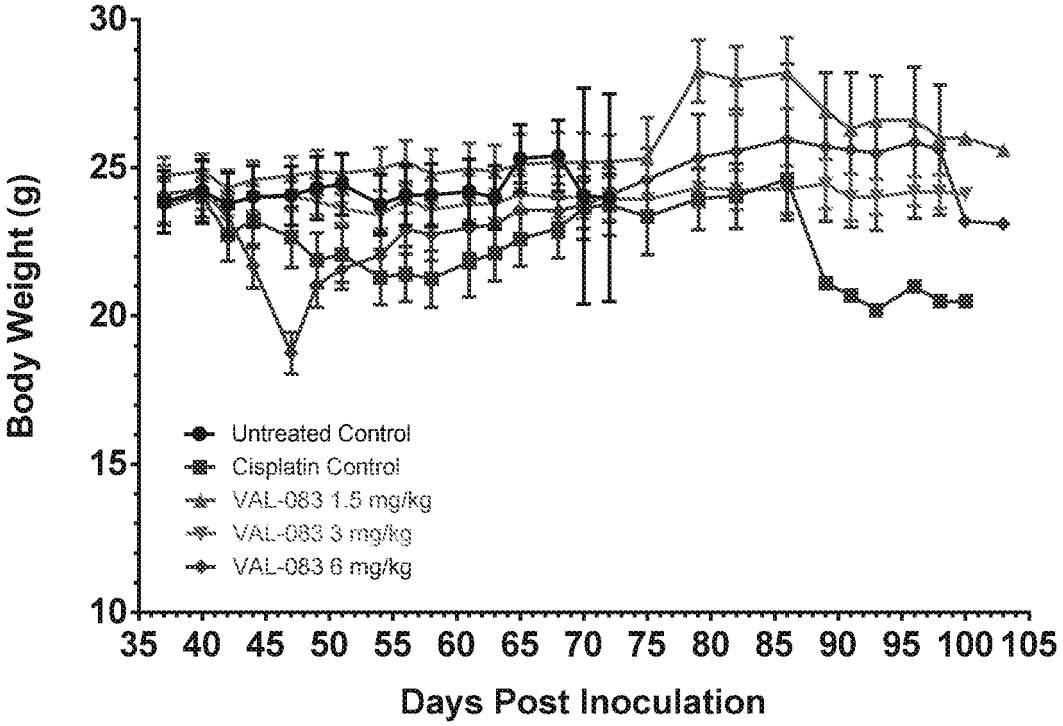
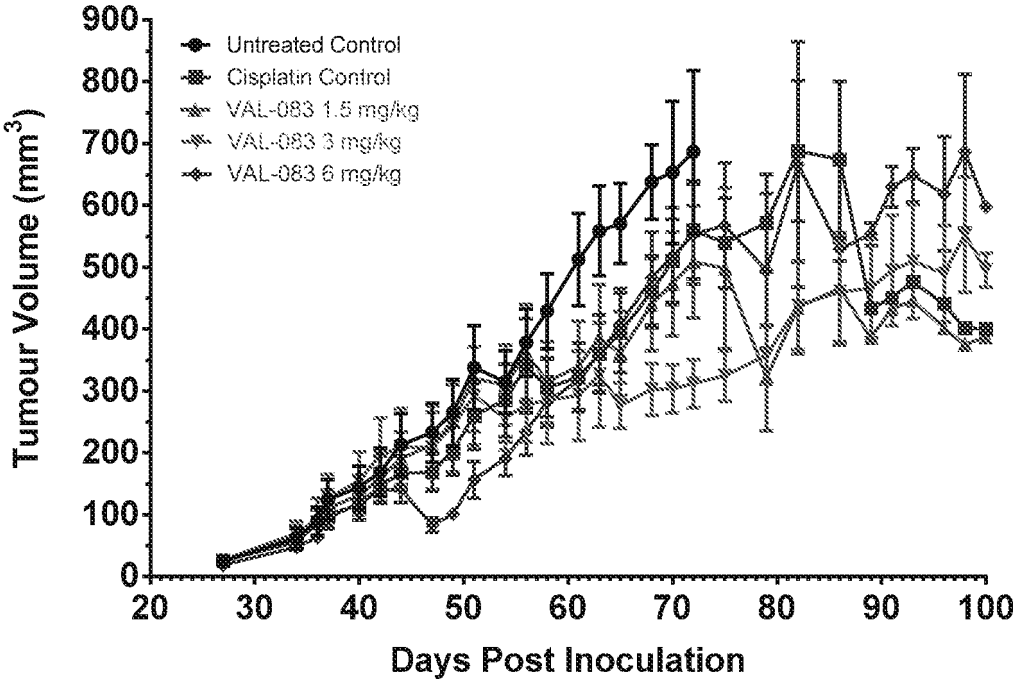

Body Weight (g)
30
25
20
15
10
35 40 45 50 55 60 65 70 75 80 85 90 95 100 105
Days Post Inoculation
Untreated Control
Cisplatin Control
VAL-083 1.5 mg/kg
VAL-083 3 mg/kg
VAL-083 6 mg/kg

Figure 1


Untreated Control
Cisplatin Control
VAL-083 1.5 mg/kg
VAL-083 3 mg/kg
VAL-083 6 mg/kg
Tumour Volume (mm3)
Days Post Inoculation
0
100
200
300
400
500
600
700
800
900
20
30
40
50
60
70
80
90
100

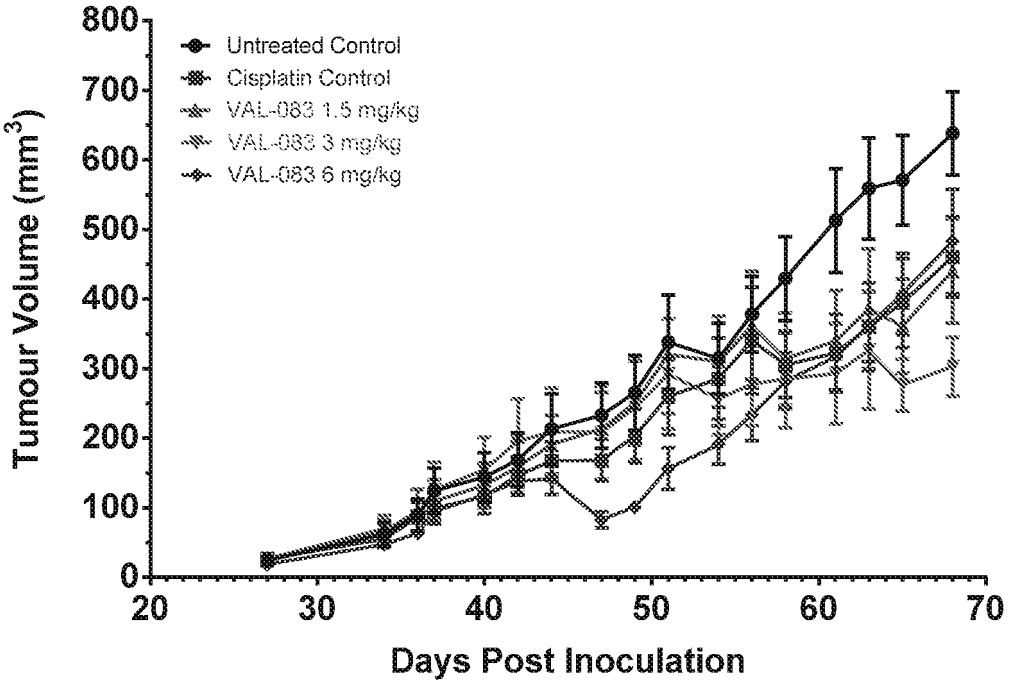

Untreated Control
Cisplatin Control
VAL-083 1.5 mg/kg
VAL-083 3 mg/kg
VAL-083 6 mg/kg
Tumour Volume (mm3)
Days Post Inoculation
0
100
200
300
400
500
600
700
800
20
30
40
50
60
70

Figure 2

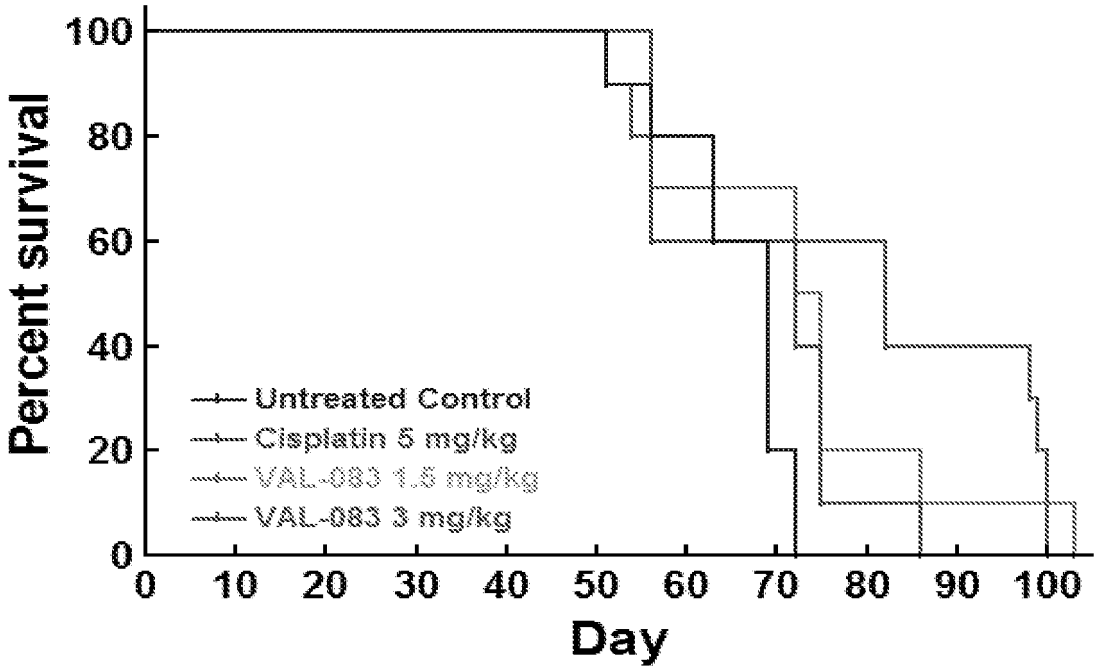

Percent survival
100
80
60
40
20
0
0
10
20
30
40
50
60
70
80
90
100
Day
Untreated Control
Cisplatin 6 mg/kg
VAL-083 1.5 mg/kg
VAL-083 3 mg/kg

