FIG. 1

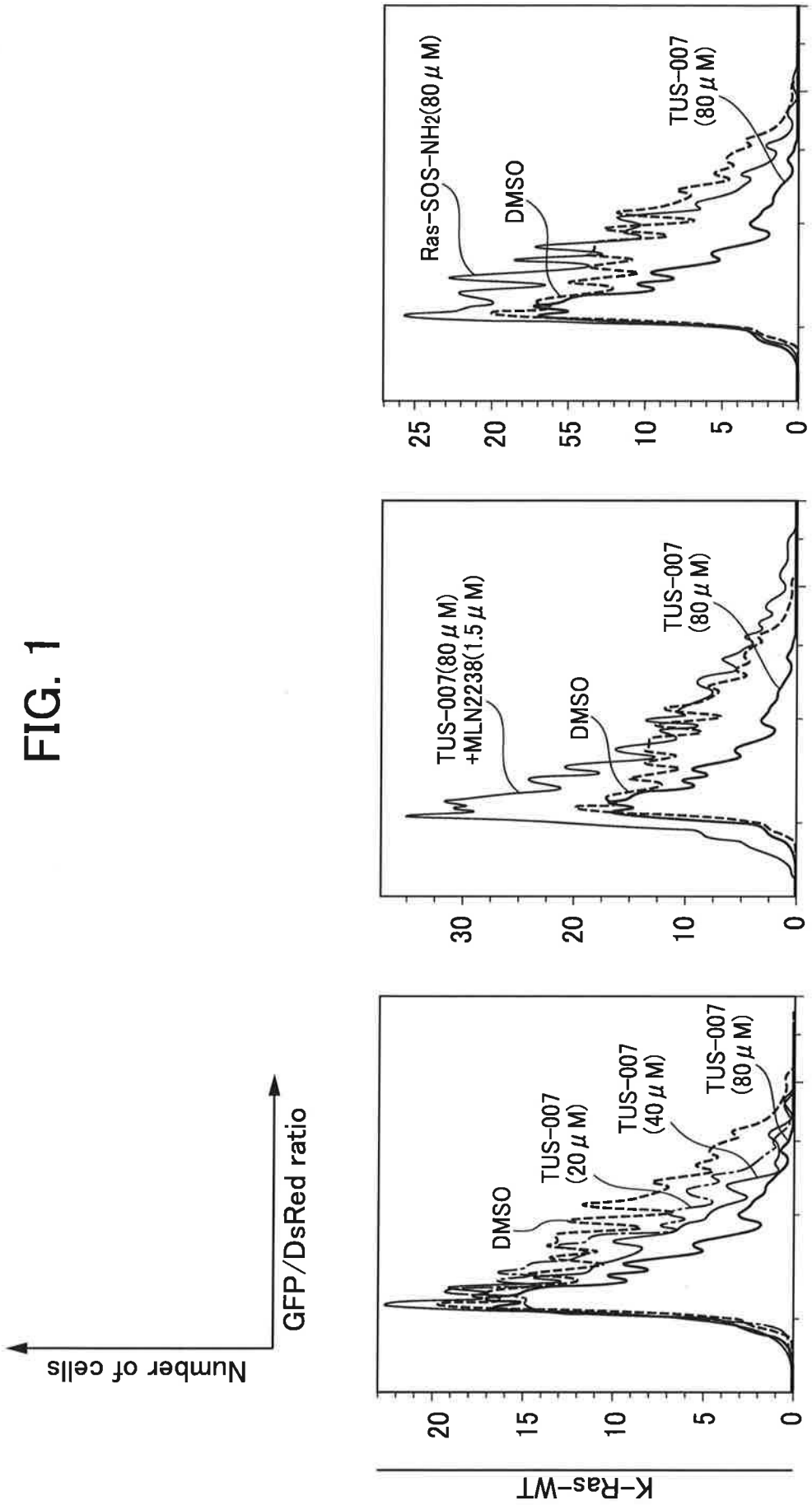

K-Ras-WT
Number of cells
GFP/DsRed ratio
DMSO
TUS-007 (20 μM)
TUS-007 (40 μM)
TUS-007 (80 μM)
TUS-007(80 μM) +MLN2238(1.5 μM)
Ras-SOS-NH2(80 μM)

FIG. 2

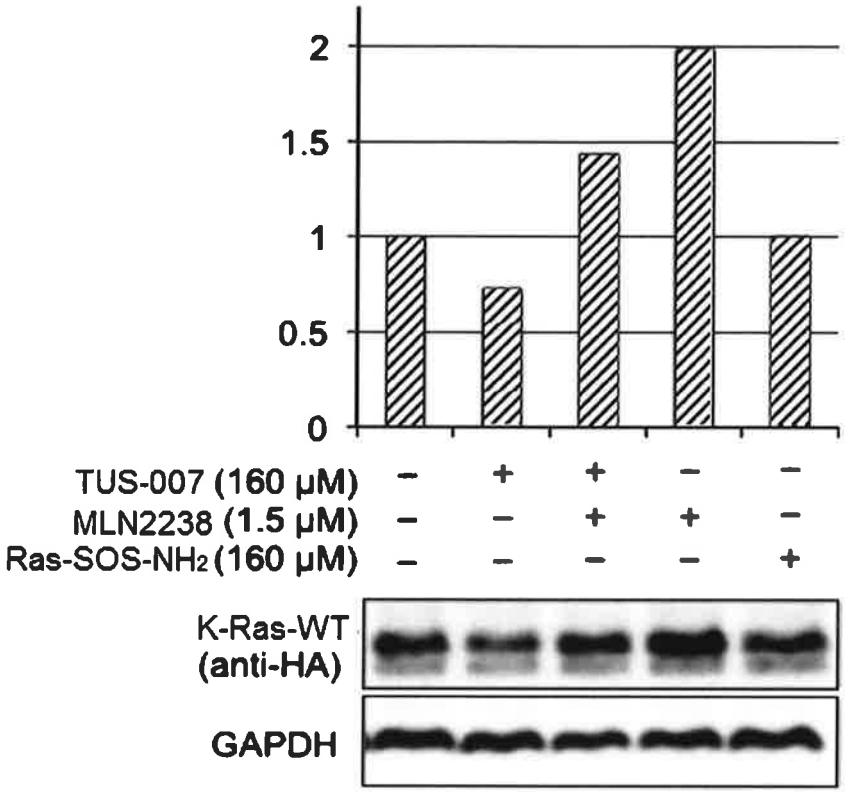

2
1.5
1
0.5
0
TUS-007 (160 μM) − + + − −
MLN2238 (1.5 μM) − − + + −
Ras-SOS-NH2 (160 μM) − − − − +
K-Ras-WT (anti-HA)
GAPDH

