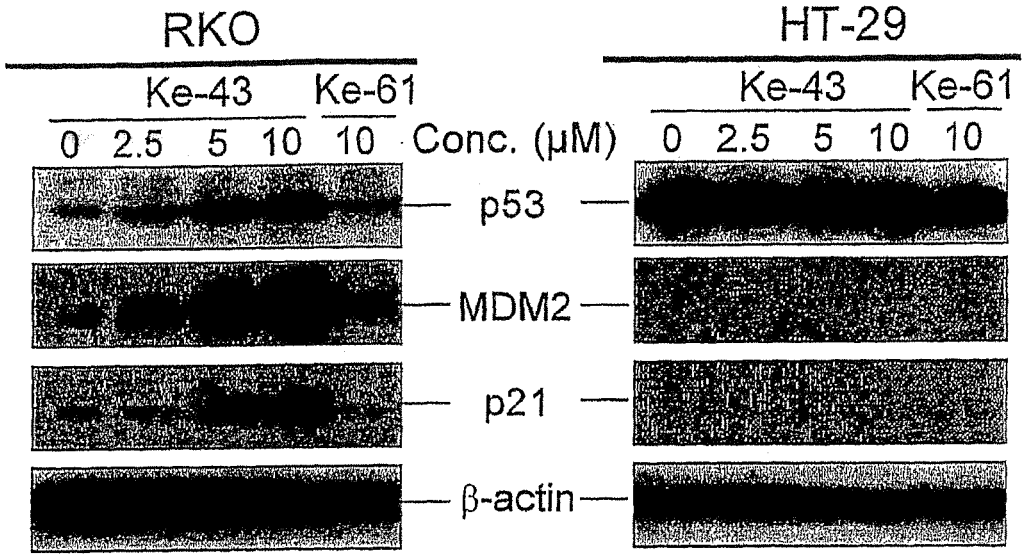

RKO
HT-29
Ke-43
Ke-61
Ke-43
Ke-61
0 2.5 5 10 10 Conc. (μM) 0 2.5 5 10 10
p53
MDM2
p21
β-actin

FIG. 12

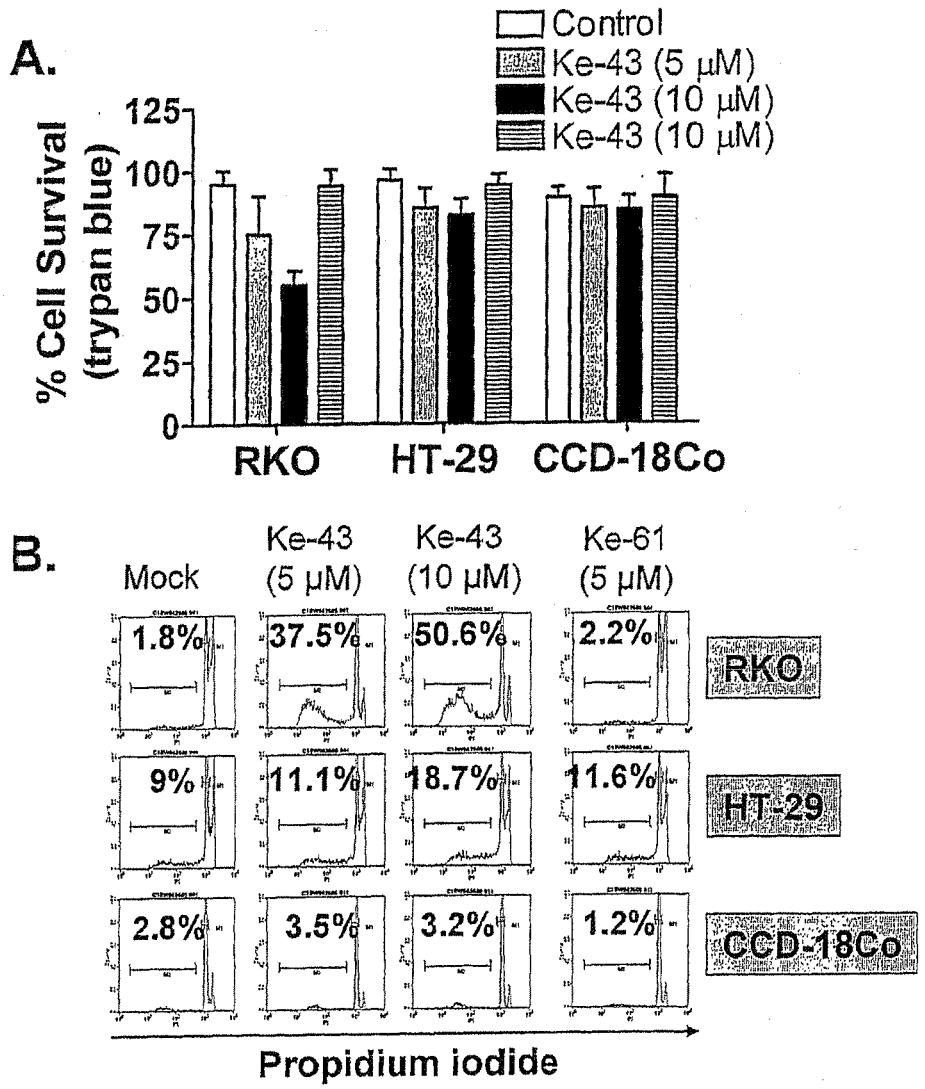

A.
Control
Ke-43 (5 μM)
Ke-43 (10 μM)
Ke-43 (10 μM)
% Cell Survival (trypan blue)
125
100
75
50
25
0
RKO
HT-29
CCD-18Co
B.
Mock
Ke-43 (5 μM)
Ke-43 (10 μM)
Ke-61 (5 μM)
1.8%
37.5%
50.6%
2.2%
RKO
9%
11.1%
18.7%
11.6%
HT-29
2.8%
3.5%
3.2%
1.2%
CCD-18Co
Propidium iodide