Figure 3

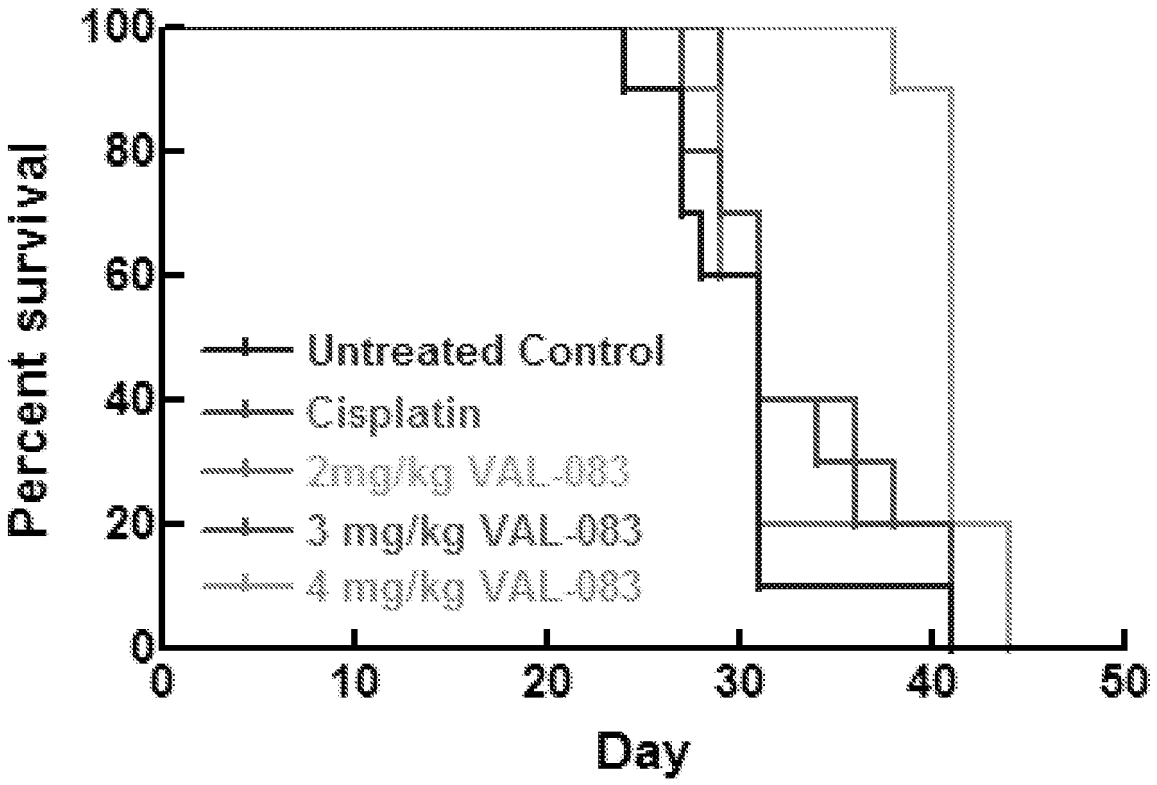

Percent survival
100
80
60
40
20
0
0
10
20
30
40
50
Day
Untreated Control
Cisplatin
2mg/kg VAL-083
3 mg/kg VAL-083
4 mg/kg VAL-083

Figure 4

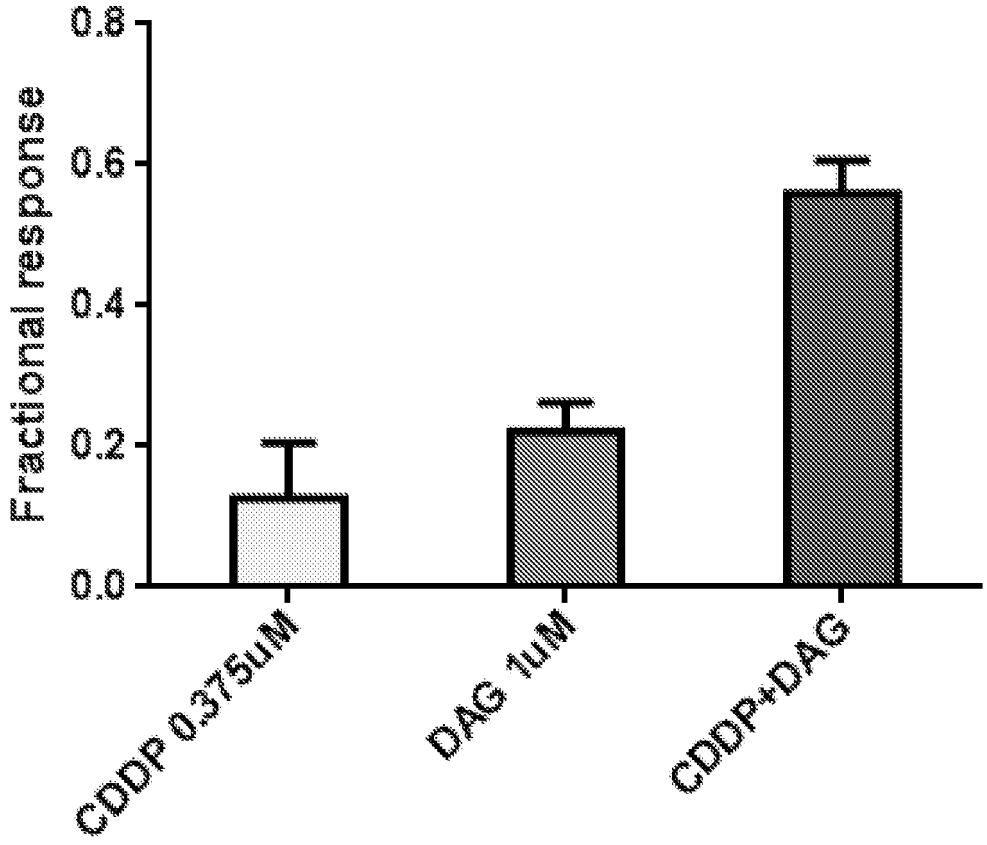

Fractional response
0.8
0.6
0.4
0.2
0.0
CDDP 0.375uM
DAG 1uM
CDDP+DAG

Figure 5A

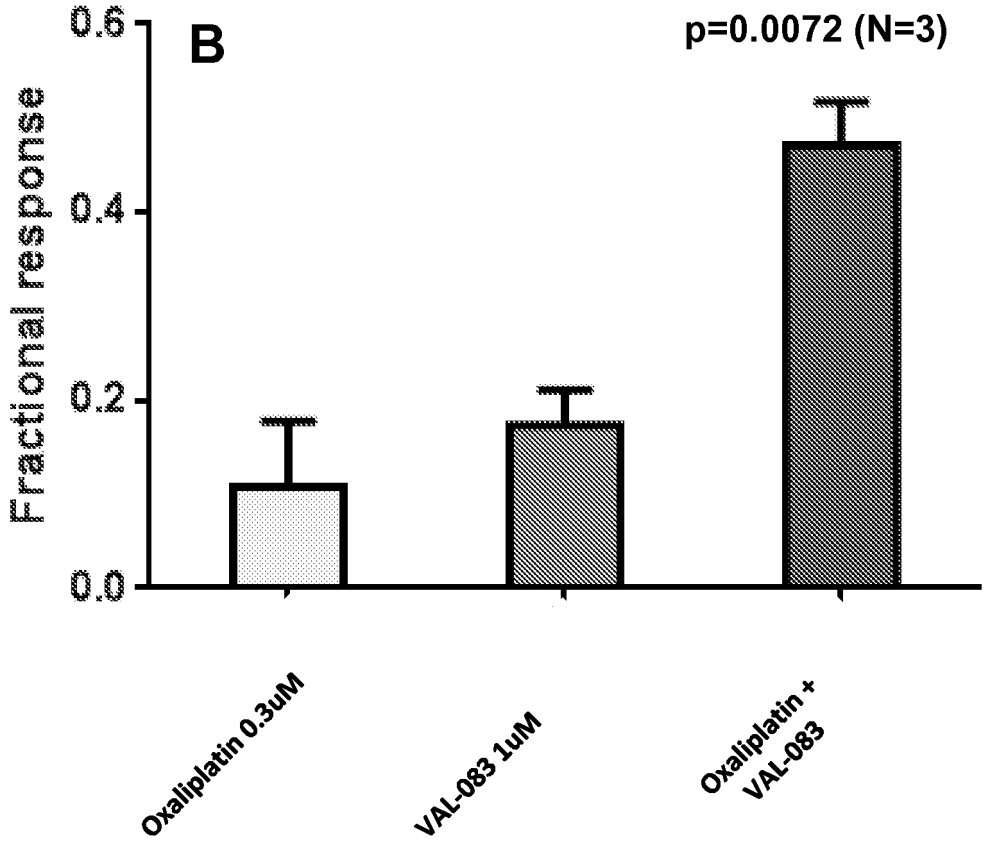

B
p=0.0072 (N=3)
Fractional response
0.6
0.4
0.2
0.0
Oxaliplatin 0.3uM
VAL-083 1uM
Oxaliplatin + VAL-083