FIG. 3

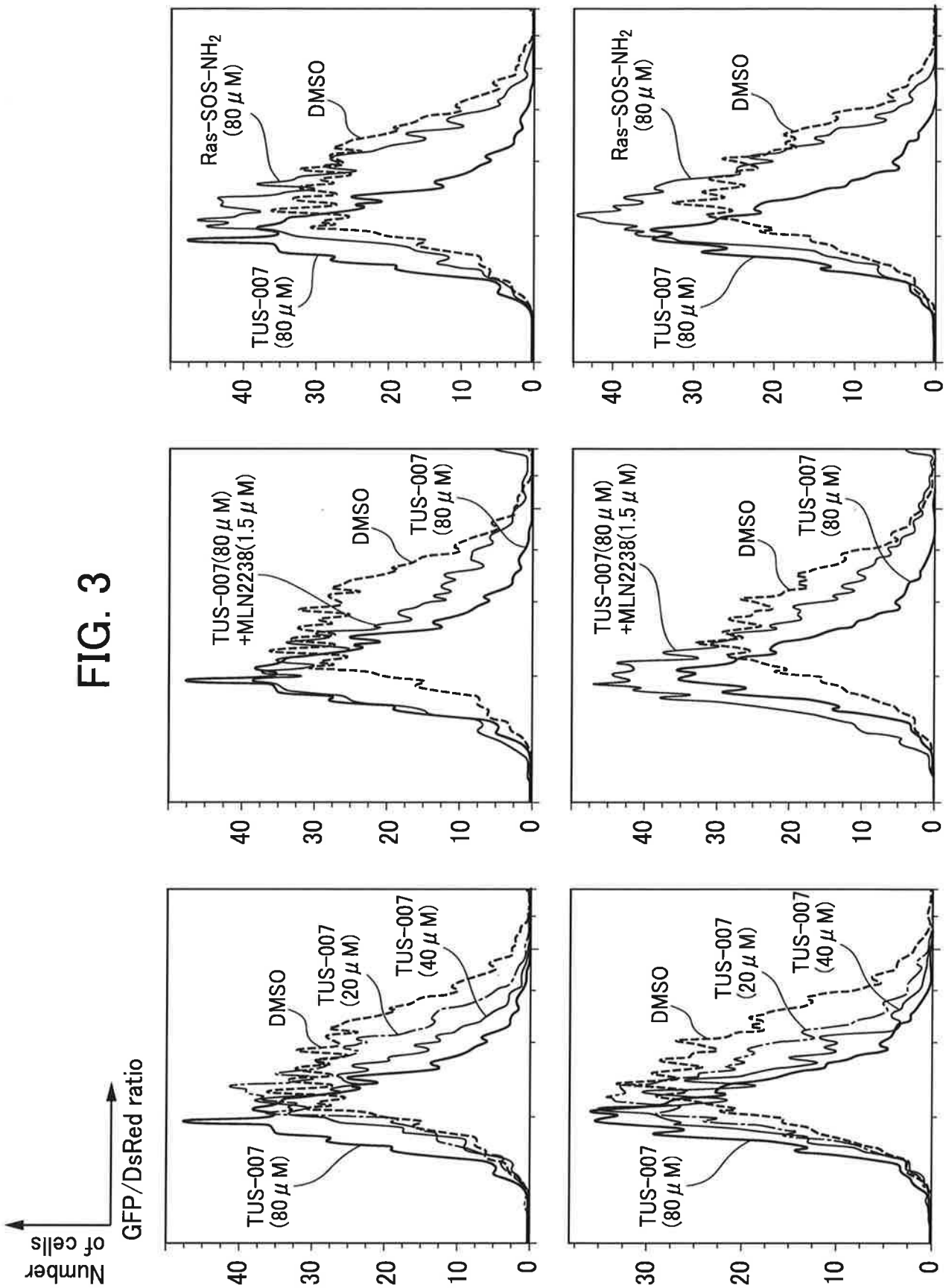

K-Ras-G12D
K-Ras-G12V
Number of cells
GFP/DsRed ratio
DMSO
TUS-007 (20 μM)
TUS-007 (40 μM)
TUS-007 (80 μM)
TUS-007(80 μM) +MLN2238(1.5 μM)
Ras-SOS-NH2 (80 μM)
0
10
20
30
40

FIG. 4

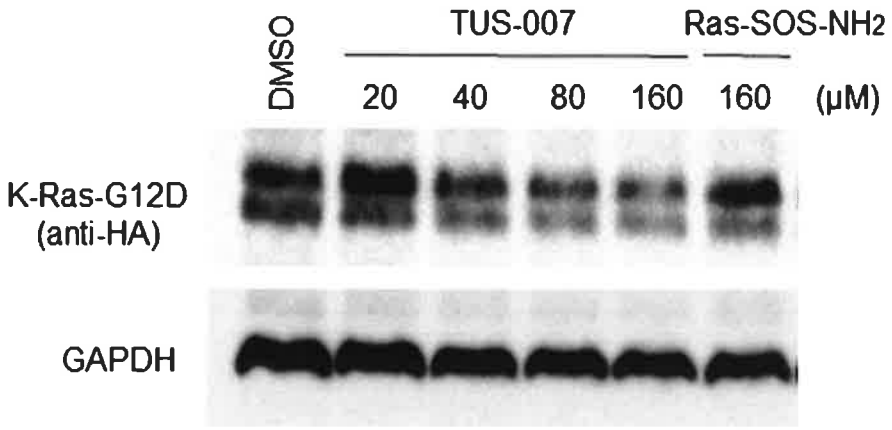

DMSO
TUS-007
Ras-SOS-NH2
20
40
80
160
160
(μM)
K-Ras-G12D
(anti-HA)
GAPDH

FIG. 5

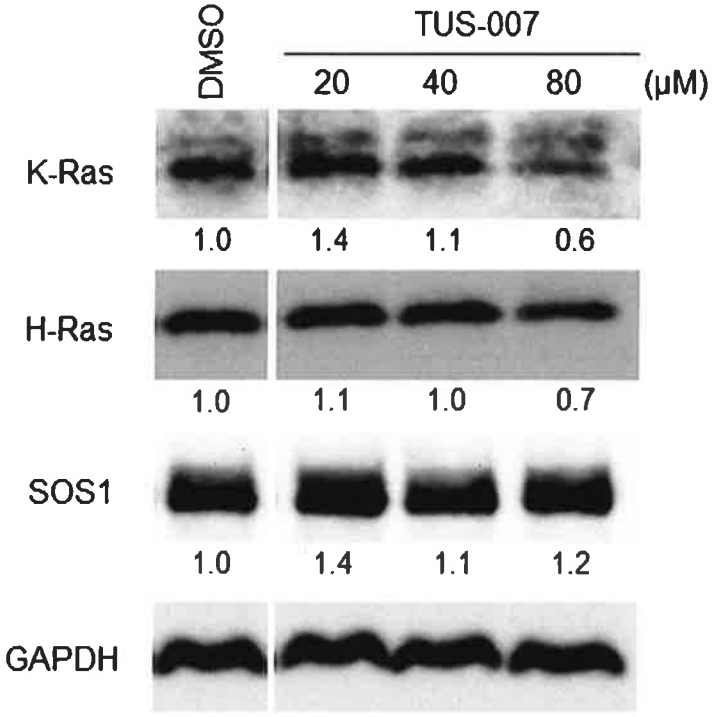

DMSO
TUS-007
20
40
80
(μM)
K-Ras
1.0
1.4
1.1
0.6
H-Ras
1.0
1.1
1.0
0.7
SOS1
1.0
1.4
1.1
1.2
GAPDH

