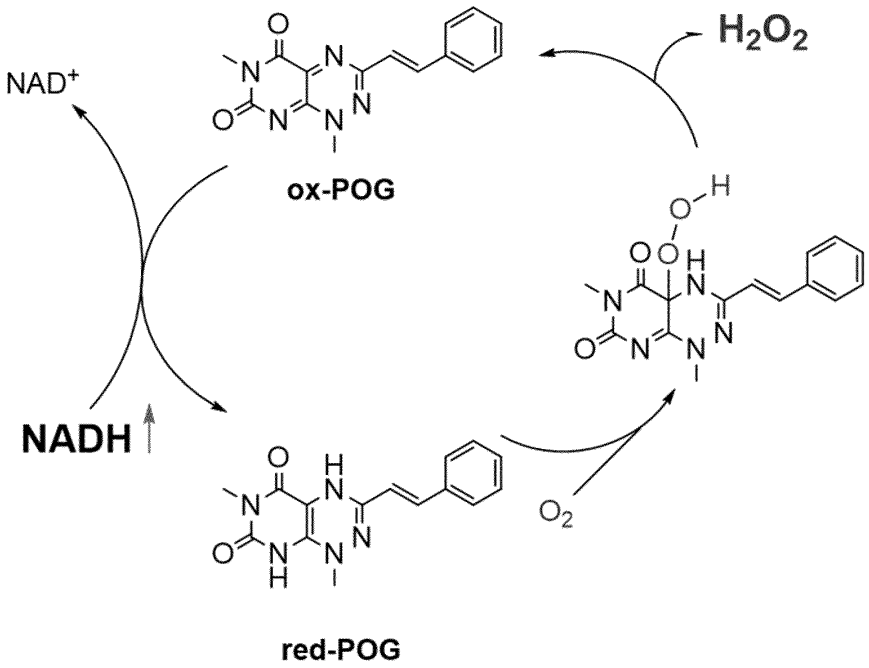

NAD+
ox-POG
H2O2
NADH
O2
red-POG

FIG 1A

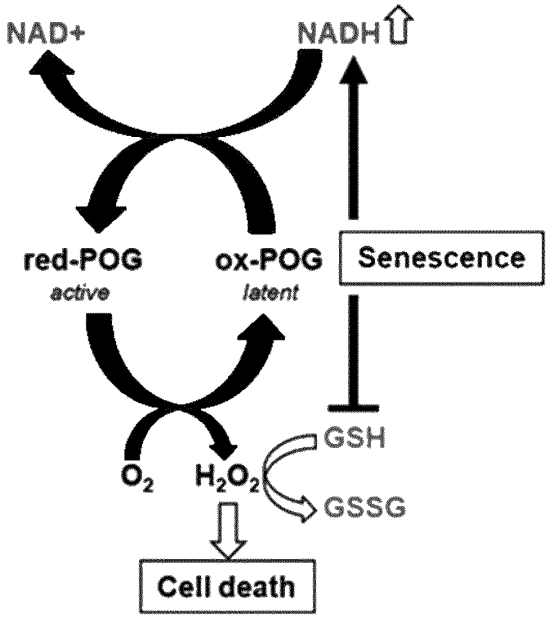

NAD+
NADH
red-POG
active
ox-POG
latent
Senescence
GSH
O2
H2O2
GSSG
Cell death

FIG 1C

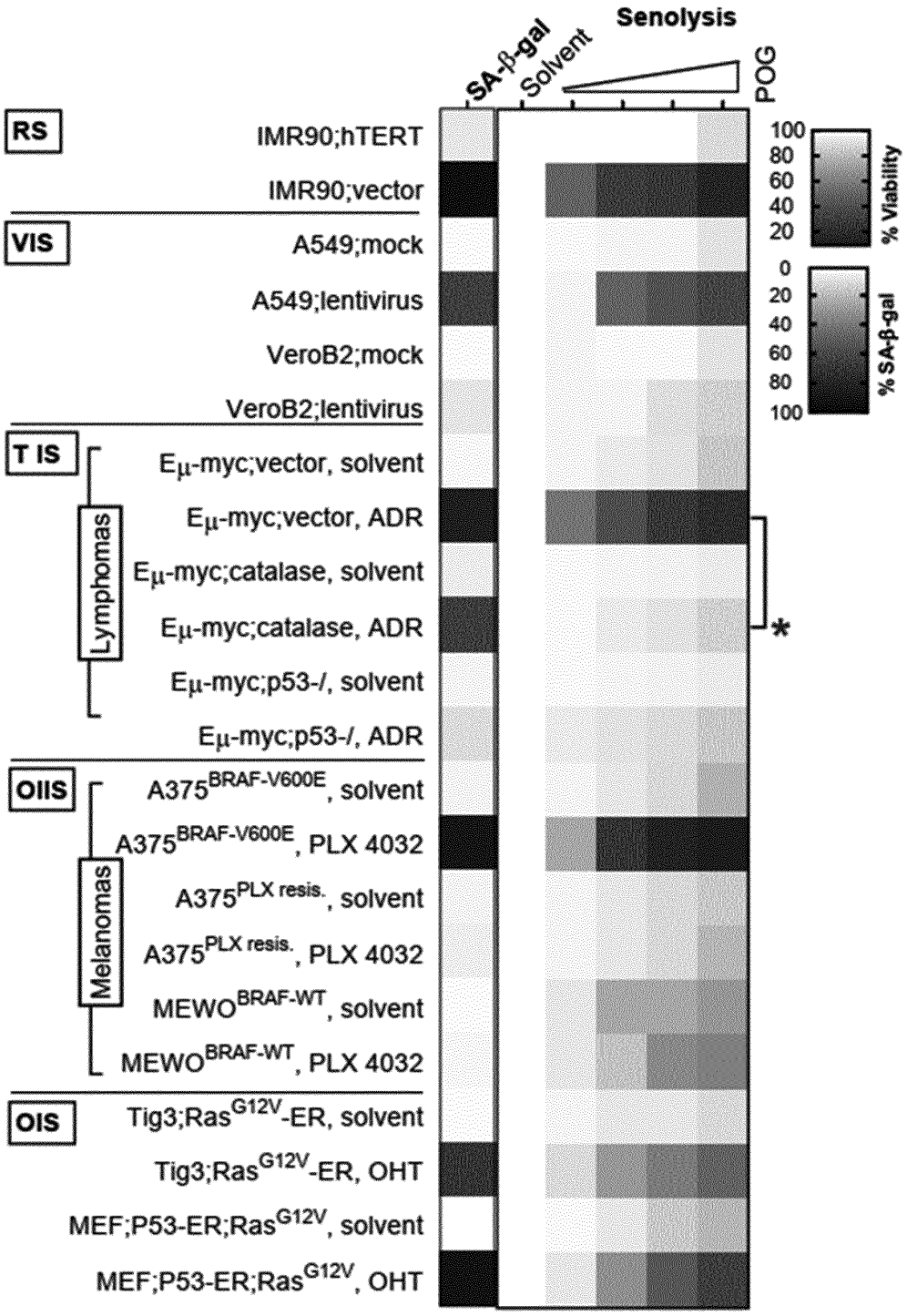

Senolysis
SA-β-gal
Solvent
POG
RS
IMR90;hTERT
IMR90;vector
VIS
A549;mock
A549;lentivirus
VeroB2;mock
VeroB2;lentivirus
T IS
Lymphomas
Eμ-myc;vector, solvent
Eμ-myc;vector, ADR
Eμ-myc;catalase, solvent
Eμ-myc;catalase, ADR
Eμ-myc;p53-/, solvent
Eμ-myc;p53-/, ADR
OIIS
Melanomas
A375BRAF-V600E, solvent
A375BRAF-V600E, PLX 4032
A375PLX resis., solvent
A375PLX resis., PLX 4032
MEWOBRAF-WT, solvent
MEWOBRAF-WT, PLX 4032
OIS
Tig3;RasG12V-ER, solvent
Tig3;RasG12V-ER, OHT
MEF;P53-ER;RasG12V, solvent
MEF;P53-ER;RasG12V, OHT
*
100
80
60
40
20
% Viability
0
20
40
60
80
100
% SA-β-gal

FIG 1B

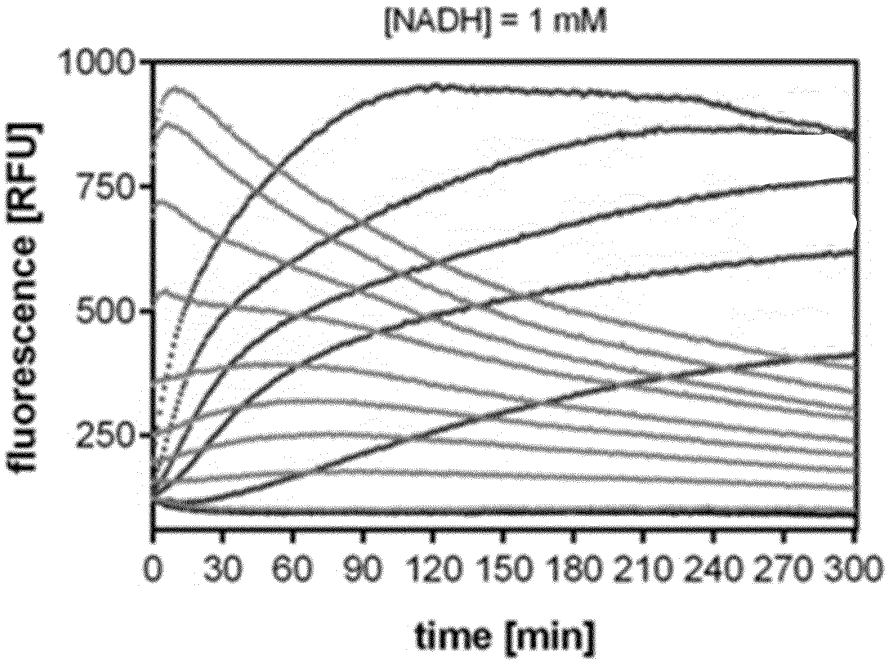

[NADH] = 1 mM
fluorescence [RFU]
1000
750
500
250
0 30 60 90 120 150 180 210 240 270 300
time [min]