Figure 5B

Figure 6A

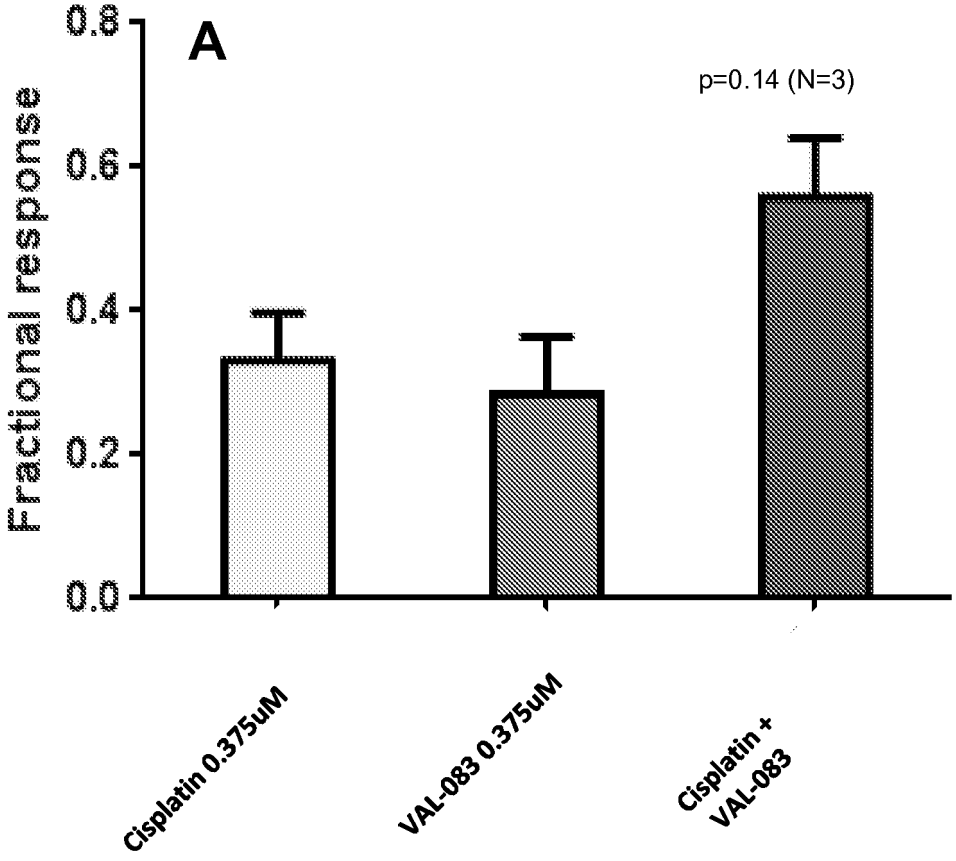
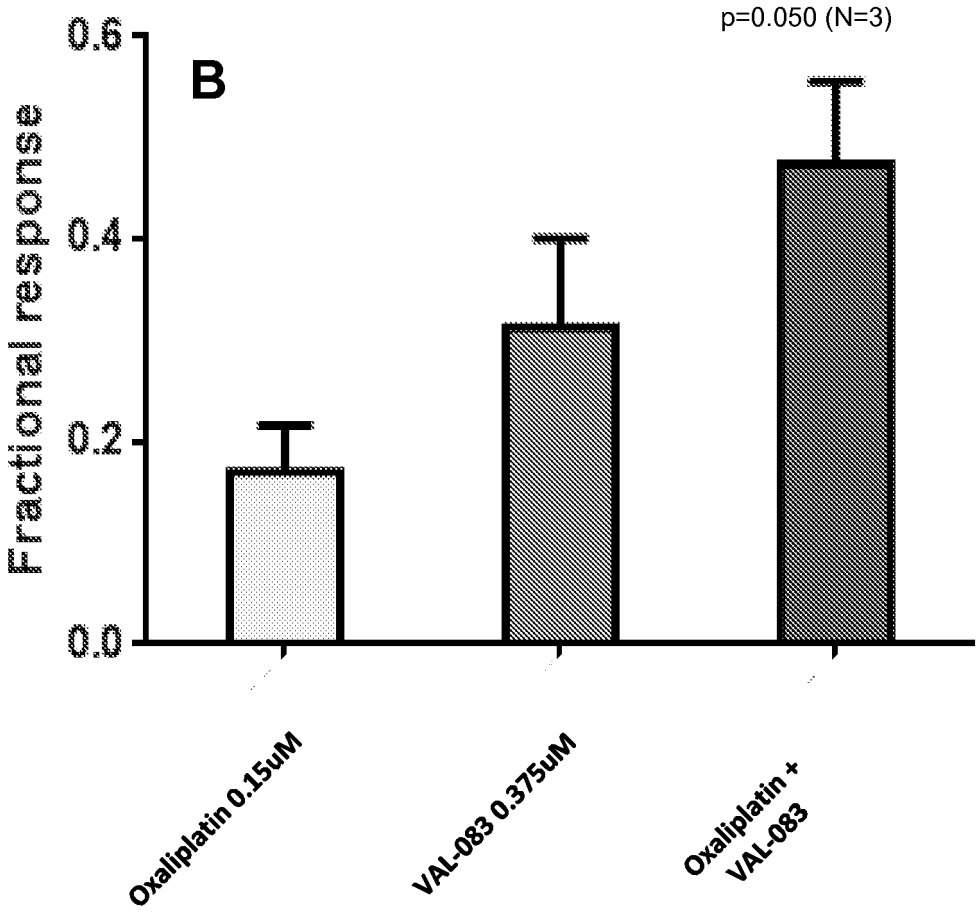

A
p=0.14 (N=3)
Fractional response
0.8
0.6
0.4
0.2
0.0
Cisplatin 0.375uM
VAL-083 0.375uM
Cisplatin + VAL-083

Figure 6B


p=0.050 (N=3)
B
Fractional response
0.6
0.4
0.2
0.0
Oxaliplatin 0.15uM
VAL-083 0.375uM
Oxaliplatin + VAL-083