FIG. 6A

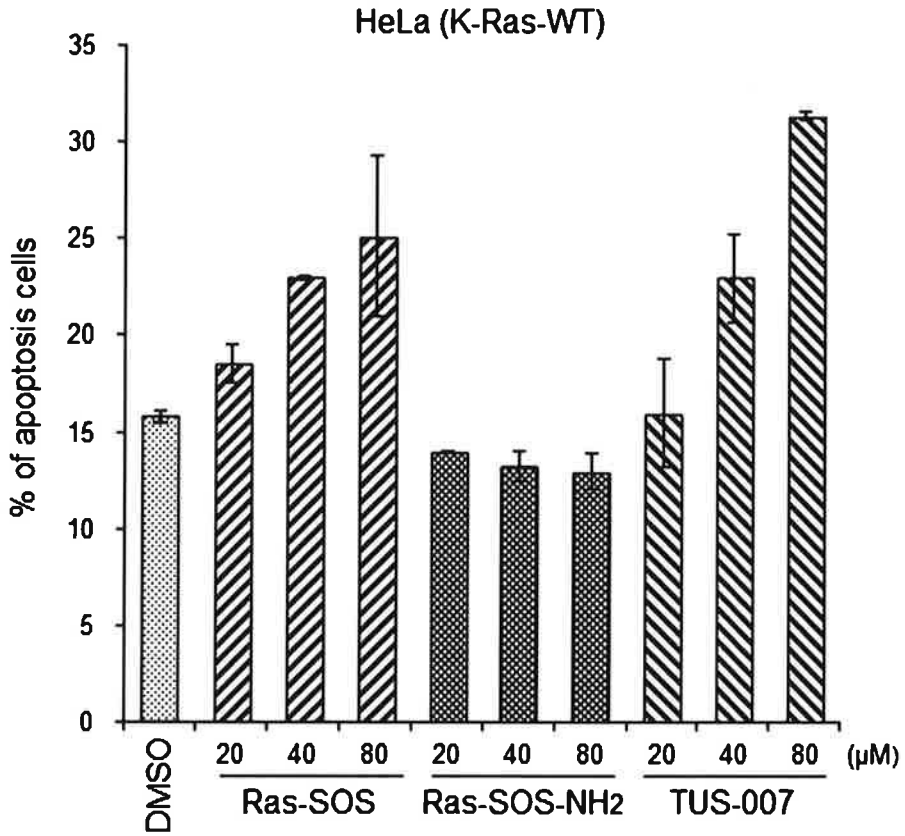

HeLa (K-Ras-WT)
% of apoptosis cells
35
30
25
20
15
10
5
0
DMSO
20
40
80
20
40
80
20
40
80
(μM)
Ras-SOS
Ras-SOS-NH2
TUS-007

FIG. 6B

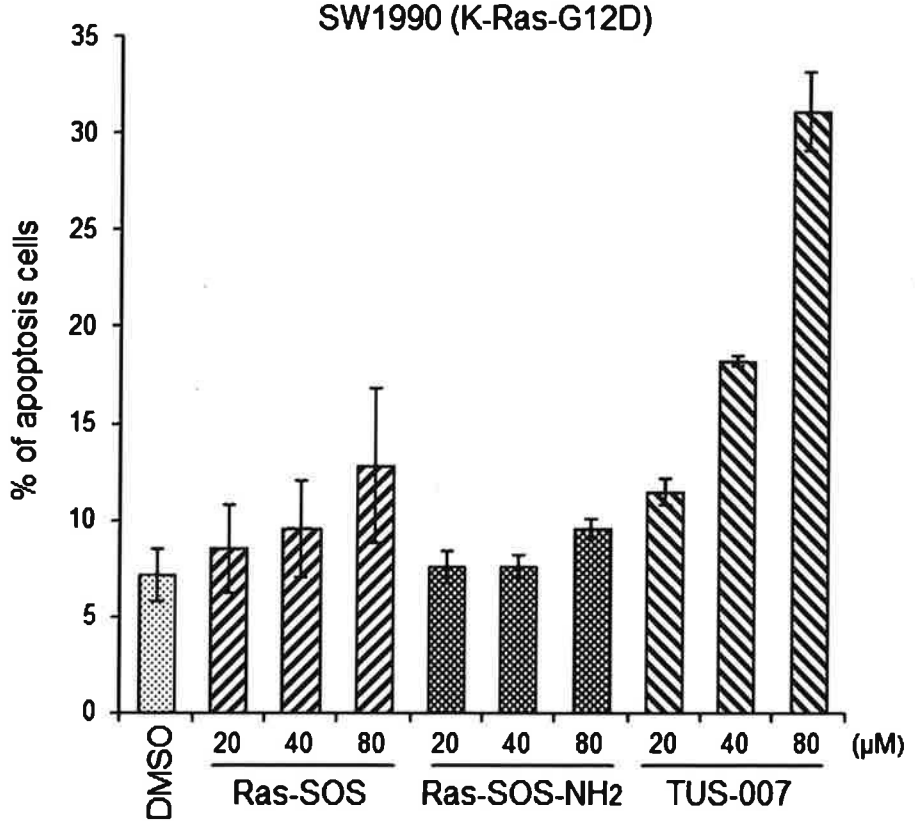

SW1990 (K-Ras-G12D)
% of apoptosis cells
35
30
25
20
15
10
5
0
DMSO
20
40
80
20
40
80
20
40
80
(μM)
Ras-SOS
Ras-SOS-NH2
TUS-007

FIG. 7A

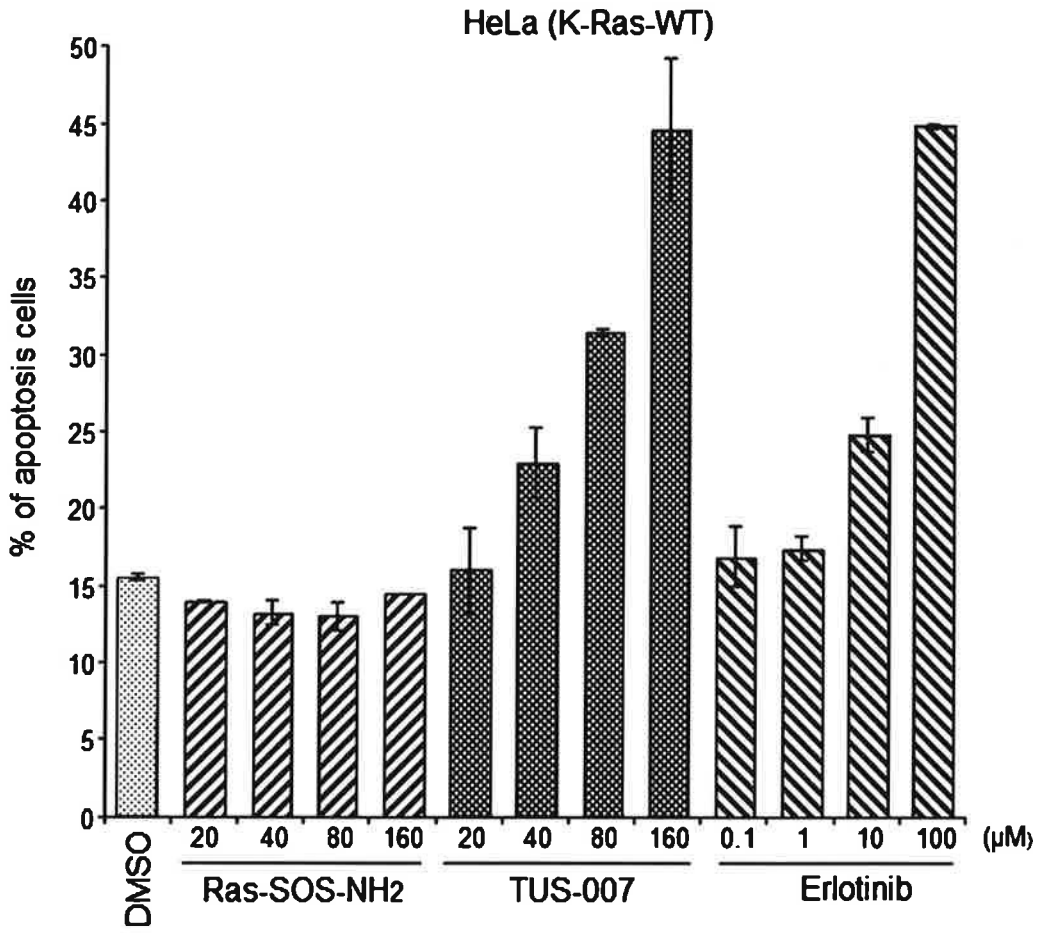

HeLa (K-Ras-WT)
% of apoptosis cells
50
45
40
35
30
25
20
15
10
5
0
DMSO
20
40
80
160
20
40
80
160
0.1
1
10
100
(μM)
Ras-SOS-NH2
TUS-007
Erlotinib