FIG 2A

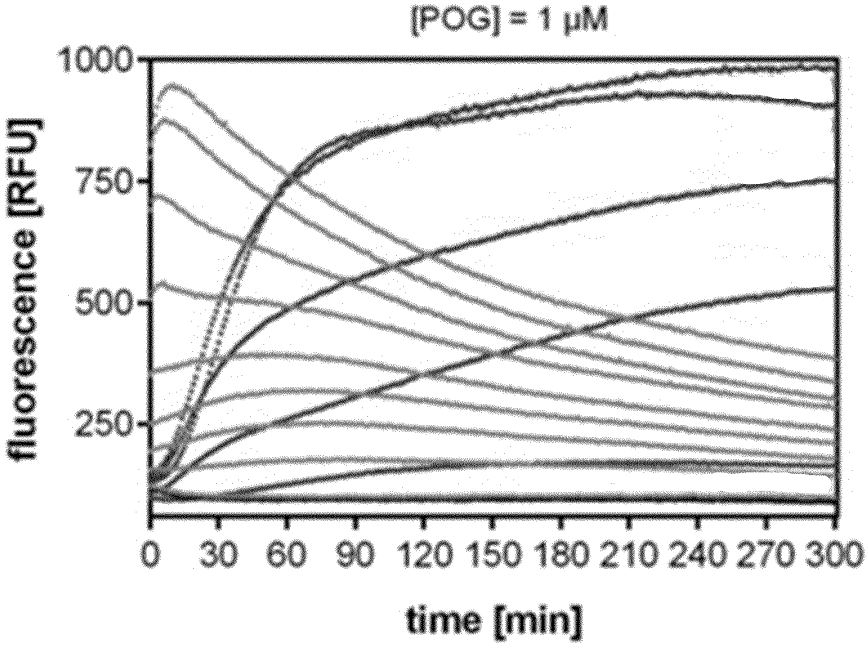

[POG] = 1 µM
fluorescence [RFU]
1000
750
500
250
0 30 60 90 120 150 180 210 240 270 300
time [min]

FIG 2B

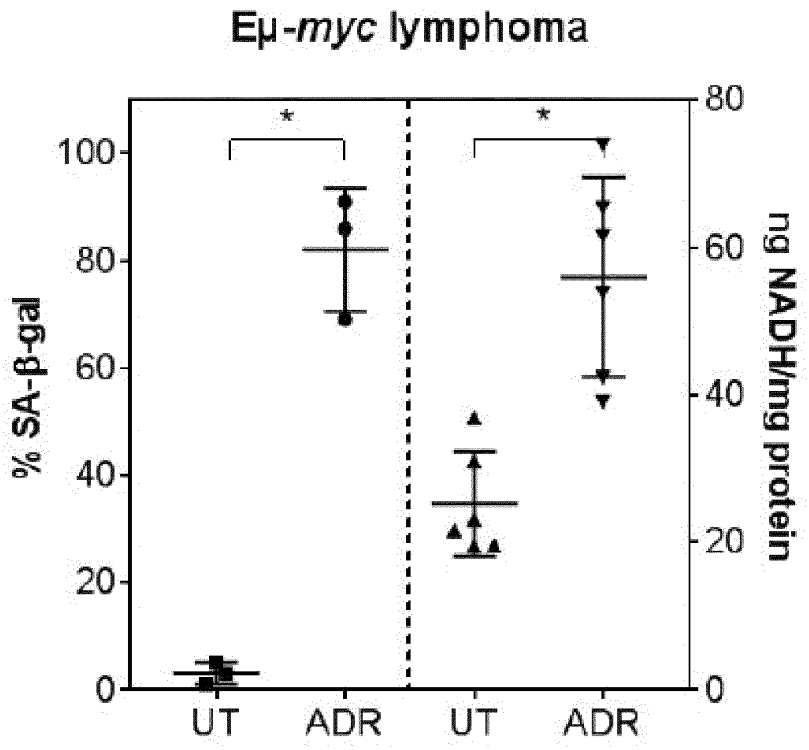

Eμ-myc lymphoma
% SA-β-gal
ng NADH/mg protein
100
80
60
40
20
0
80
60
40
20
0
*
*
UT
ADR
UT
ADR

FIG 3

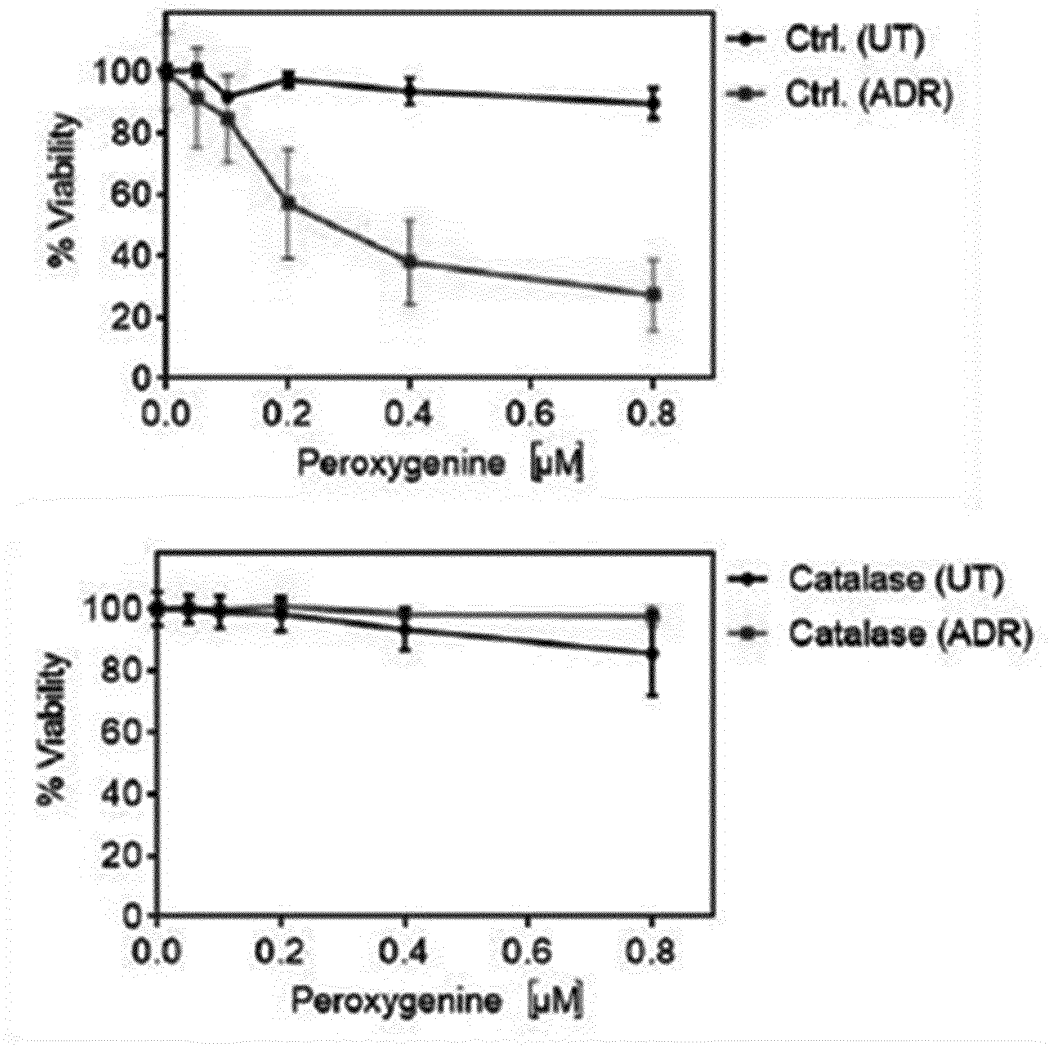

Ctrl. (UT)
Ctrl. (ADR)
% Viability
100
80
60
40
20
0
0.0
0.2
0.4
0.6
0.8
Peroxygenine [µM]
Catalase (UT)
Catalase (ADR)
% Viability
100
80
60
40
20
0
0.0
0.2
0.4
0.6
0.8
Peroxygenine [µM]