FIG. 13

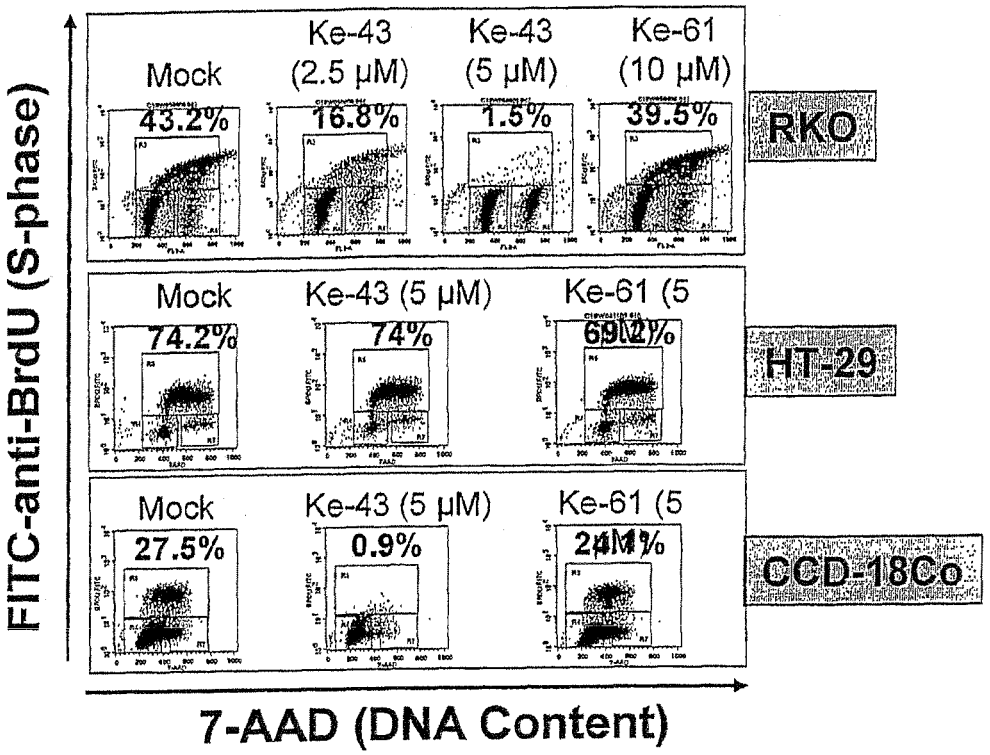

Mock
Ke-43 (2.5 μM)
Ke-43 (5 μM)
Ke-61 (10 μM)
43.2%
16.8%
1.5%
39.5%
RKO
Mock
Ke-43 (5 μM)
Ke-61 (5
74.2%
74%
69.2%
HT-29
Mock
Ke-43 (5 μM)
Ke-61 (5
27.5%
0.9%
CCD-18Co
FITC-anti-BrdU (S-phase)
7-AAD (DNA Content)

FIG. 14

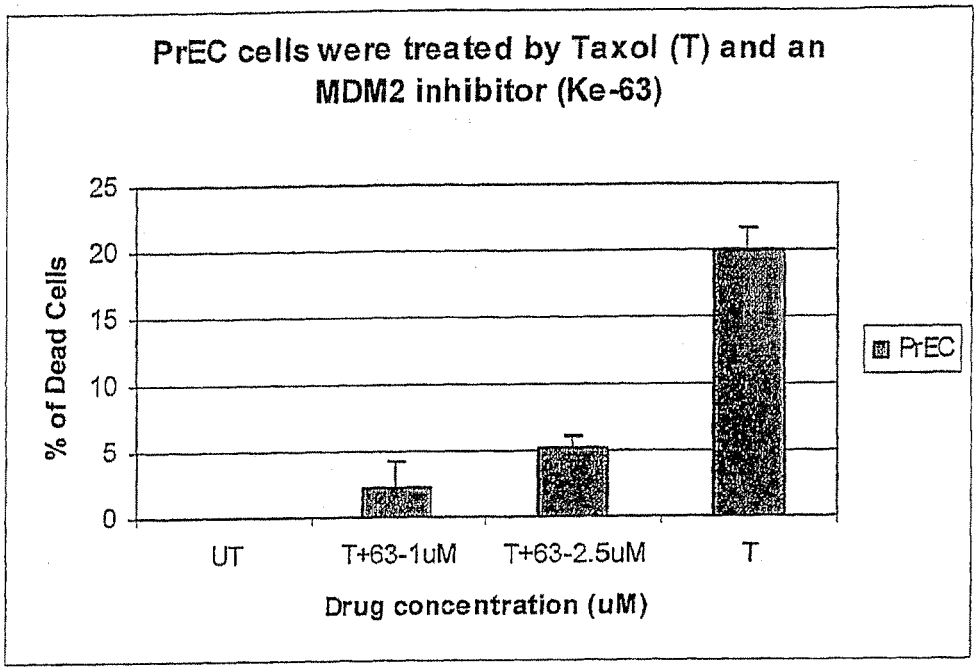

PrEC cells were treated by Taxol (T) and an MDM2 inhibitor (Ke-63)
% of Dead Cells
25
20
15
10
5
0
UT
T+63-1uM
T+63-2.5uM
T
Drug concentration (uM)
PrEC

FIG. 15