FIG. 7B

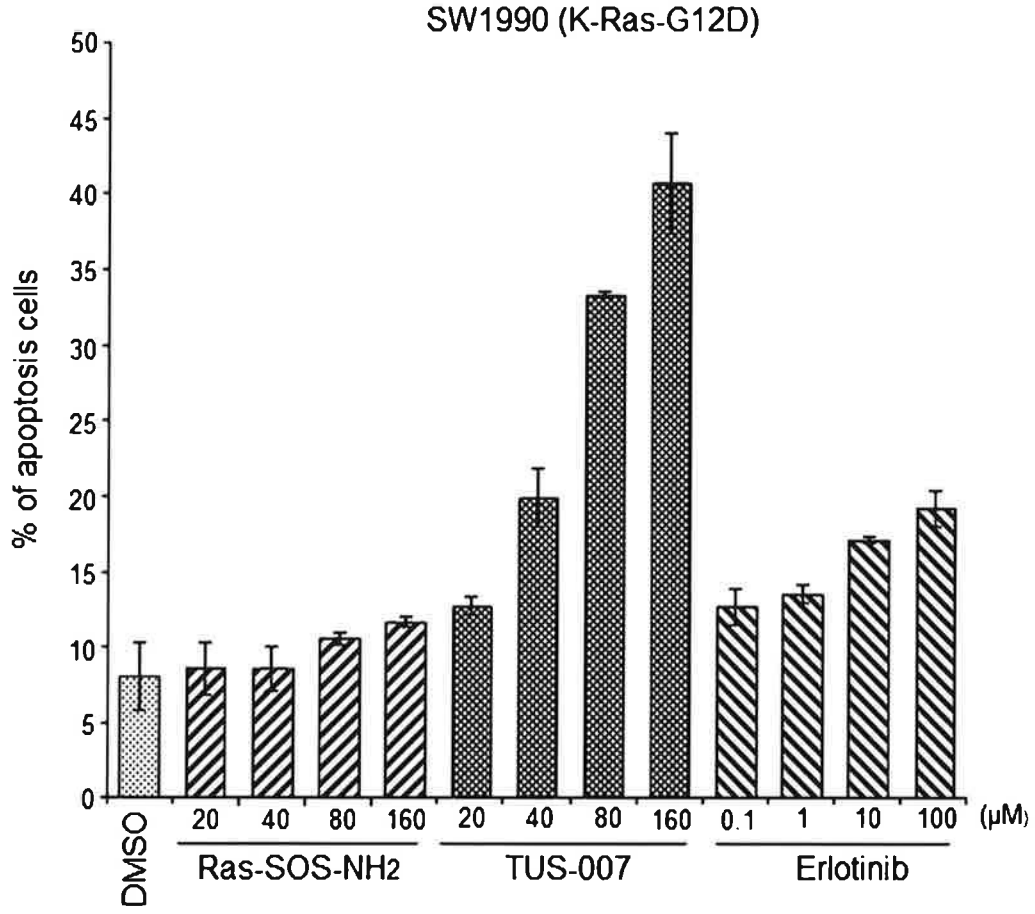

SW1990 (K-Ras-G12D)
% of apoptosis cells
50
45
40
35
30
25
20
15
10
5
0
DMSO
20
40
80
160
20
40
80
160
0.1
1
10
100
(μM)
Ras-SOS-NH2
TUS-007
Erlotinib

FIG. 8

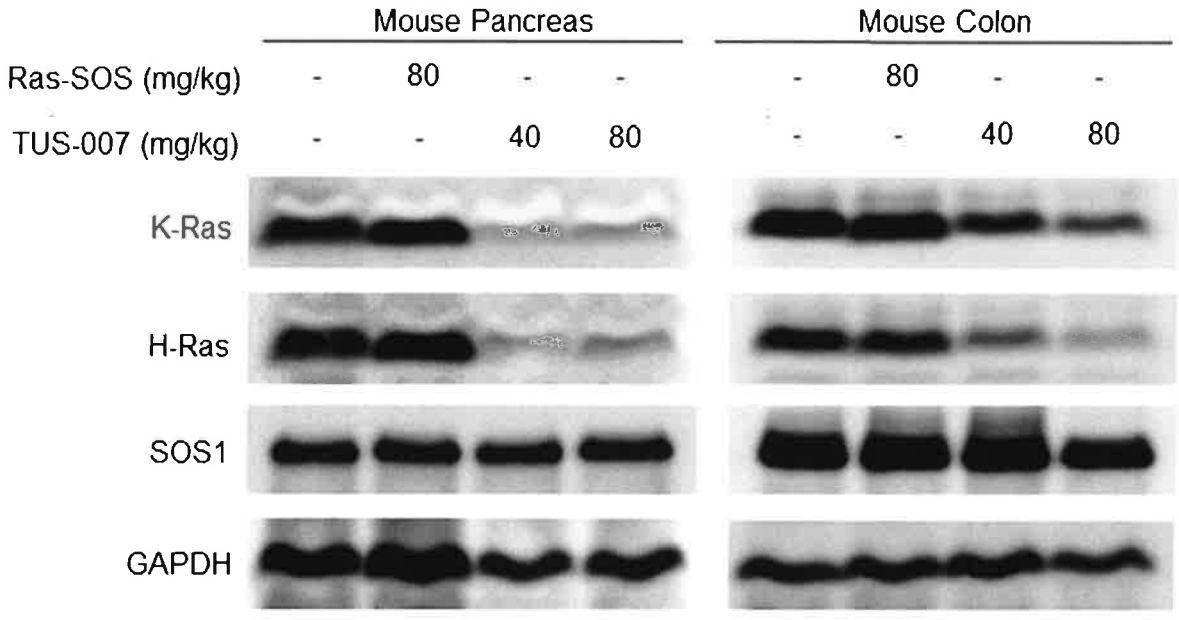

Mouse Pancreas
Mouse Colon
Ras-SOS (mg/kg)
- 80 - -
- 80 - -
TUS-007 (mg/kg)
- - 40 80
- - 40 80
K-Ras
H-Ras
SOS1
GAPDH

FIG. 9A

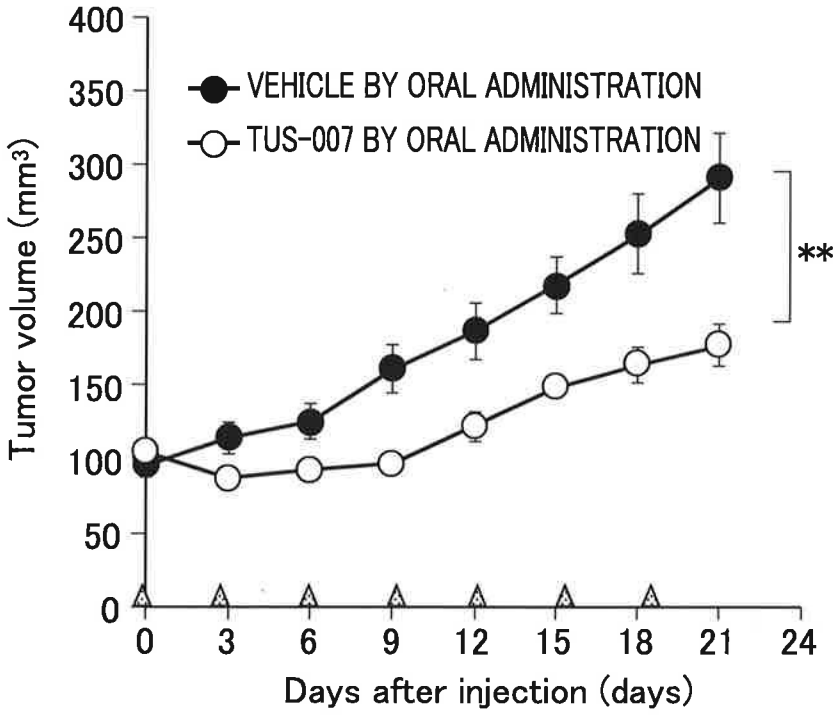

400
350
300
250
200
150
100
50
0
Tumor volume (mm³)
VEHICLE BY ORAL ADMINISTRATION
TUS-007 BY ORAL ADMINISTRATION
**
0
3
6
9
12
15
18
21
24
Days after injection (days)