FIG 4

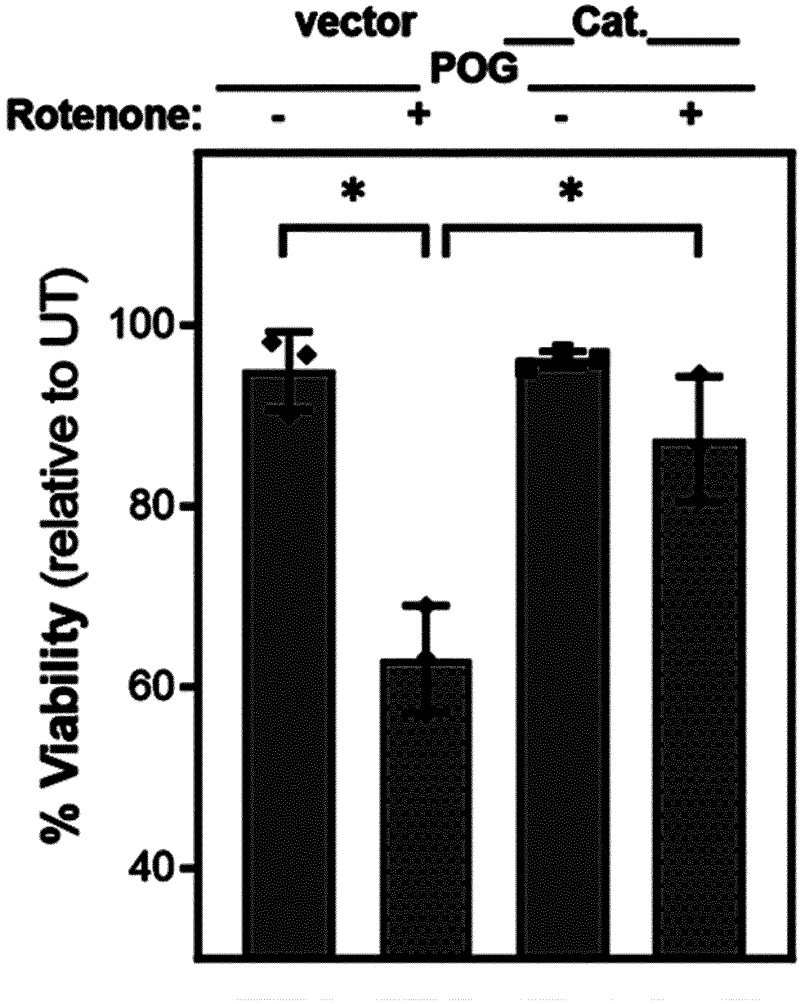

vector
Cat.
POG
Rotenone:
-
+
-
+
*
*
% Viability (relative to UT)
100
80
60
40

FIG 5

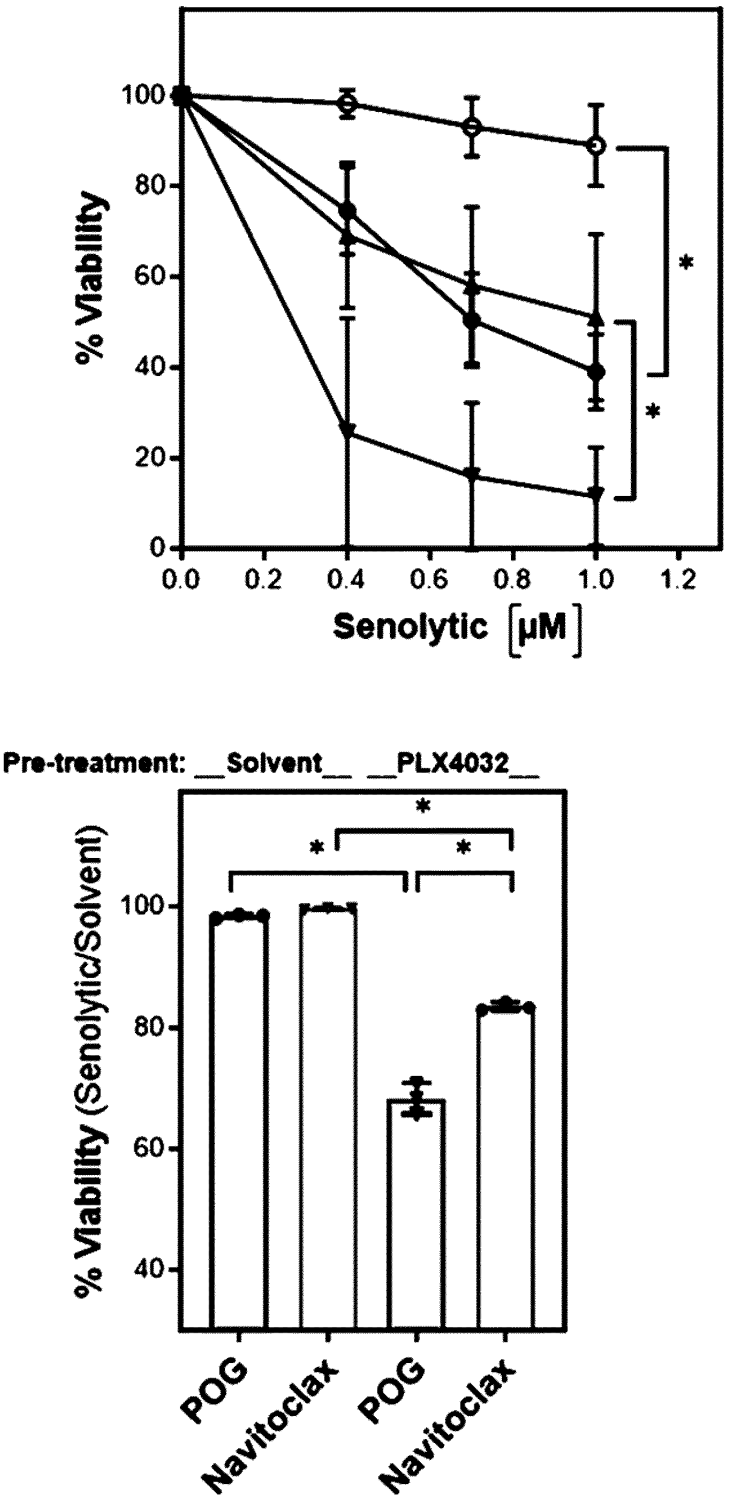

% Viability
100
80
60
40
20
0
0.0
0.2
0.4
0.6
0.8
1.0
1.2
Senolytic [µM]
*
*
Pre-treatment: __Solvent__ __PLX4032__
% Viability (Senolytic/Solvent)
100
80
60
40
*
*
*
POG
Navitoclax
POG
Navitoclax

FIG 6

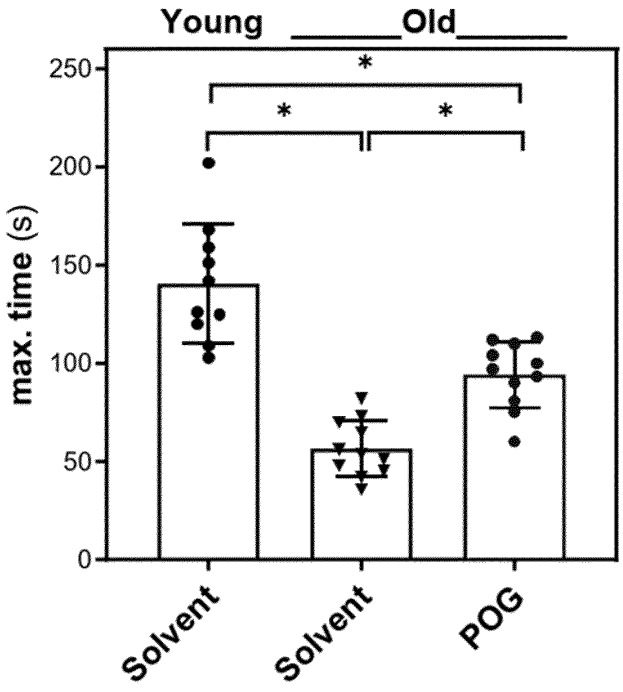

Young
Old
max. time (s)
250
200
150
100
50
0
*
*
*
Solvent
Solvent
POG

FIG 7A

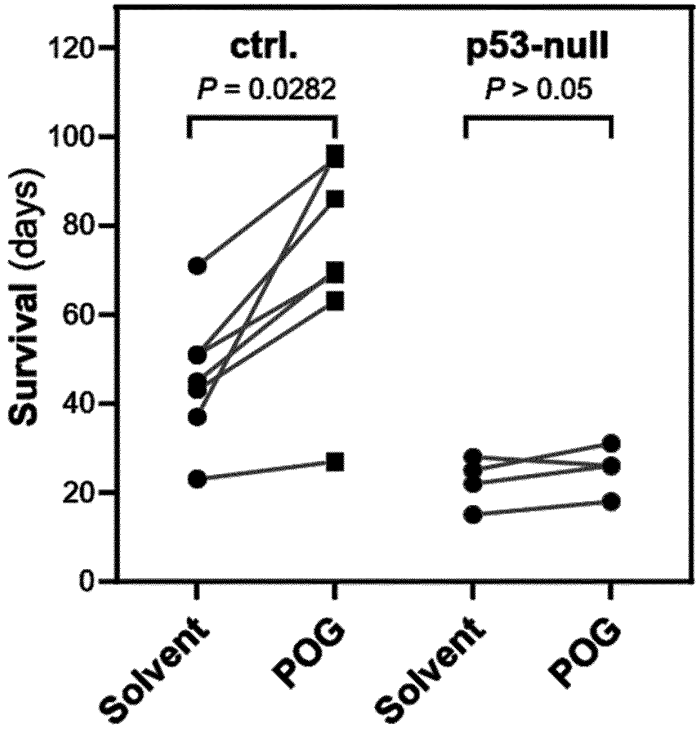

ctrl.
P = 0.0282
p53-null
P > 0.05
Survival (days)
120
100
80
60
40
20
0
Solvent
POG
Solvent
POG