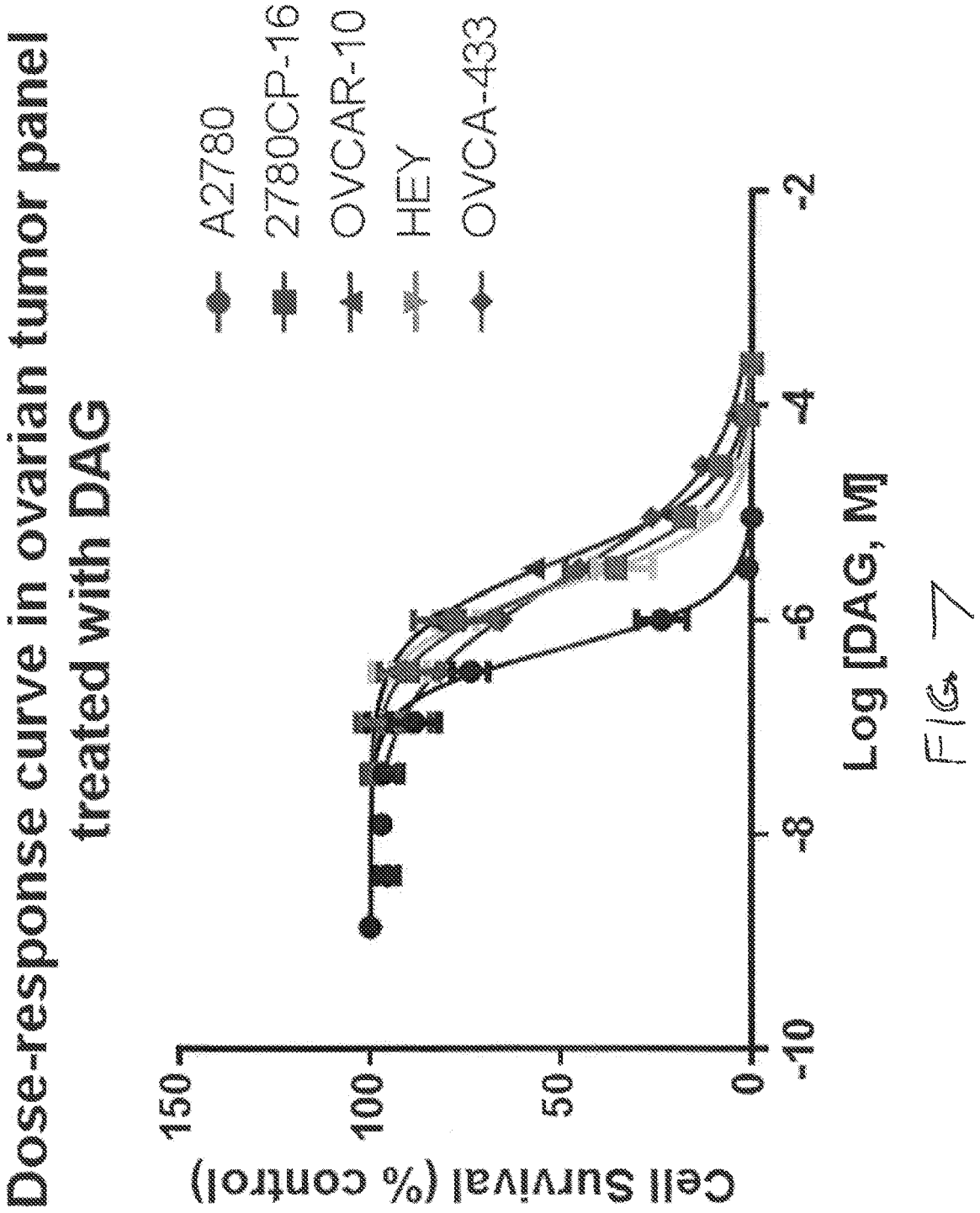

Dose-response curve in ovarian tumor panel
treated with DAG
A2780
2780CP-16
OVCAR-10
HEY
OVCA-433
Cell Survival (% control)
150
100
50
0
-10
-8
-6
-4
-2
Log [DAG, M]

FIG 7

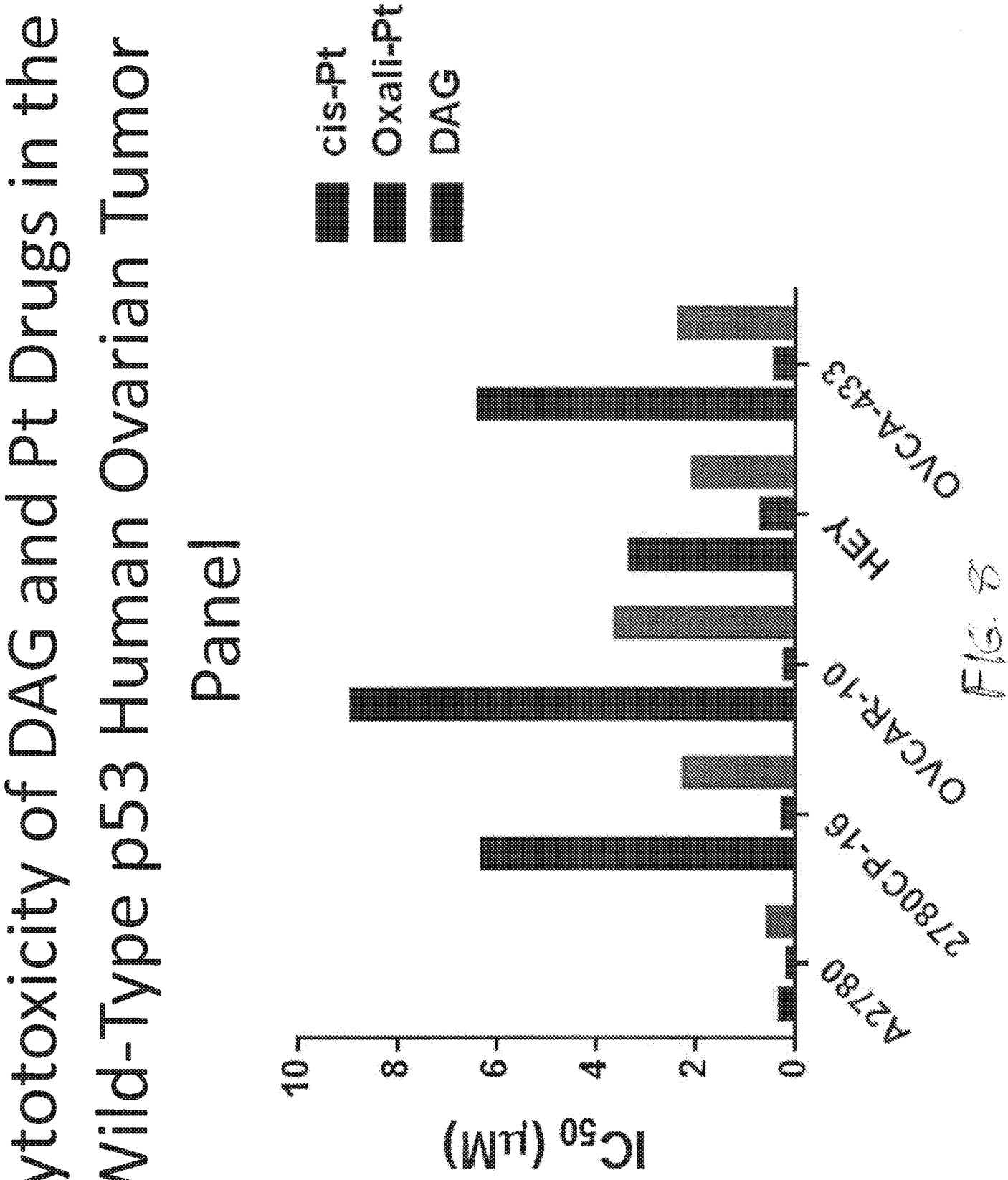

Cytotoxicity of DAG and Pt Drugs in the Wild-Type p53 Human Ovarian Tumor Panel
cis-Pt
Oxali-Pt
DAG
IC50 (μM)
0
2
4
6
8
10
A2780
2780CP-16
OVCAR-10
HEY
OVCA-433

Fig. 8

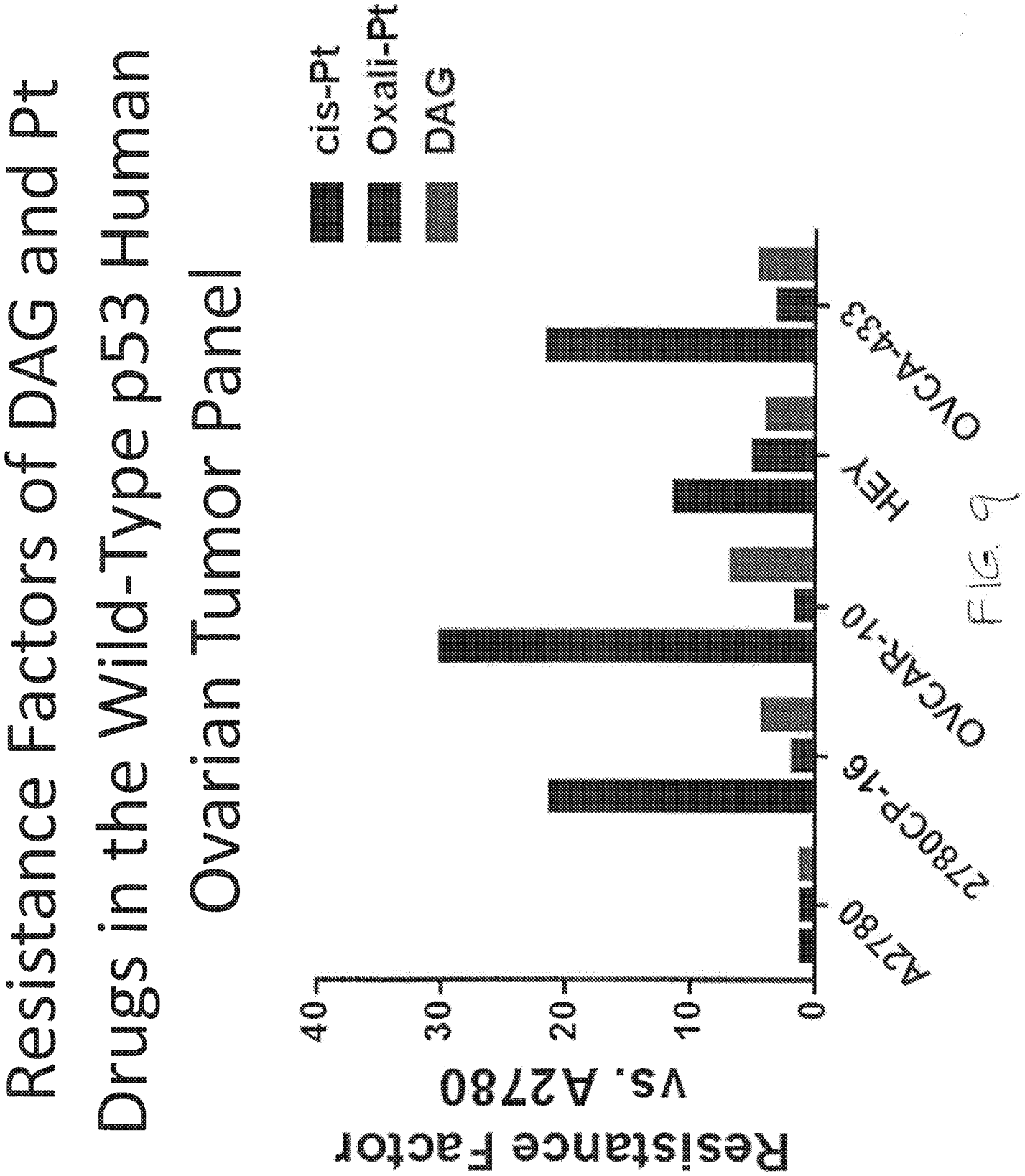

Resistance Factors of DAG and Pt Drugs in the Wild-Type p53 Human Ovarian Tumor Panel
cis-Pt
Oxali-Pt
DAG
Resistance Factor vs. A2780
40
30
20
10
0
A2780
2780CP-16
OVCAR-10
HEY
OVCA-433