FIG. 9B

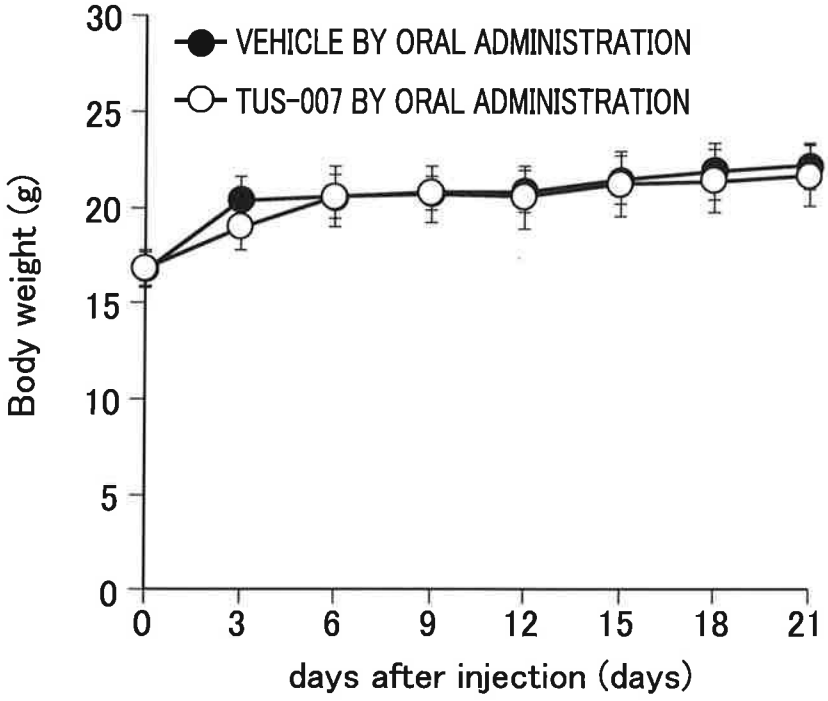

30
25
20
15
10
5
0
Body weight (g)
VEHICLE BY ORAL ADMINISTRATION
TUS-007 BY ORAL ADMINISTRATION
0
3
6
9
12
15
18
21
days after injection (days)