FIG 7B

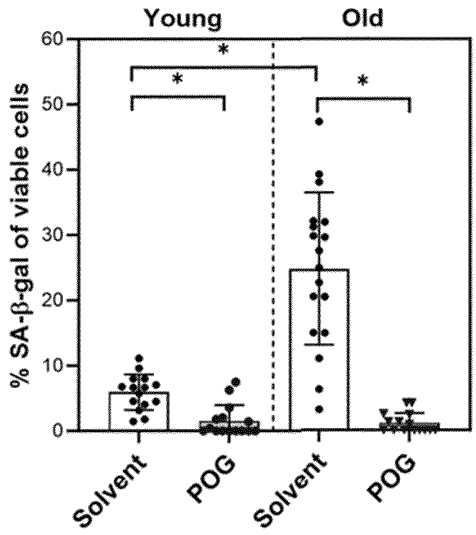


FIG 8A

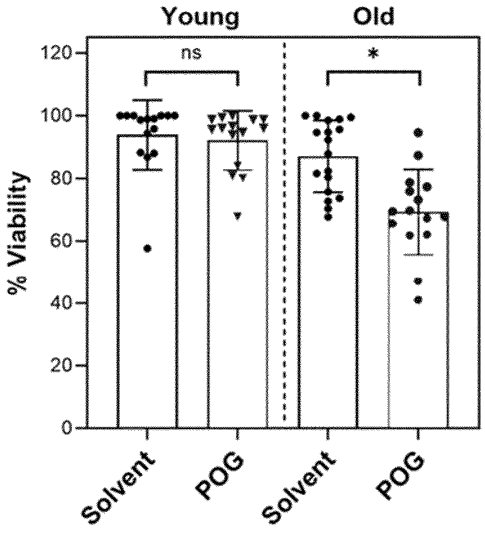


FIG 8B

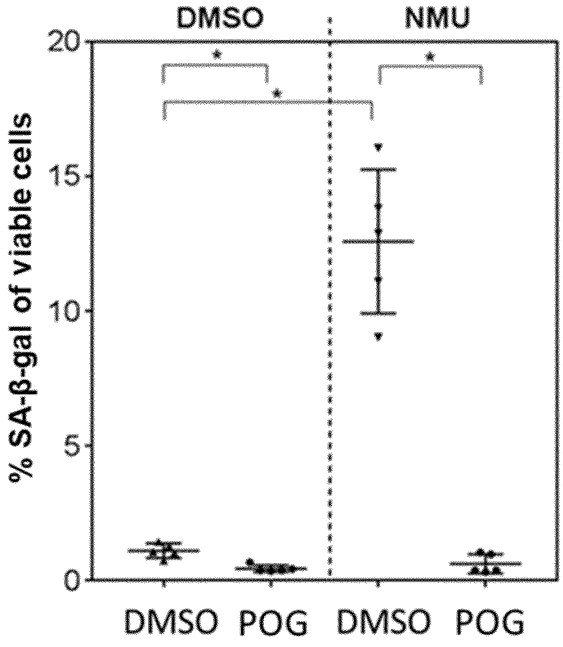


FIG 9A

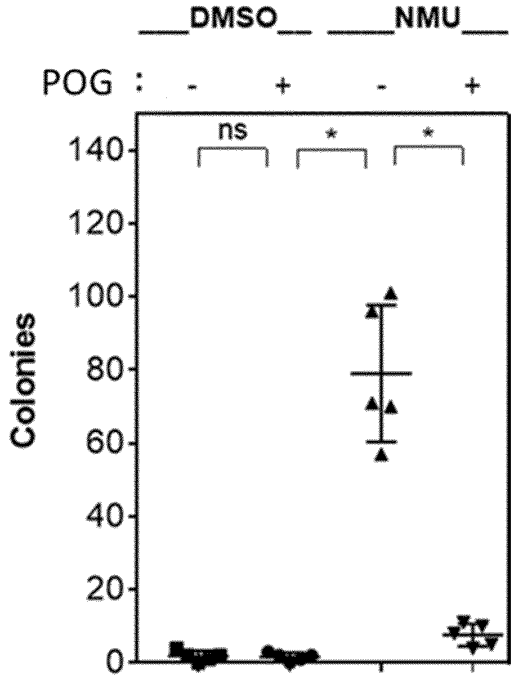

DMSO
NMU
POG : - + - +
ns
*
*
Colonies
140
120
100
80
60
40
20
0

FIG 9B

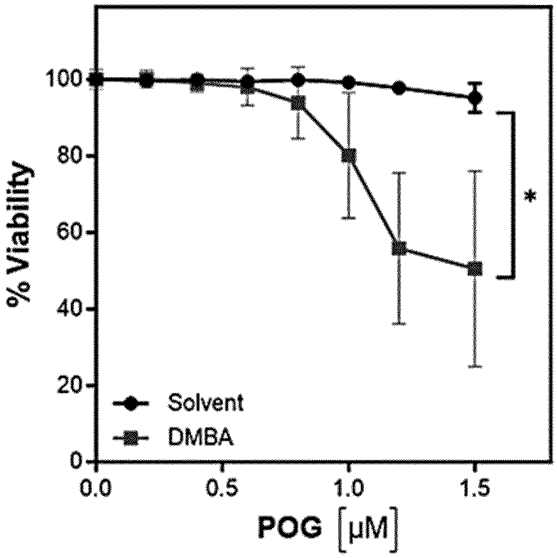

% Viability
100
80
60
40
20
0
0.0
0.5
1.0
1.5
POG [µM]
Solvent
DMBA
*

FIG 10

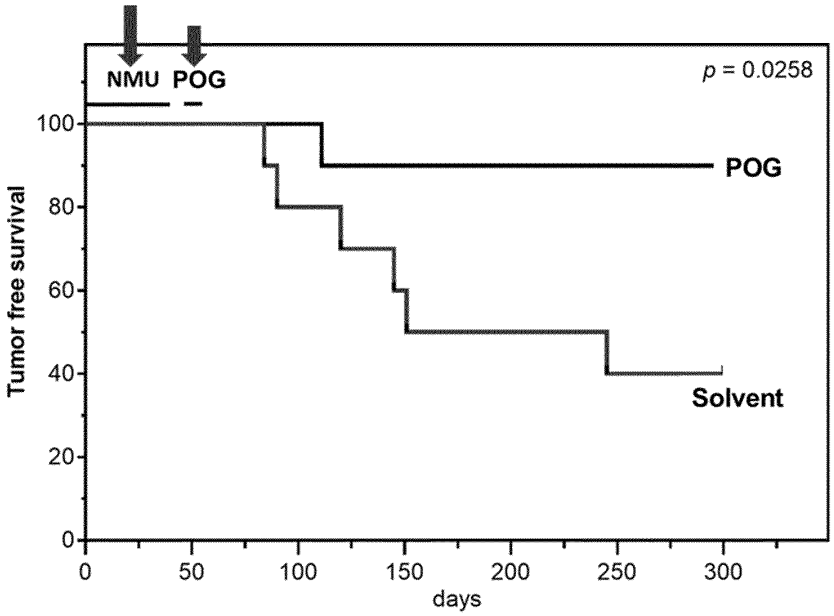

NMU
POG
p = 0.0258
POG
Solvent
Tumor free survival
100
80
60
40
20
0
0
50
100
150
200
250
300
days

FIG 11

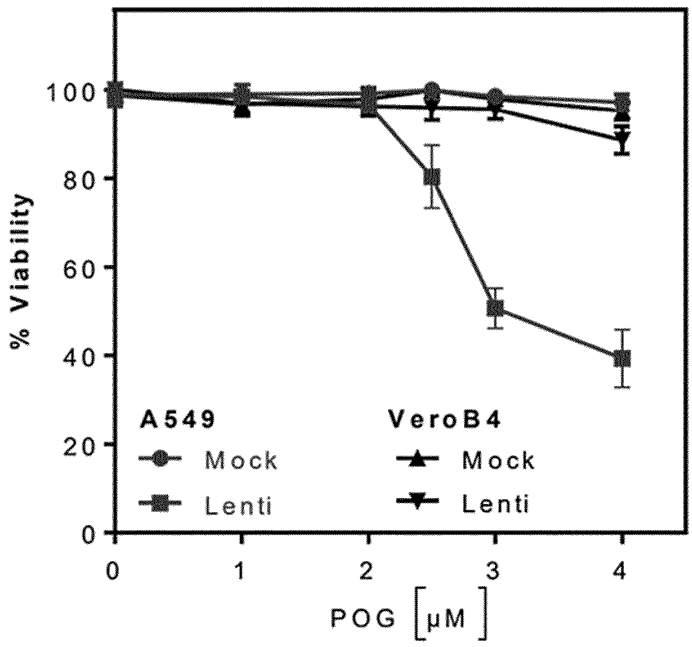

% Viability
100
80
60
40
20
0
A549
Mock
Lenti
VeroB4
Mock
Lenti
0
1
2
3
4
POG [µM]