FIG. 7

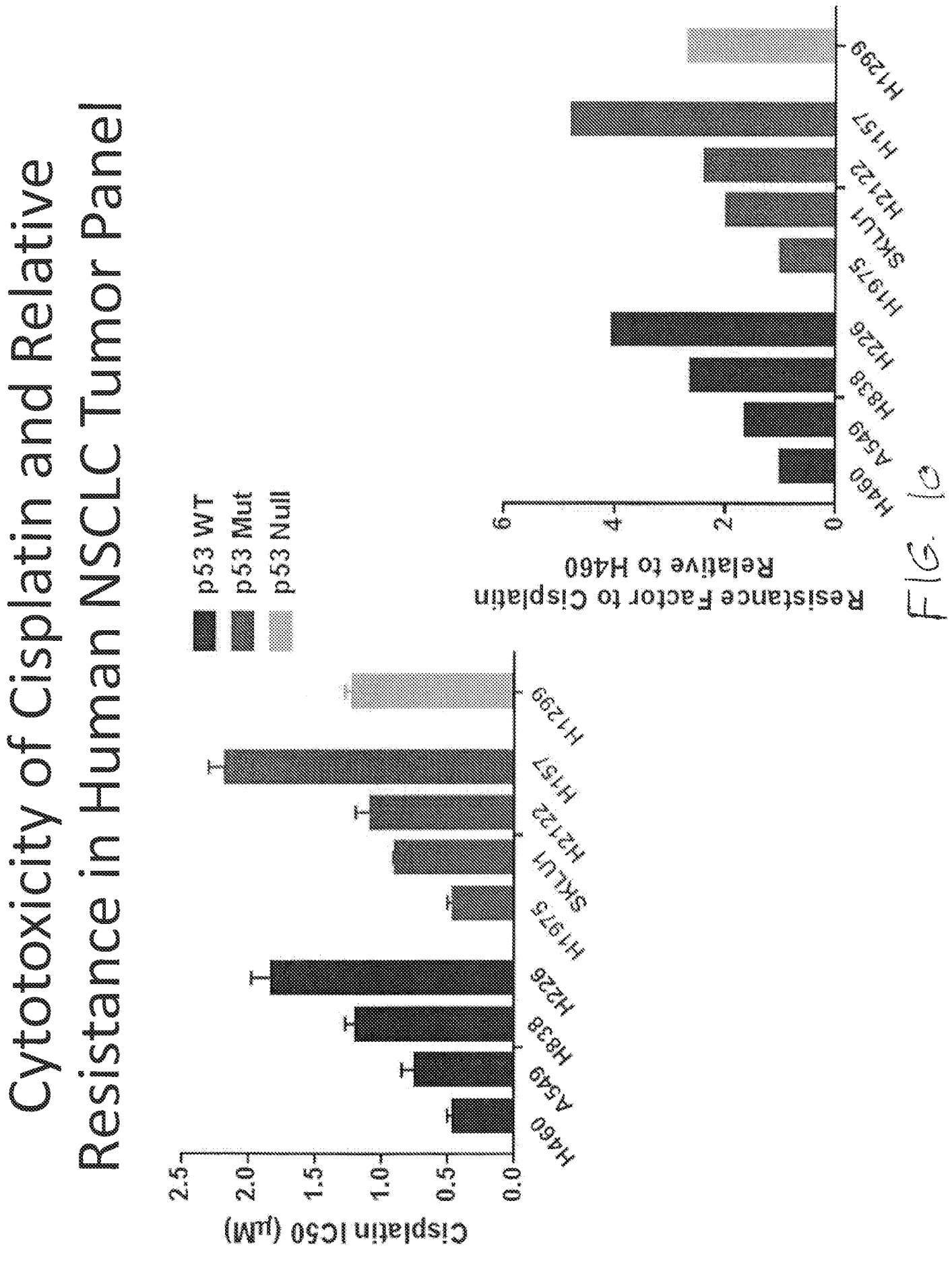
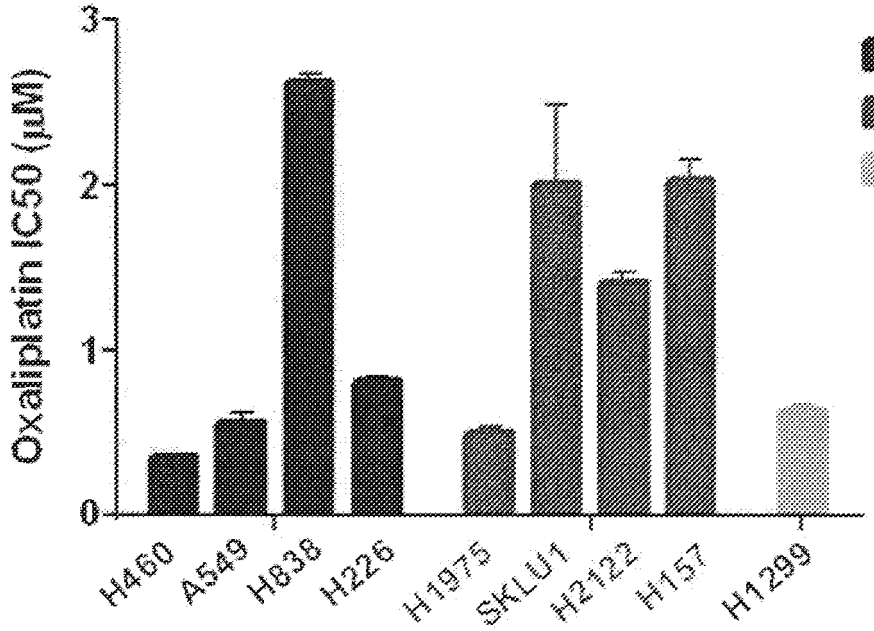

Cytotoxicity of Cisplatin and Relative Resistance in Human NSCLC Tumor Panel
p53 WT
p53 Mut
p53 Null
Cisplatin IC50 (μM)
0.0
0.5
1.0
1.5
2.0
2.5
H460
A549
H838
H226
H1975
SKLU1
H2122
H157
H1299
Resistance Factor to Cisplatin Relative to H460
0
2
4
6
H460
A549
H838
H226
H1975
SKLU1
H2122
H157
H1299