FIG. 10A

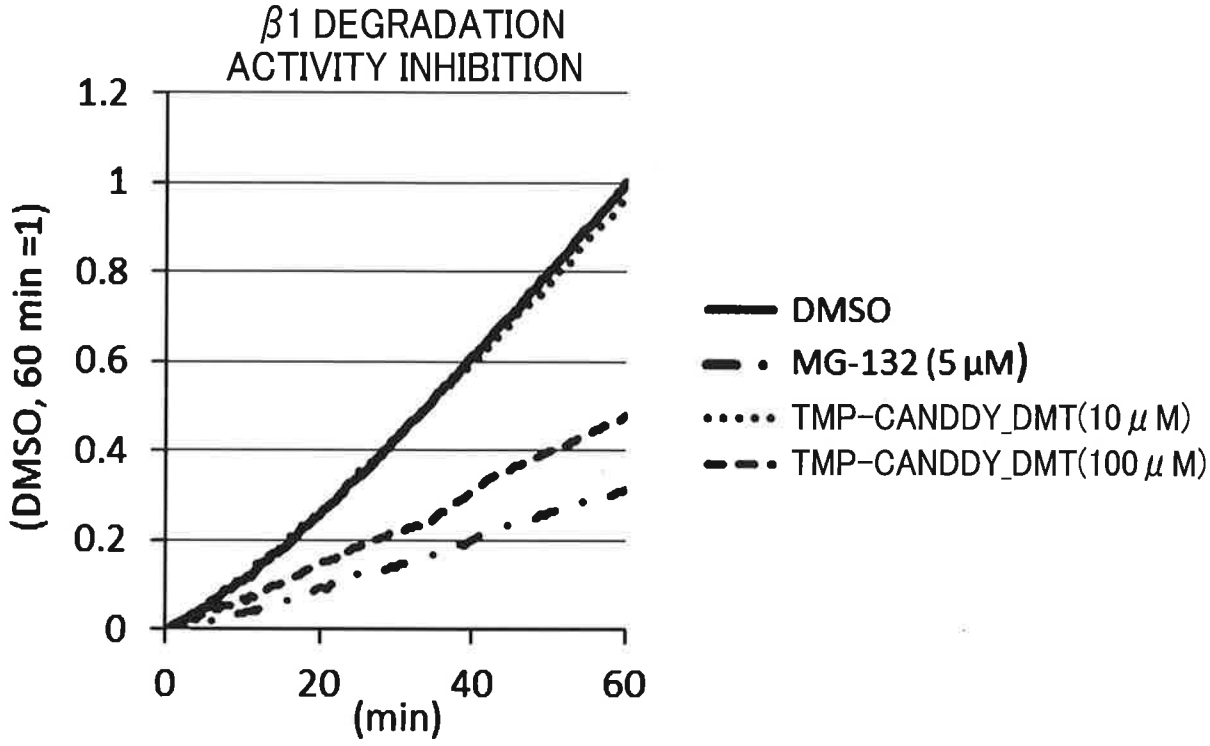


FIG. 10B

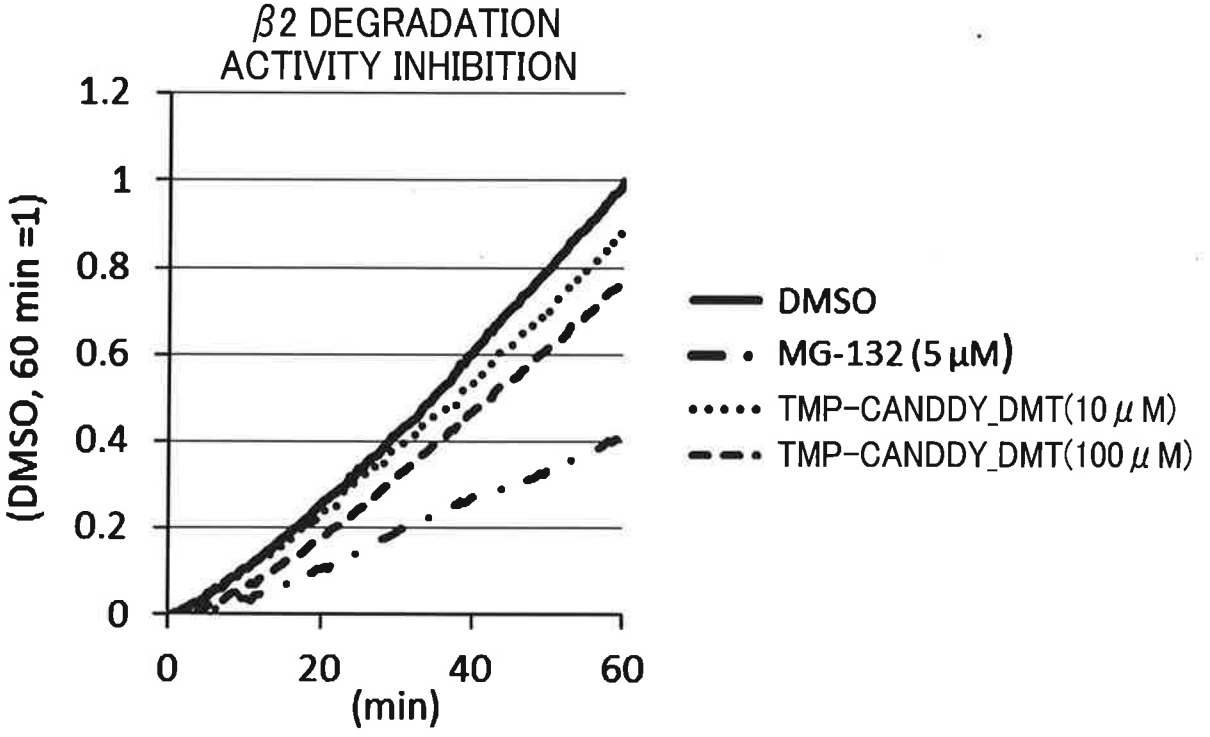


FIG. 10C

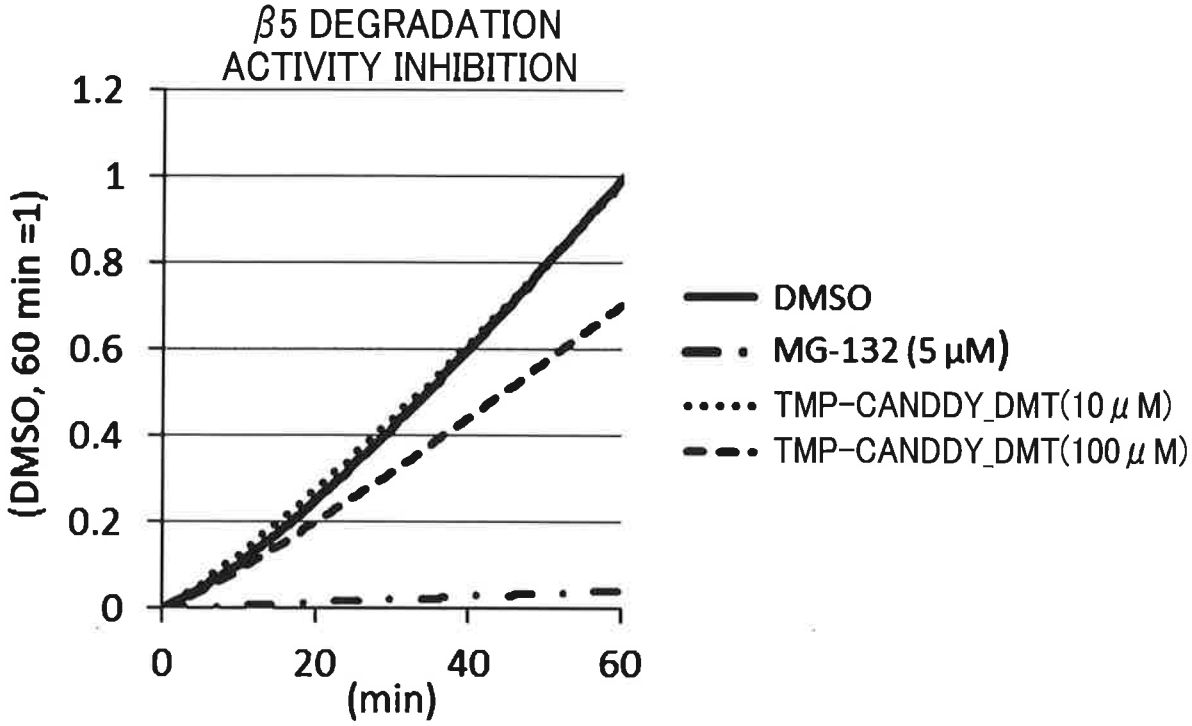

β5 DEGRADATION ACTIVITY INHIBITION
(DMSO, 60 min =1)
1.2
1
0.8
0.6
0.4
0.2
0
0
20
40
60
(min)
DMSO
MG-132 (5 μM)
TMP-CANDDY_DMT(10 μ M)
TMP-CANDDY_DMT(100 μ M)

FIG. 11

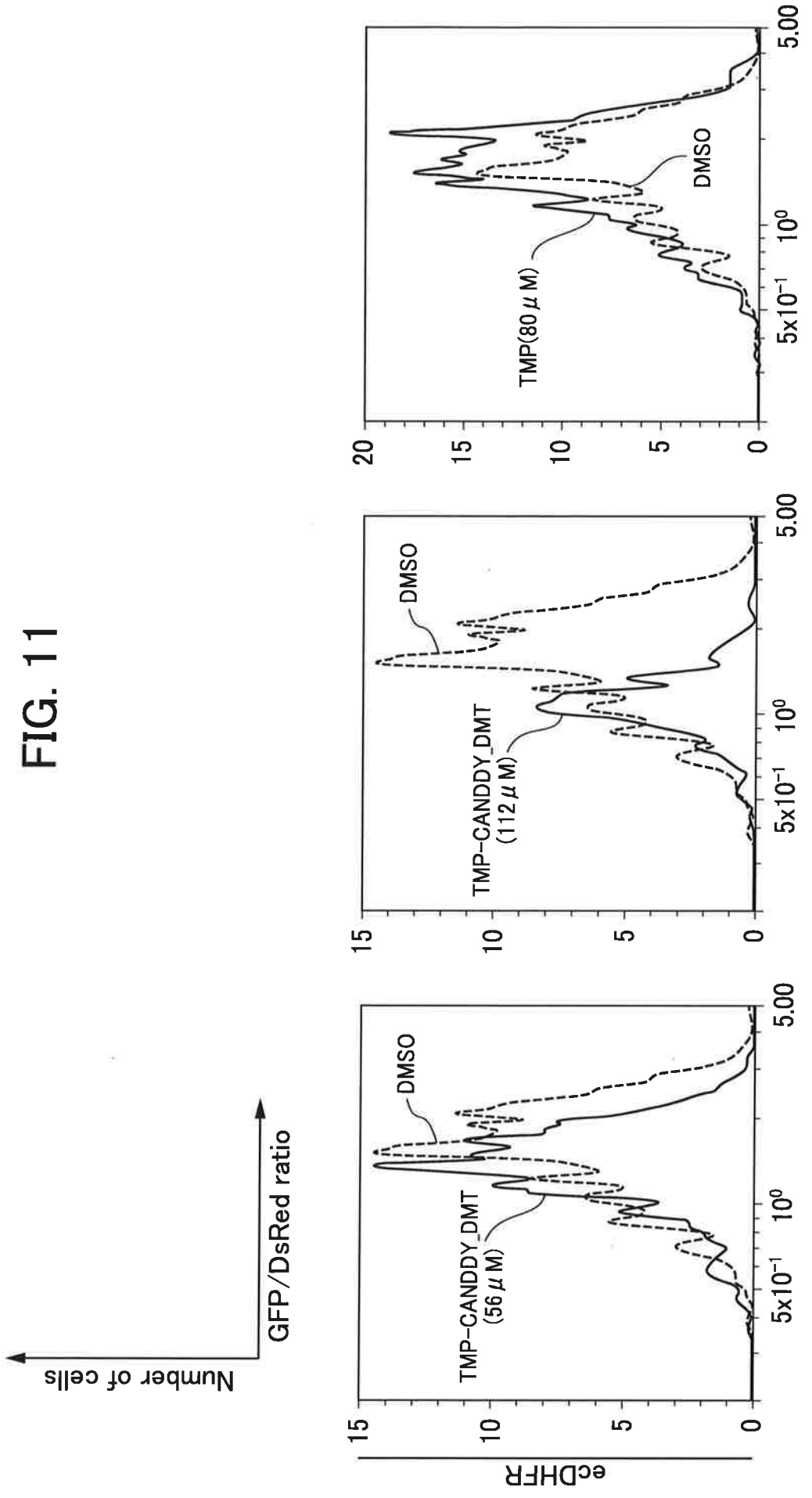

ecDHFR
GFP/DsRed ratio
Number of cells
TMP-CANDDY_DMT (56 μM)
DMSO
TMP-CANDDY_DMT (112 μM)
DMSO
TMP(80 μM)
DMSO
0
5
10
15
20
5x10⁻¹
10⁰
5.00