FIG 12

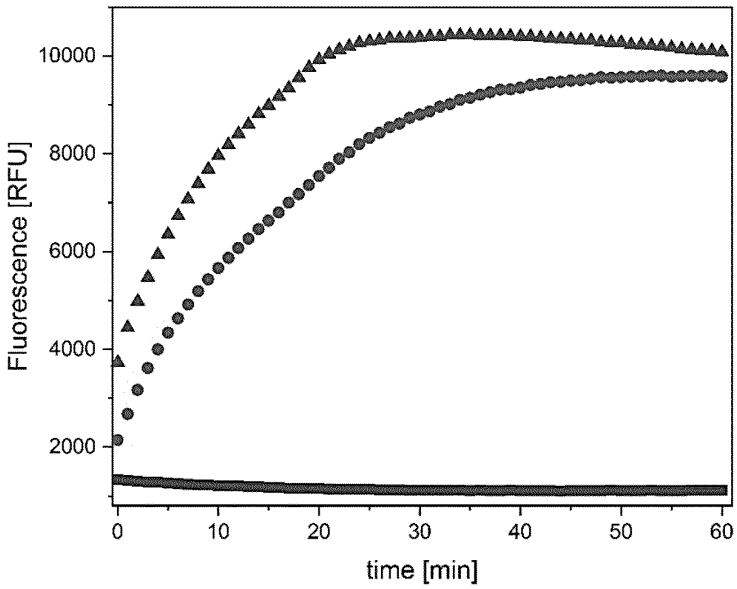

Fluorescence [RFU]
10000
8000
6000
4000
2000
0
10
20
30
40
50
60
time [min]

FIG 13

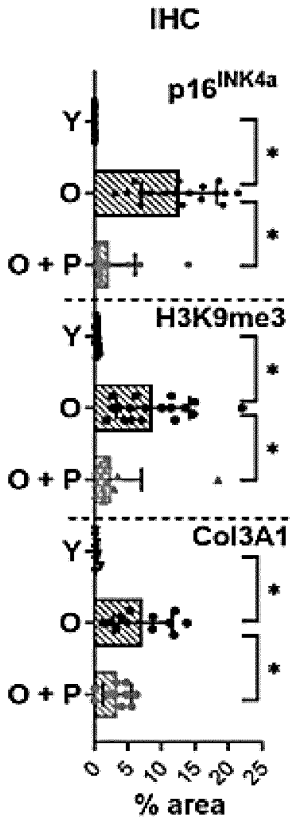

IHC
p16INK4a
Y
O
O + P
H3K9me3
Y
O
O + P
Col3A1
Y
O
O + P
*
*
*
*
*
*
0
5
10
15
20
25
% area