FIG. 1C

Cytotoxicity of Oxaliplatin and Relative Resistance in Human NSCLC Tumor Panel



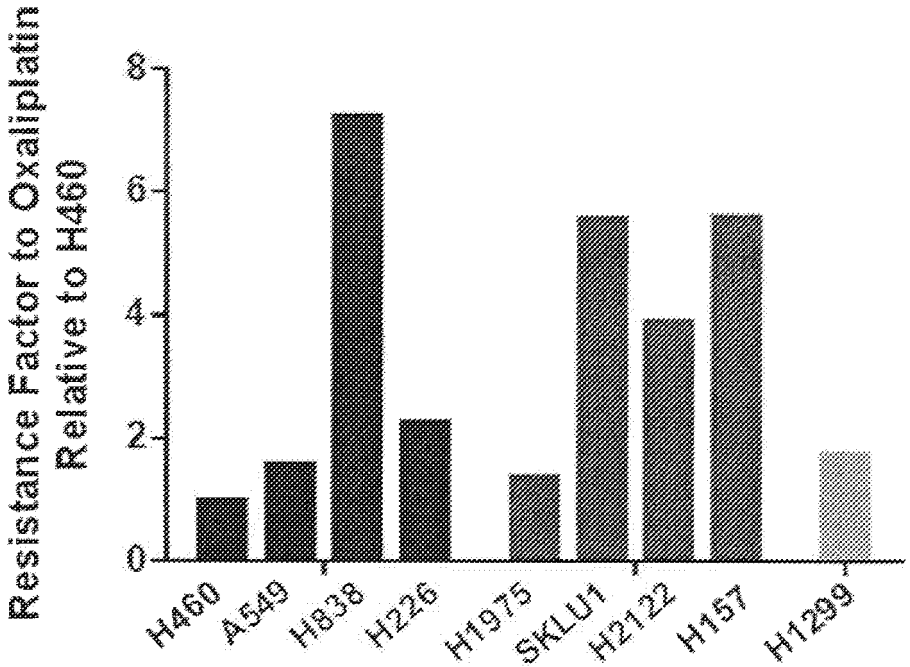


FIG. 11

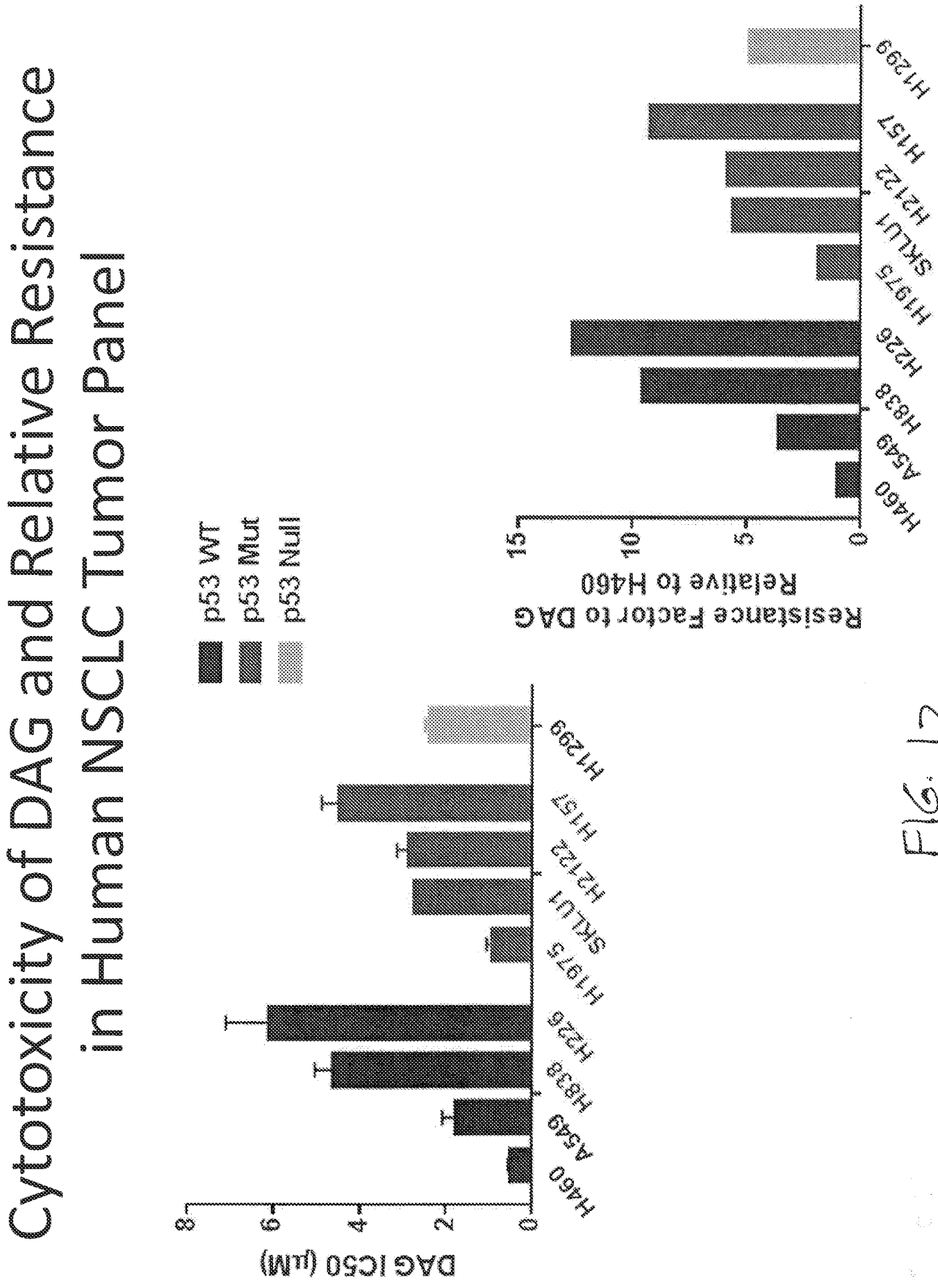

Cytotoxicity of DAG and Relative Resistance
in Human NSCLC Tumor Panel
p53 WT
p53 Mut
p53 Null
DAG IC50 (μM)
0
2
4
6
8
H460
A549
H838
H226
H1975
SKLU1
H2122
H157
H1299
Resistance Factor to DAG
Relative to H460
0
5
10
15
H460
A549
H838
H226
H1975
SKLU1
H2122
H157
H1299

Fig. 12

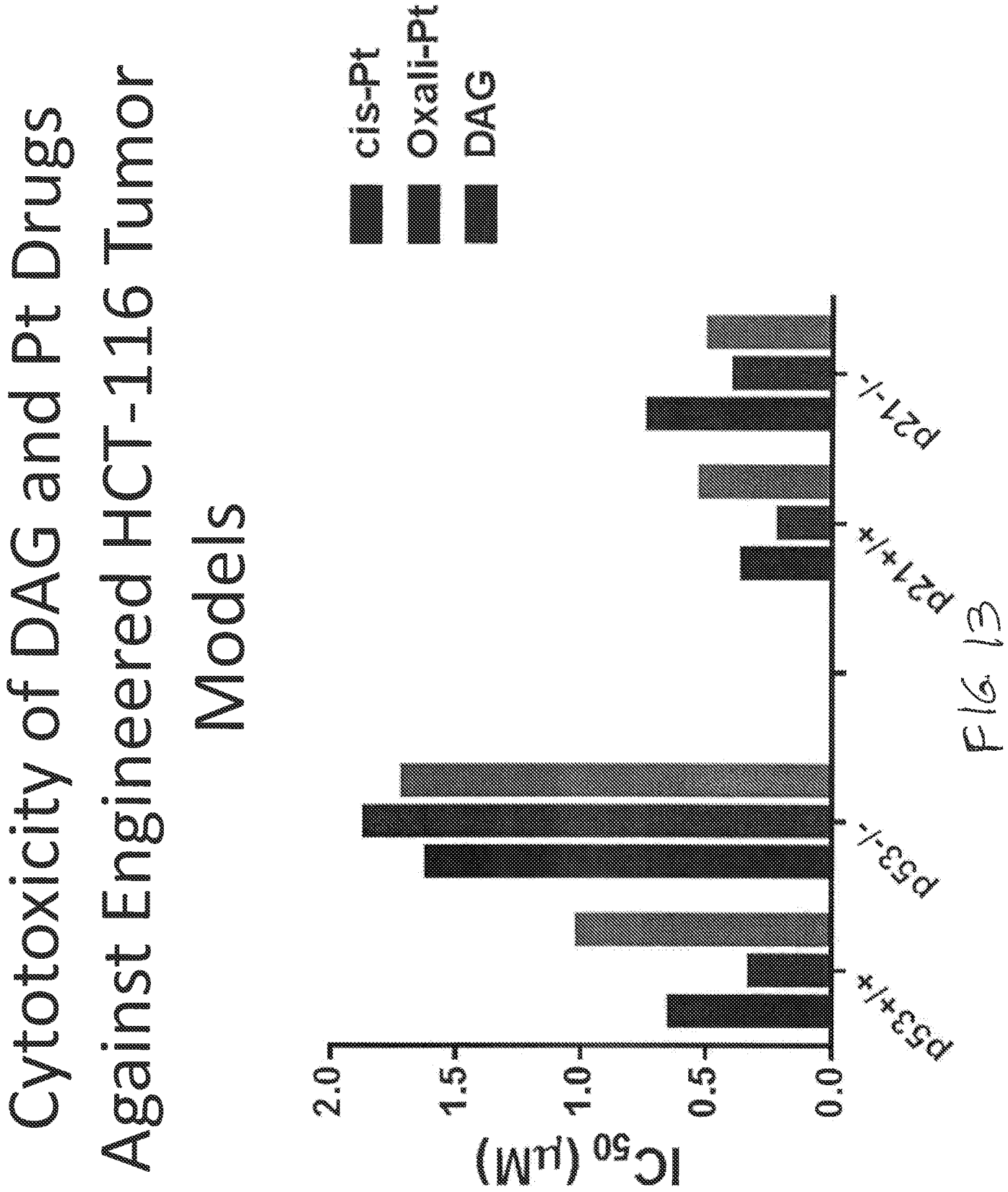

Cytotoxicity of DAG and Pt Drugs
Against Engineered HCT-116 Tumor
Models
cis-Pt
Oxali-Pt
DAG
IC50 (μM)
2.0
1.5
1.0
0.5
0.0
p53+/+
p53-/-
p21+/+
p21-/-