FIG. 12A

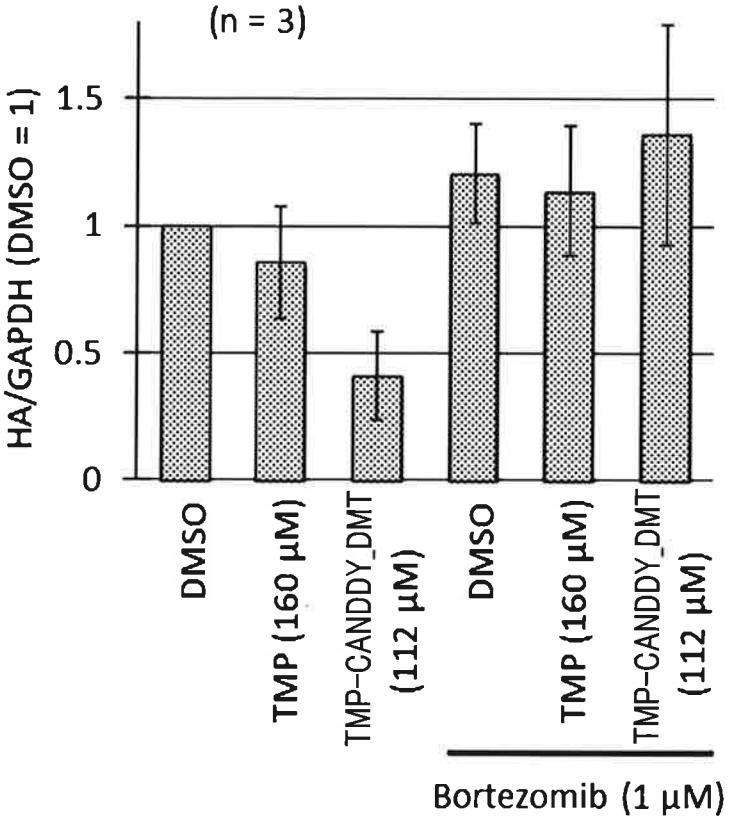


FIG. 12B

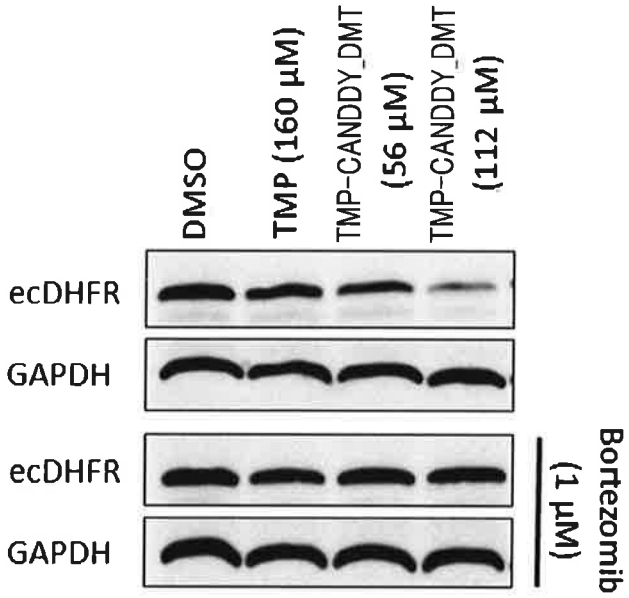


FIG. 13A

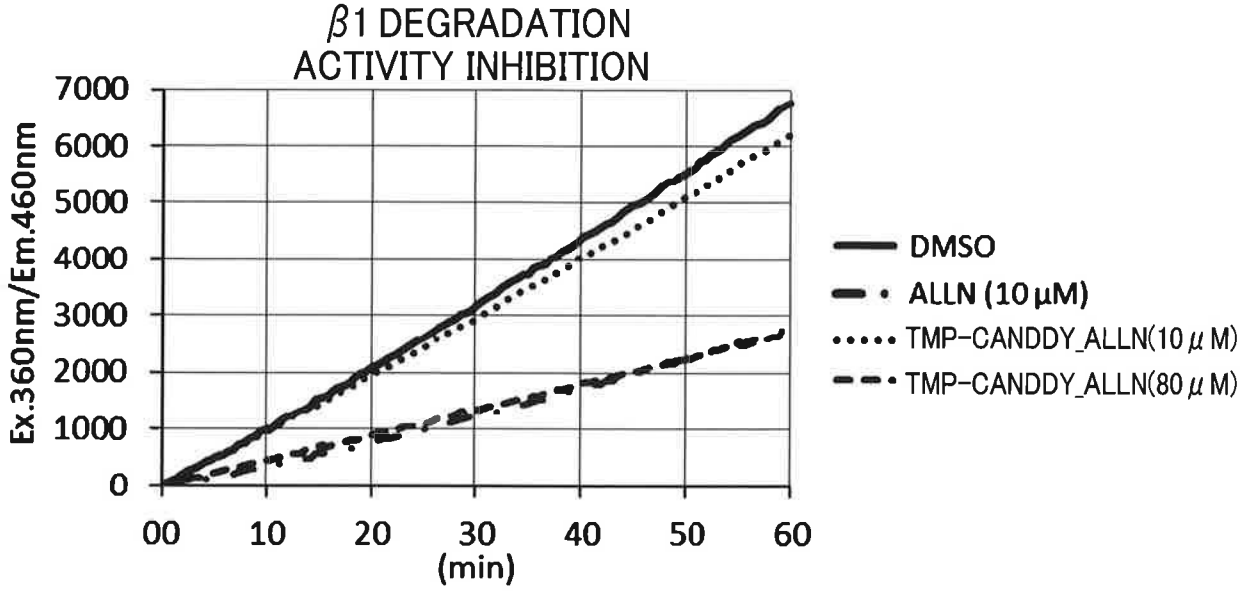


FIG. 13B

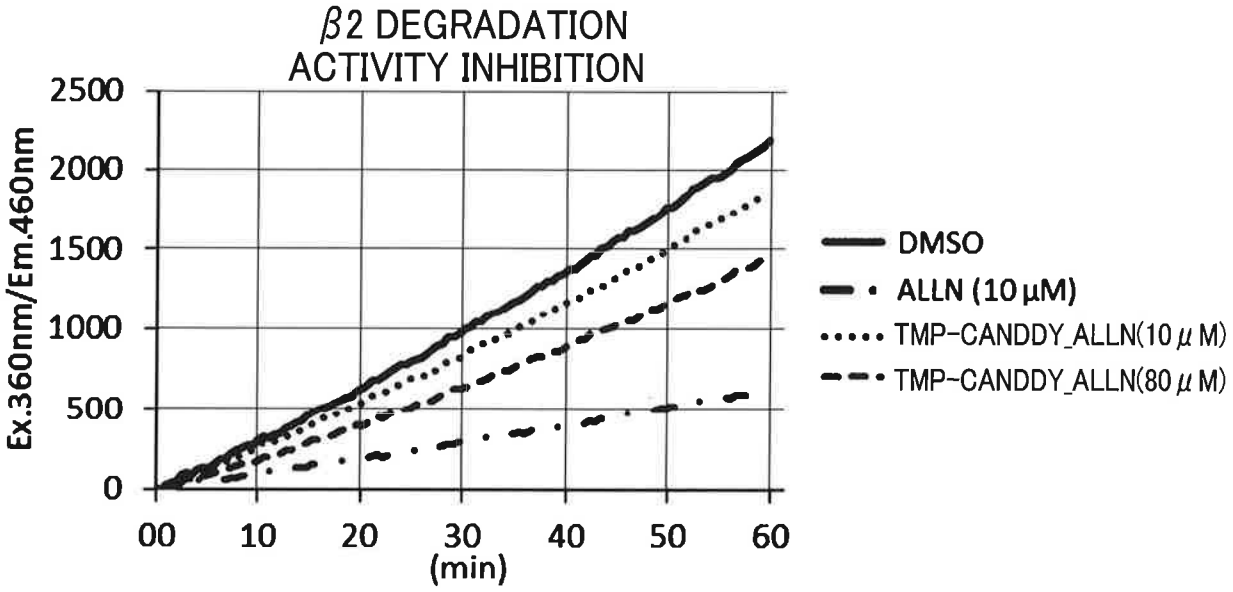


FIG. 13C

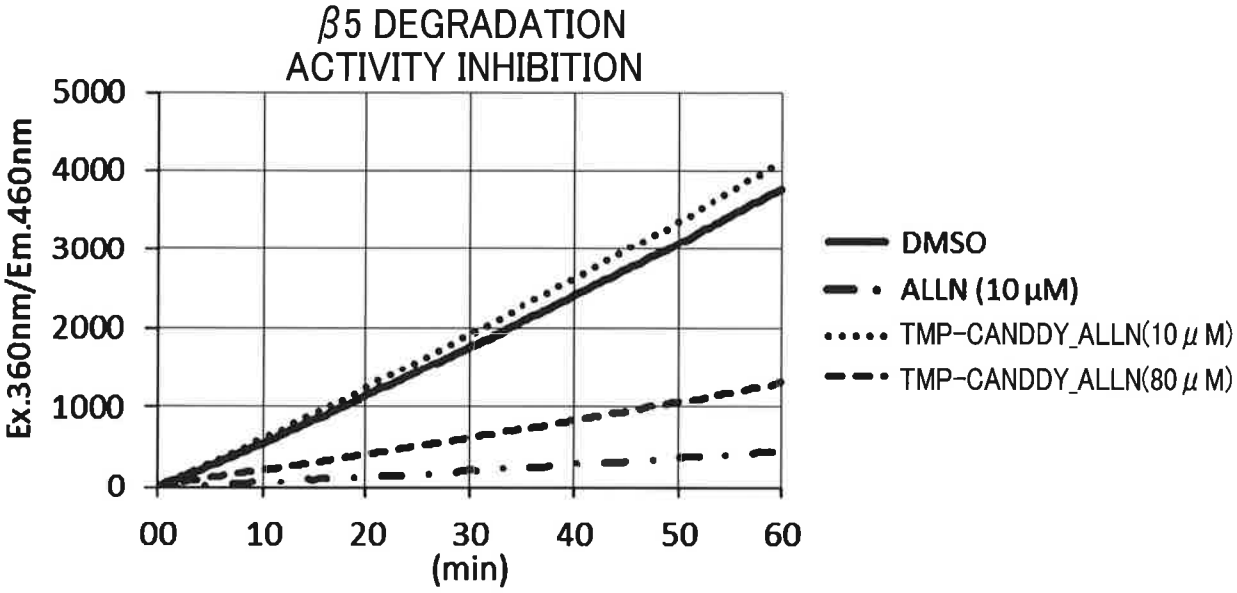
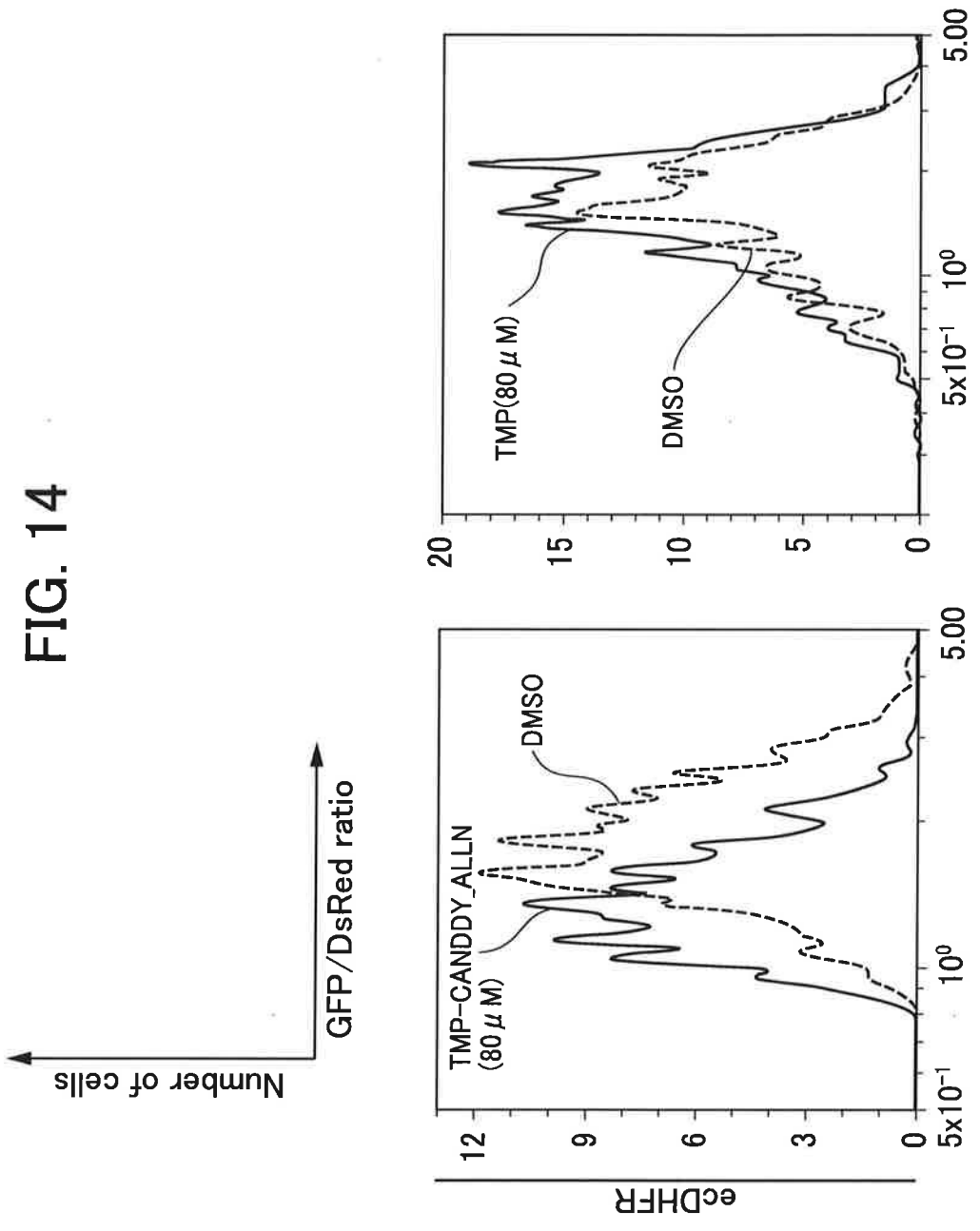

β5 DEGRADATION
ACTIVITY INHIBITION
Ex.360nm/Em.460nm
5000
4000
3000
2000
1000
0
00
10
20
30
40
50
60
(min)
DMSO
ALLN (10 μM)
TMP-CANDDY_ALLN(10 μ M)
TMP-CANDDY_ALLN(80 μ M)

FIG. 14


ecDHFR
12
9
6
3
0
5x10⁻¹
10⁰
5.00
TMP-CANDDY_ALLN
(80 μ M)
DMSO
20
15
10
5
0
TMP(80 μ M)
DMSO
Number of cells
GFP/DsRed ratio