FIG 14

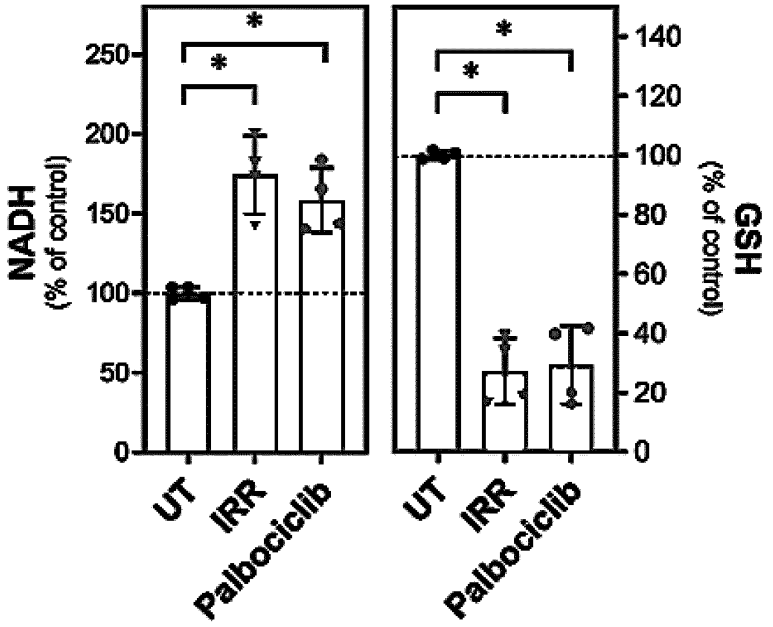


FIG 15A

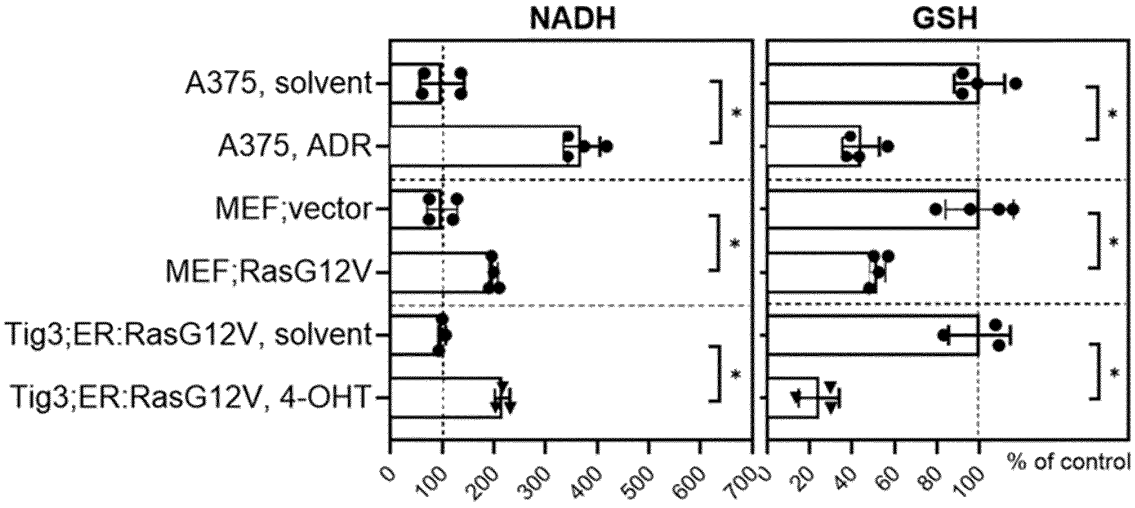


FIG 15B

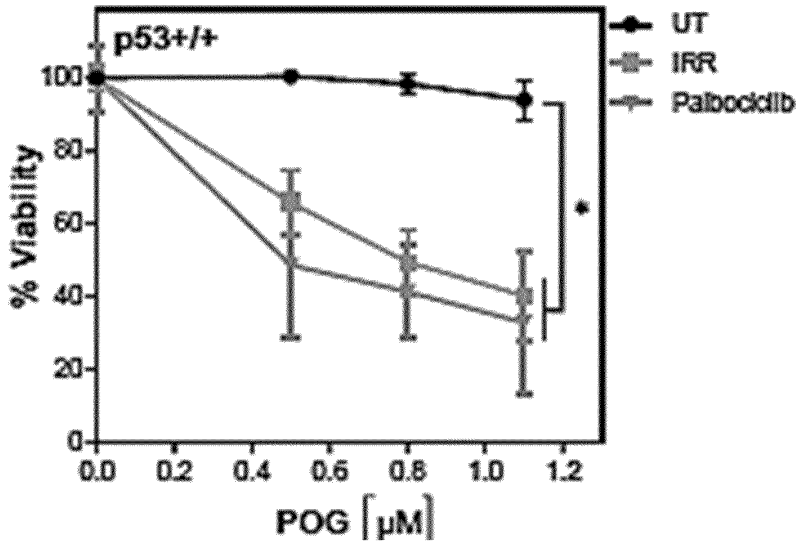


FIG 16

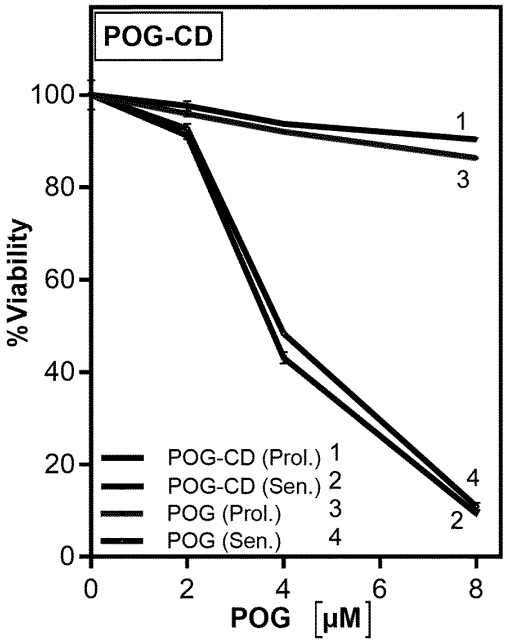


FIG 17A

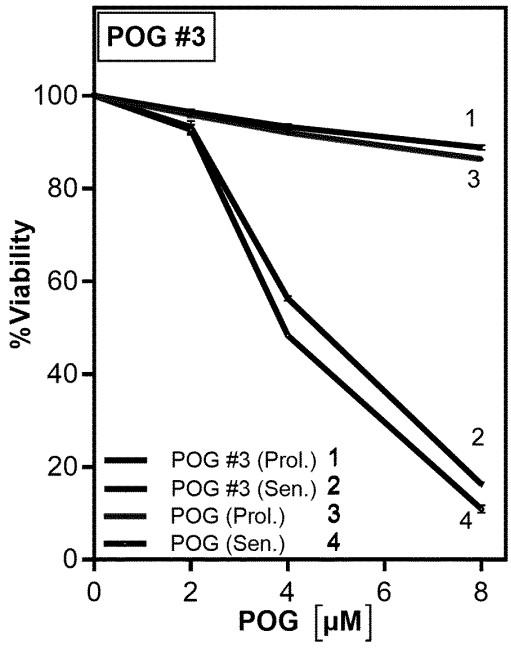


FIG 17B

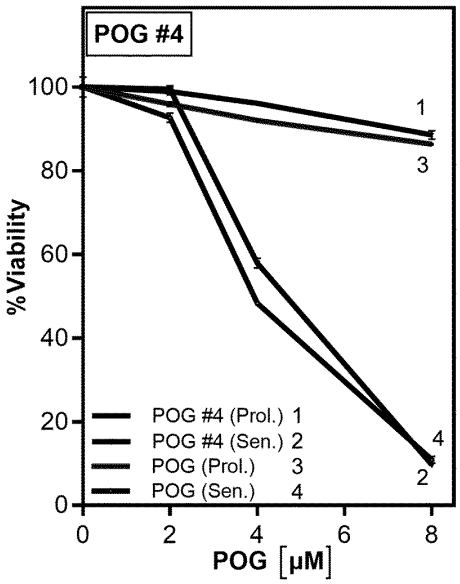


FIG 17C

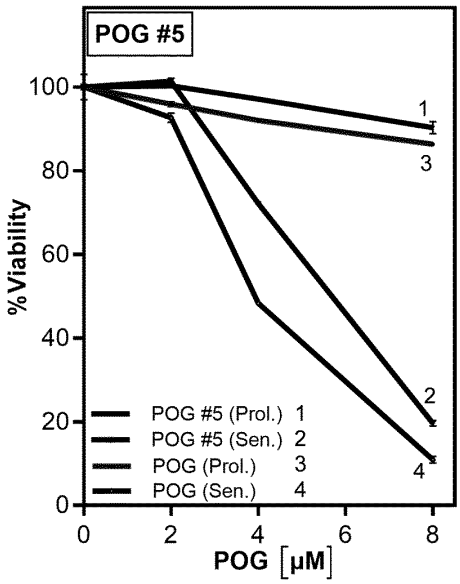


FIG 17D

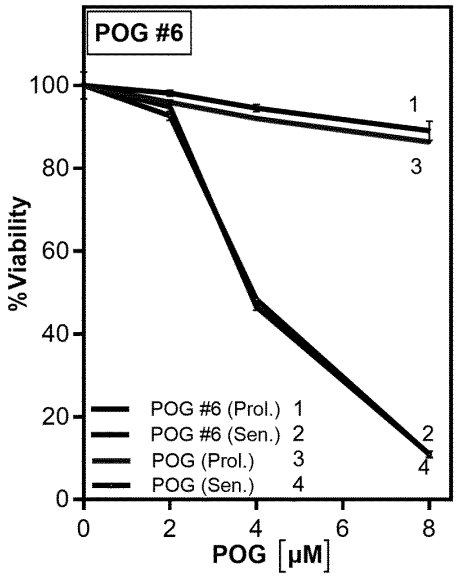


FIG 17E

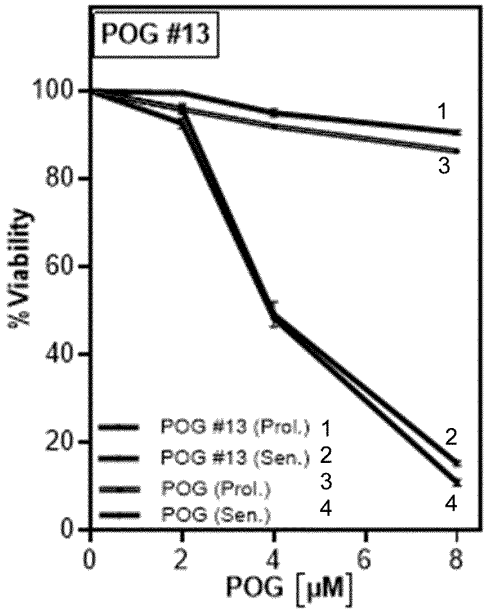


FIG 17F

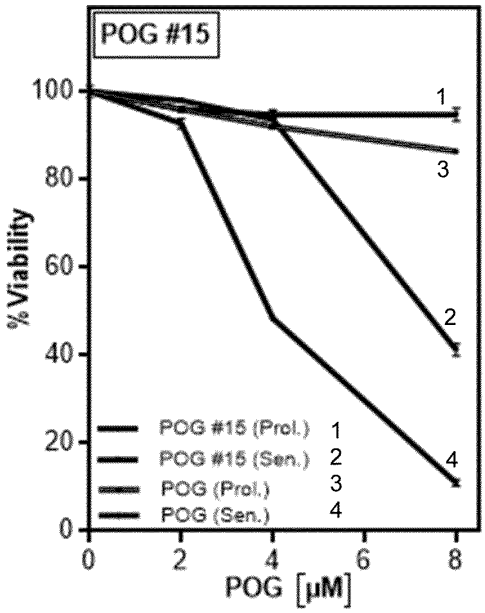


FIG 17G

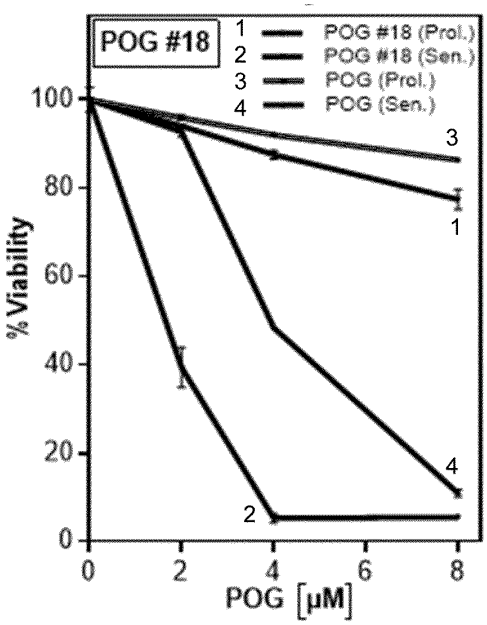


FIG 17H

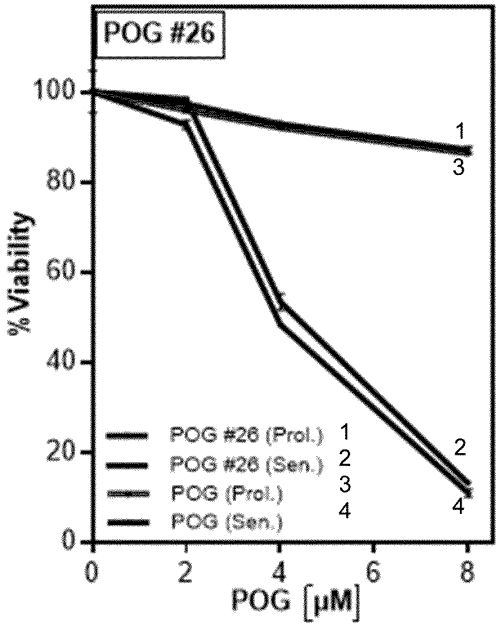