Fig 13

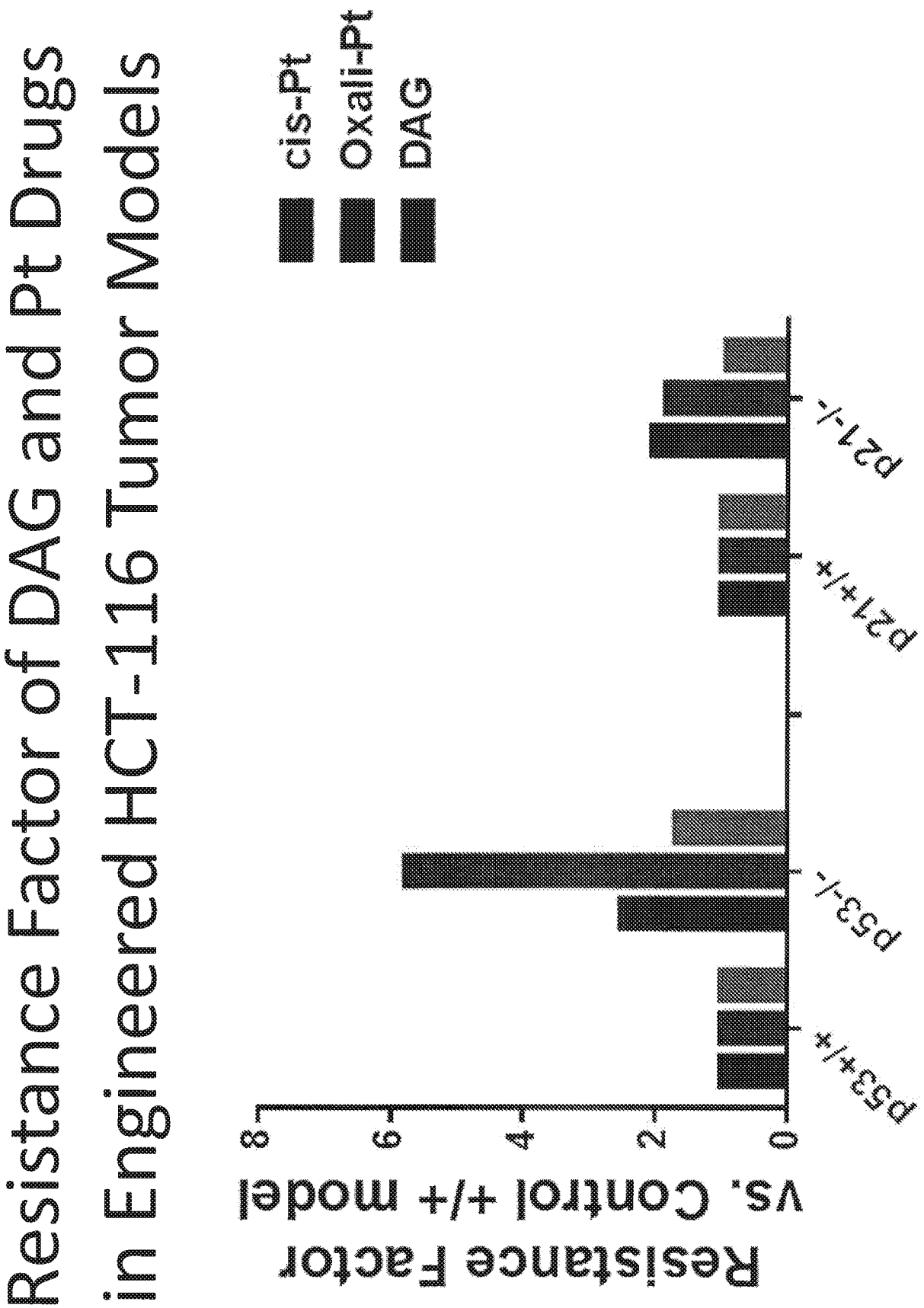
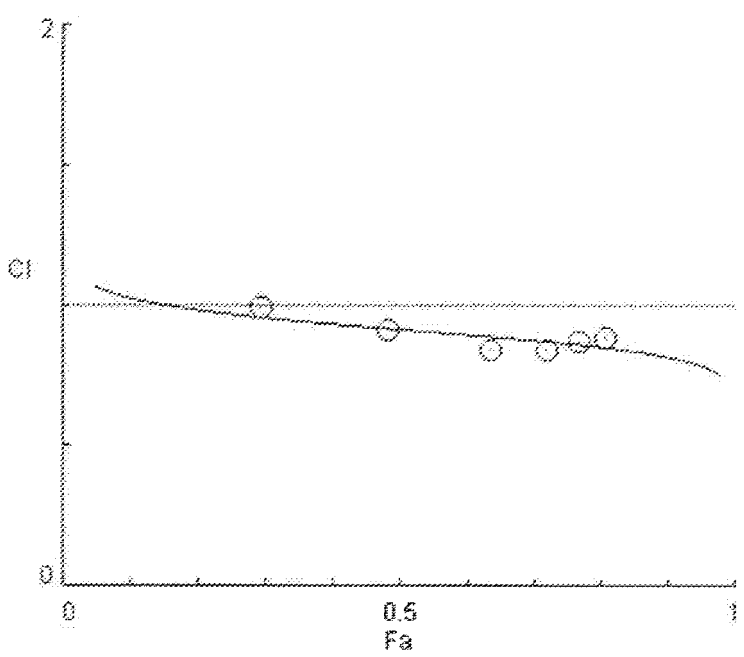

Resistance Factor of DAG and Pt Drugs
in Engineered HCT-116 Tumor Models
cis-Pt
Oxali-Pt
DAG
Resistance Factor
vs. Control +/+ model
0
2
4
6
8
p53+/+
p53-/-
p21+/+
p21-/-

FIG. 14

Combination Index of DAG with Cisplatin or Oxaliplatin in Human A549 NSCLC Model

Combination of CDDP and DAG

Note: Each data point is a mean of 4 independent determinations



CI: DAG + CisPt	
ED50	0.91697
ED75	0.86643
ED90	0.81882
ED95	0.78802

CI: DAG + OxPt	
ED50	1.05625
ED75	0.90984
ED90	0.78388
ED95	0.70840

Combination of Oxaliplatin and DAG

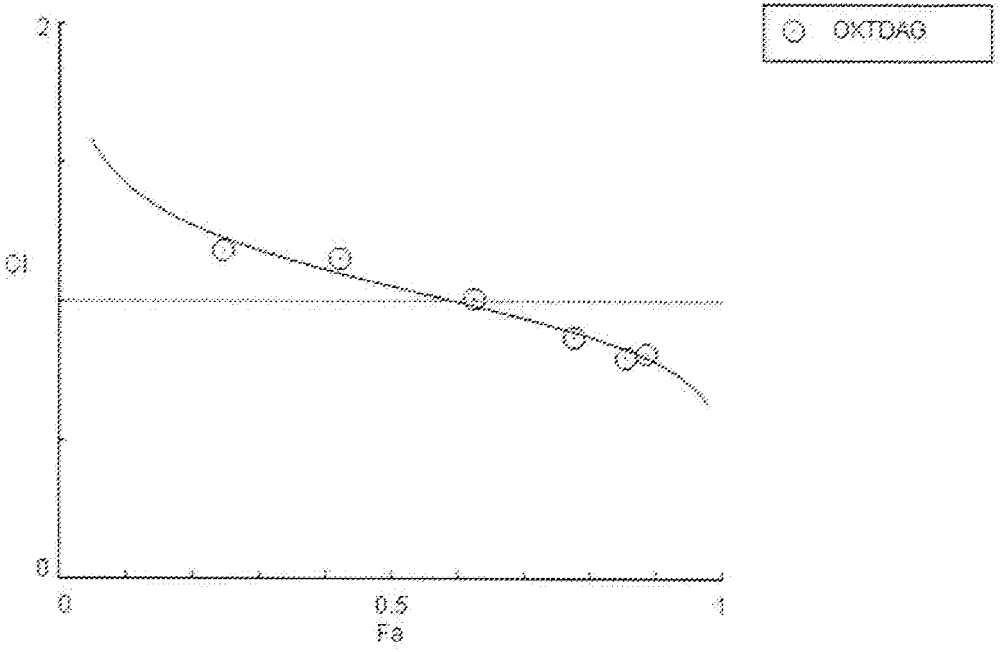


FIG. 15

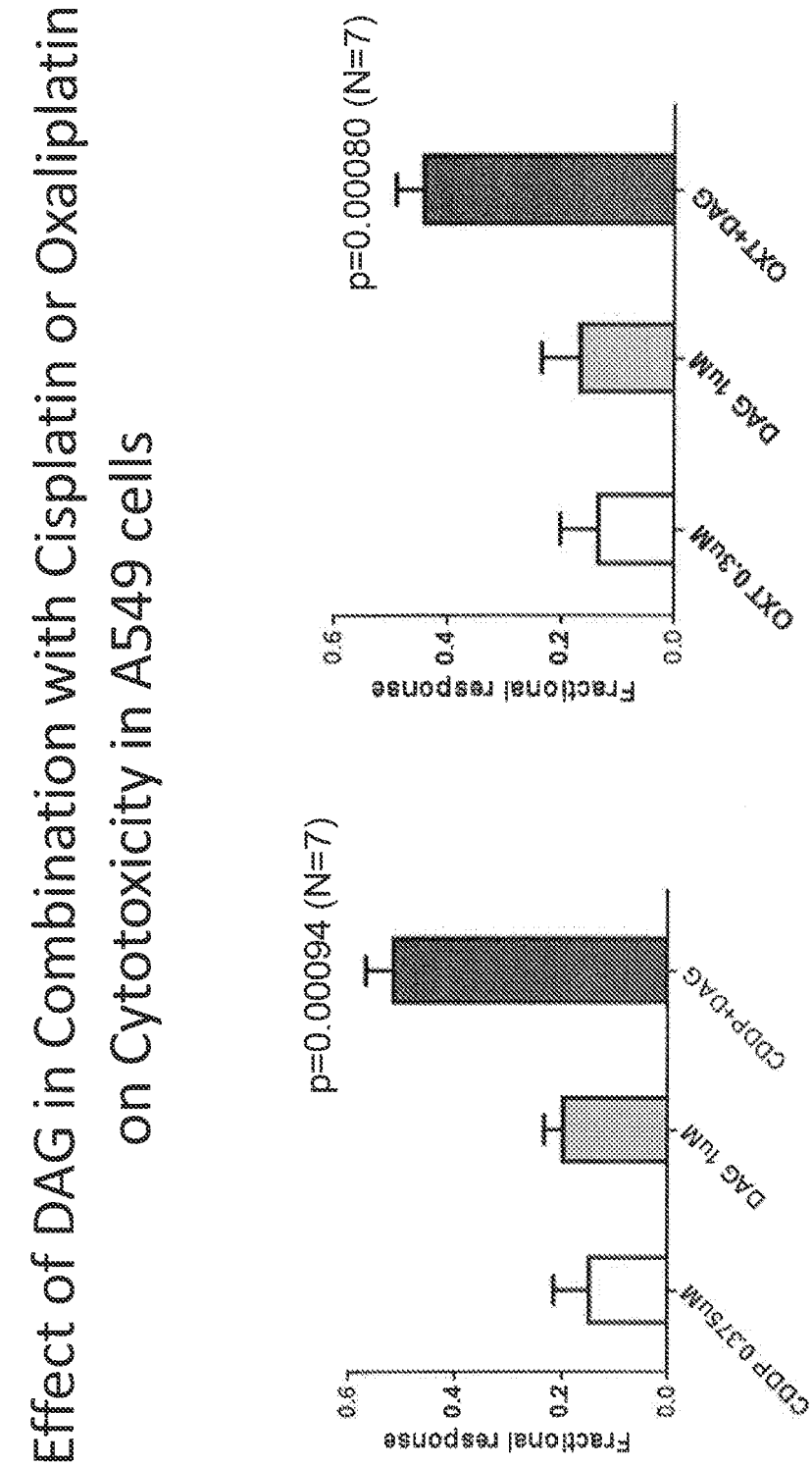

The Effect of DAG in Combination with Cisplatin or Oxaliplatin on Cytotoxicity in A549 cells
p=0.00094 (N=7)
Fractional response
0.0
0.2
0.4
0.6
CDDP 0.375uM
DAG 1uM
CDDP+DAG
p=0.00080 (N=7)
Fractional response
0.0
0.2
0.4
0.6
OXT 0.3uM
DAG 1uM
OXT+DAG