FIG 17J

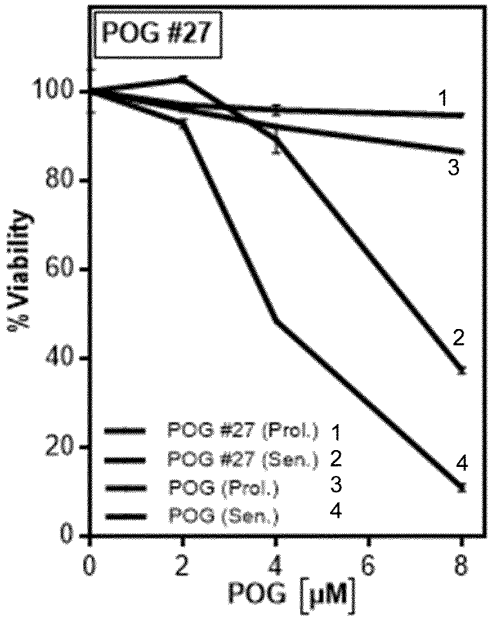


FIG 17K

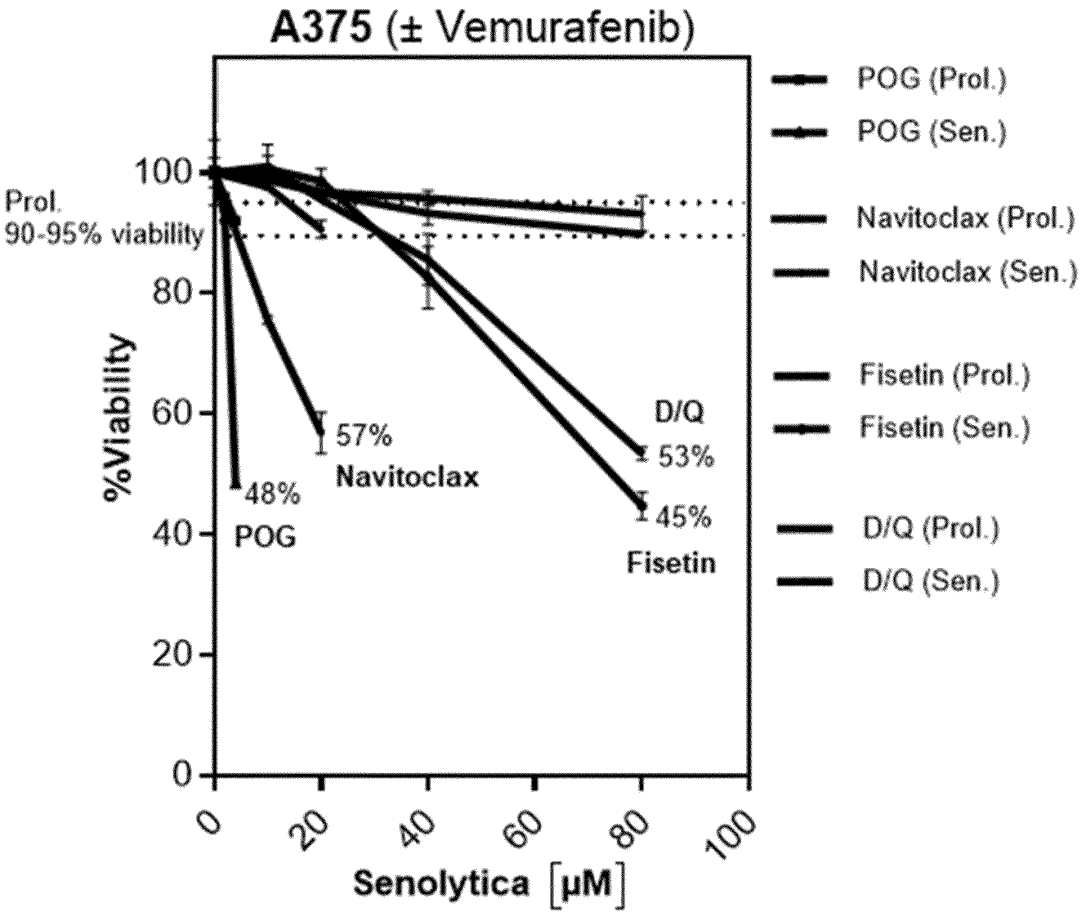

A375 (± Vemurafenib)
POG (Prol.)
POG (Sen.)
Navitoclax (Prol.)
Navitoclax (Sen.)
Fisetin (Prol.)
Fisetin (Sen.)
D/Q (Prol.)
D/Q (Sen.)
Prol.
90-95% viability
%Viability
100
80
60
40
20
0
0
20
40
60
80
100
Senolytica [µM]
48%
POG
57%
Navitoclax
D/Q
53%
45%
Fisetin

FIG 18

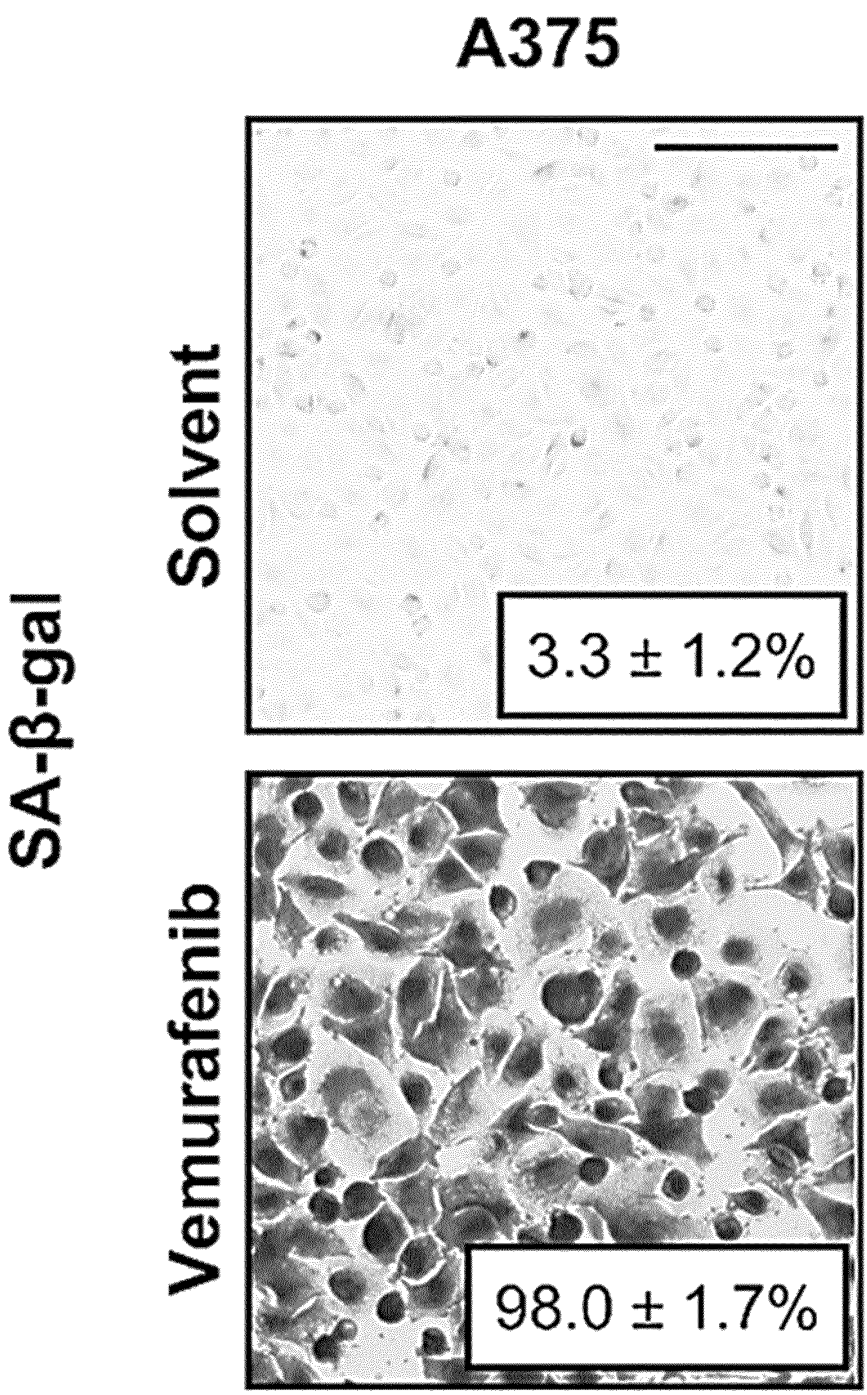


FIG 19

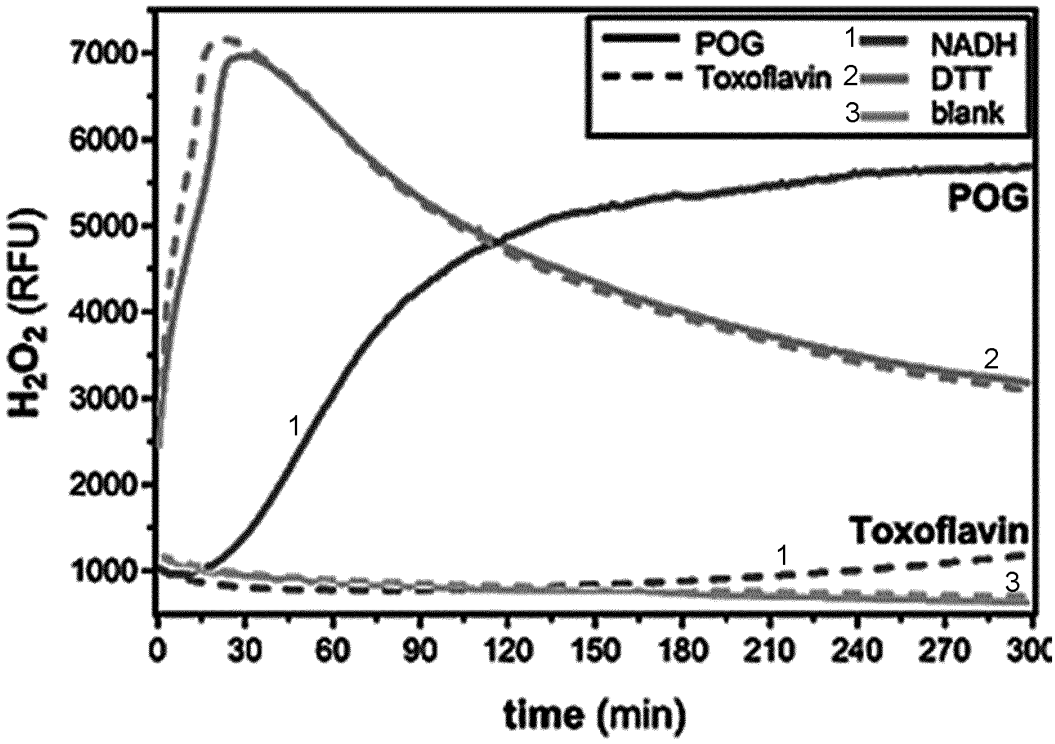

POG
Toxoflavin
1 NADH
2 DTT
3 blank
H_2O_2 (RFU)
7000
6000
5000
4000
3000
2000
1000
0
30
60
90
120
150
180
210
240
270
300
time (min)
POG
Toxoflavin
1
2
3