FIG. 16

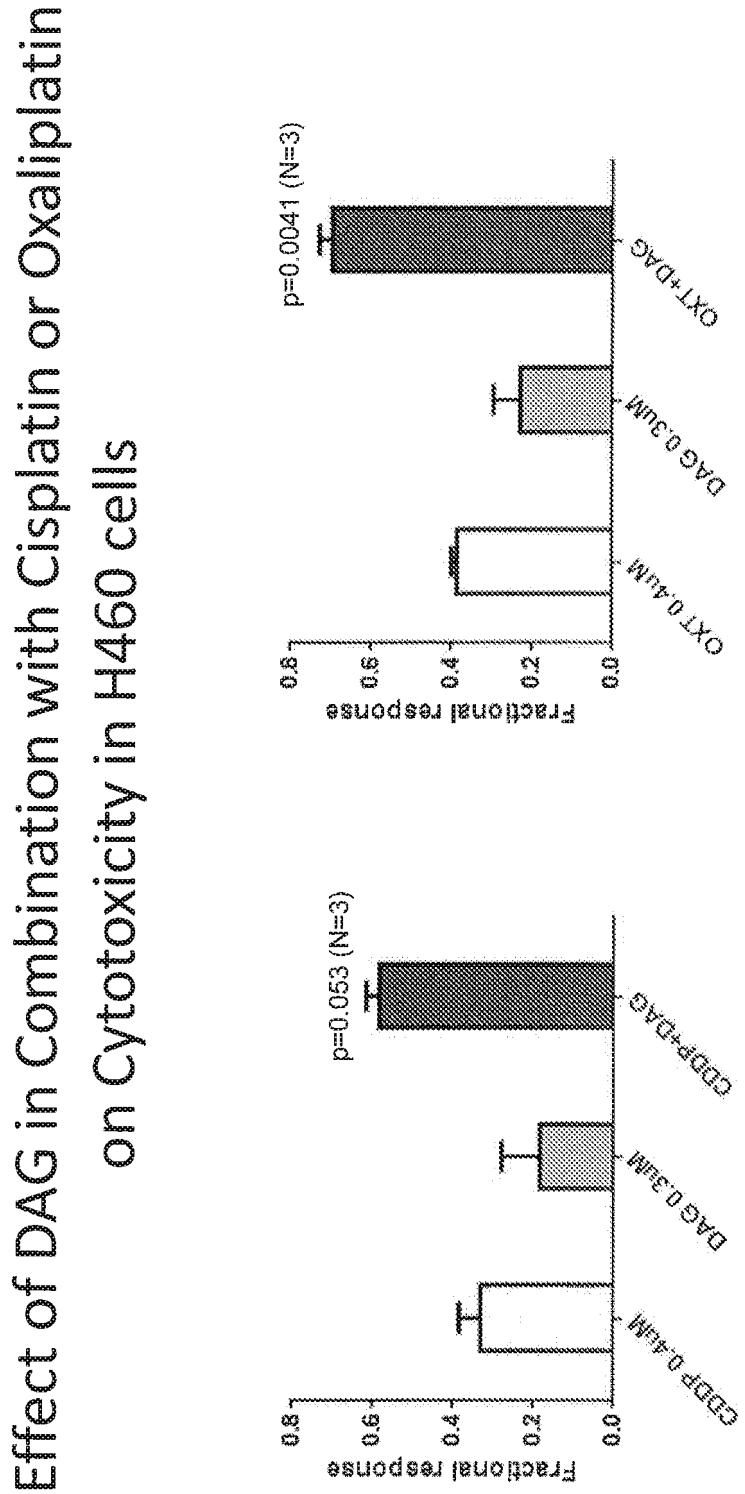

The Effect of DAG in Combination with Cisplatin or Oxaliplatin on Cytotoxicity in H460 cells
p=0.053 (N=3)
Fractional response
0.0
0.2
0.4
0.6
0.8
CDDP 0.4uM
DAG 0.3uM
CDDP+DAG
p=0.0041 (N=3)
Fractional response
0.0
0.2
0.4
0.6
0.8
OXT 0.4uM
DAG 0.3uM
OXT+DAG

FIG. 17

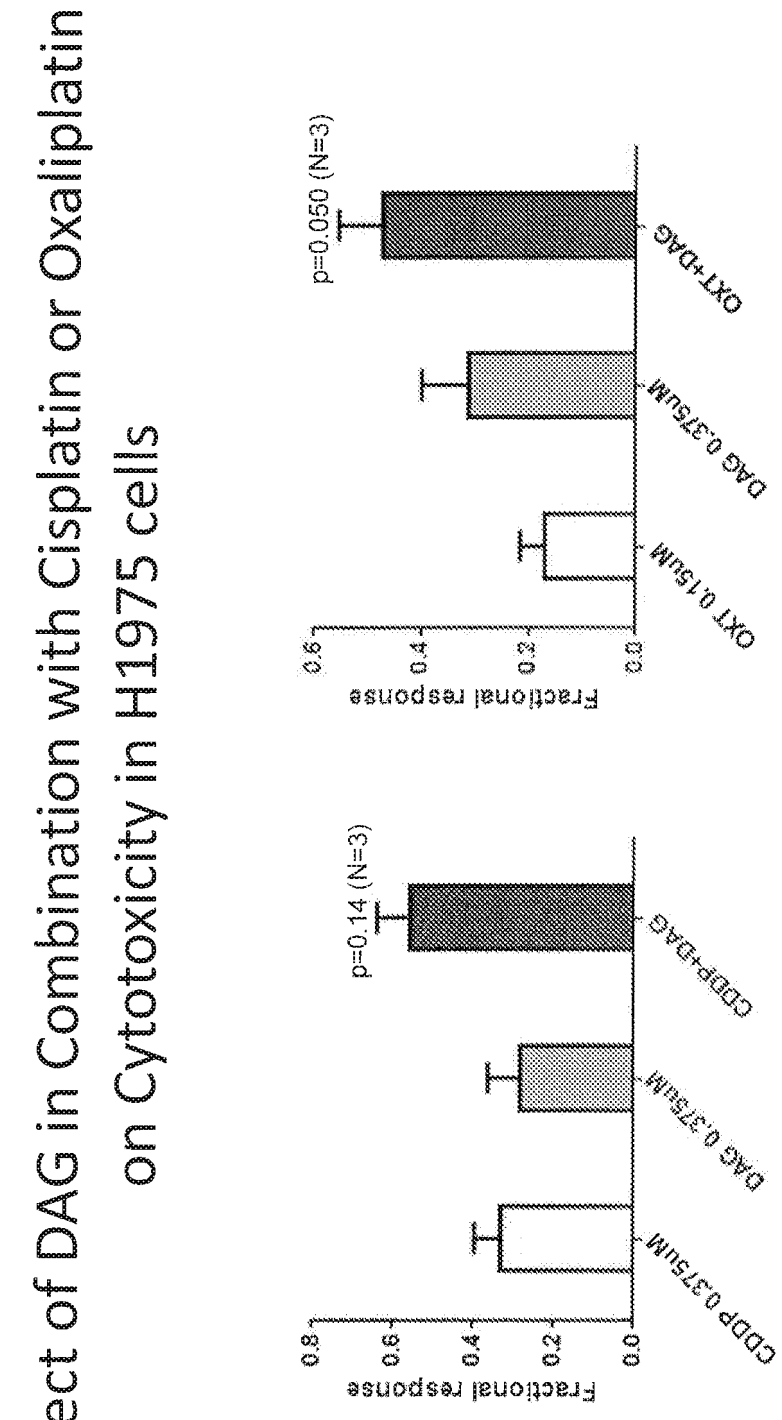

The Effect of DAG in Combination with Cisplatin or Oxaliplatin on Cytotoxicity in H1975 cells
Fractional response
0.0
0.2
0.4
0.6
0.8
p=0.14 (N=3)
CDDP 0.375uM
DAG 0.375uM
CDDP+DAG
Fractional response
0.0
0.2
0.4
0.6
p=0.050 (N=3)
OXT 0.15uM
DAG 0.375uM
OXT+DAG

FIG. 18