FIG 20

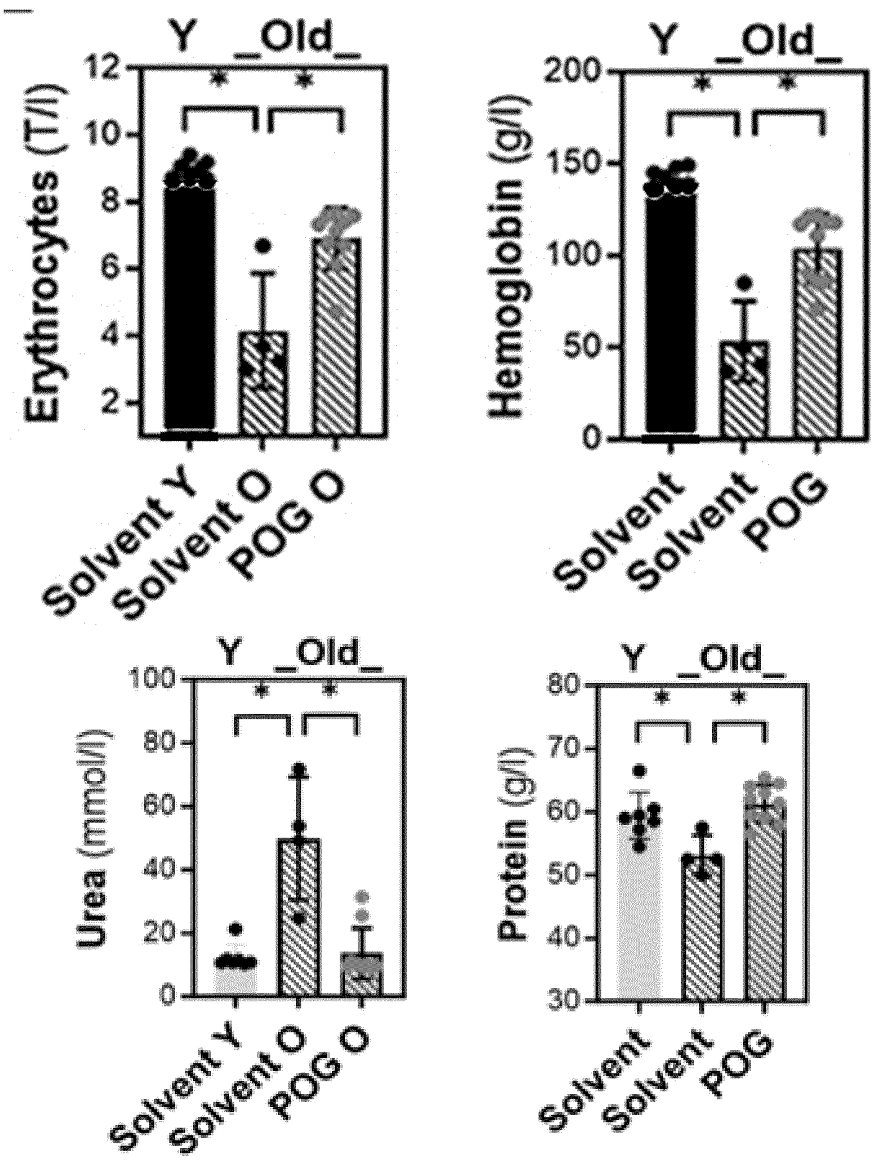

Y _Old_
Erythrocytes (T/l)
12
10
8
6
4
2
Solvent Y
Solvent O
POG O
Y _Old_
Hemoglobin (g/l)
200
150
100
50
0
Solvent
Solvent
POG
Y _Old_
Urea (mmol/l)
100
80
60
40
20
0
Solvent Y
Solvent O
POG O
Y _Old_
Protein (g/l)
80
70
60
50
40
30
Solvent
Solvent
POG

FIG 21

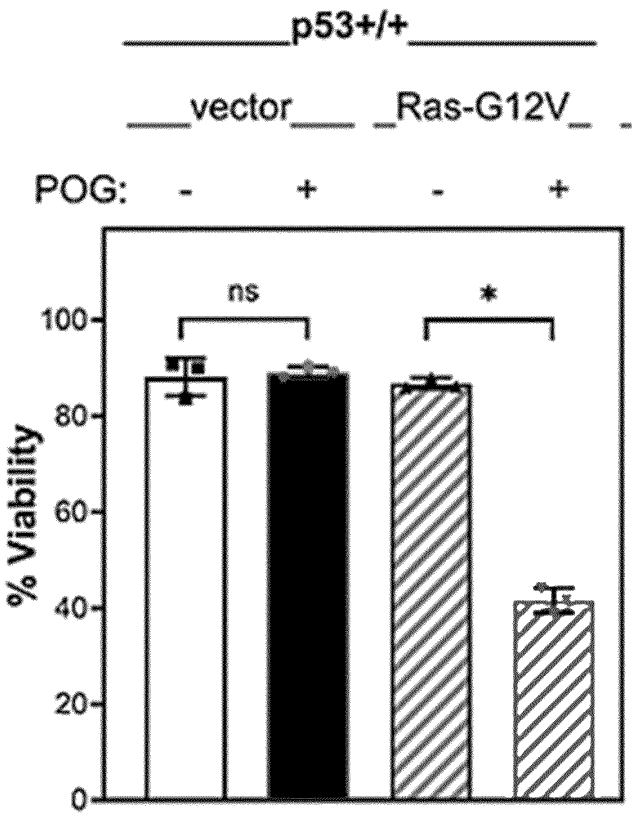


FIG 22A

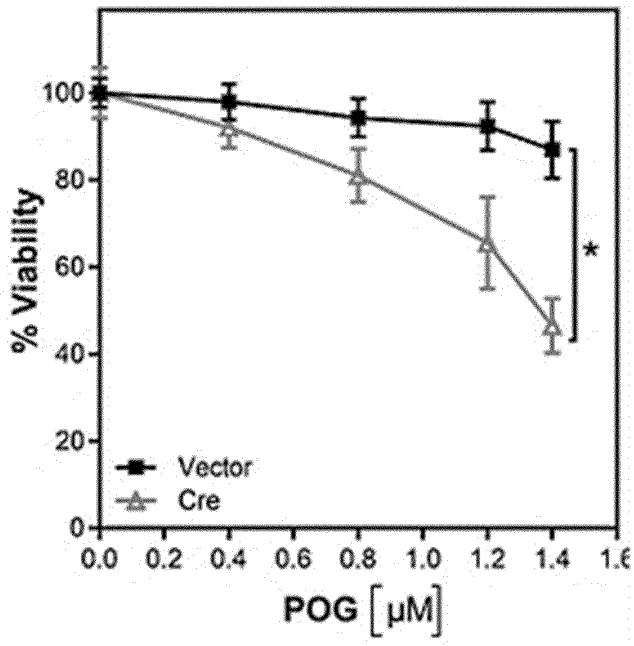


FIG 22B

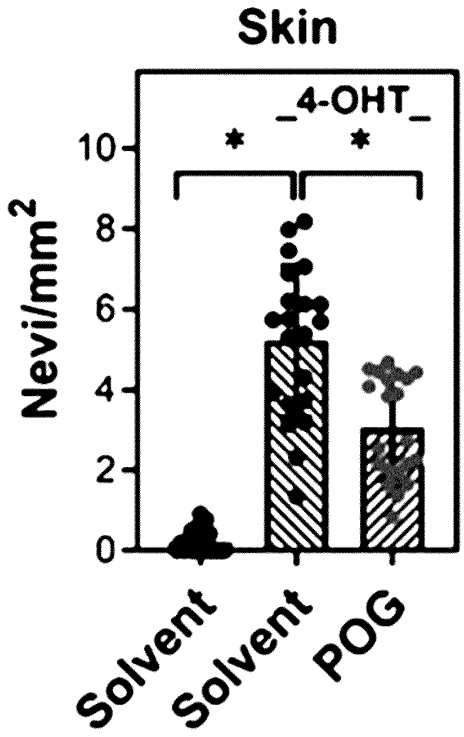


FIG 23A

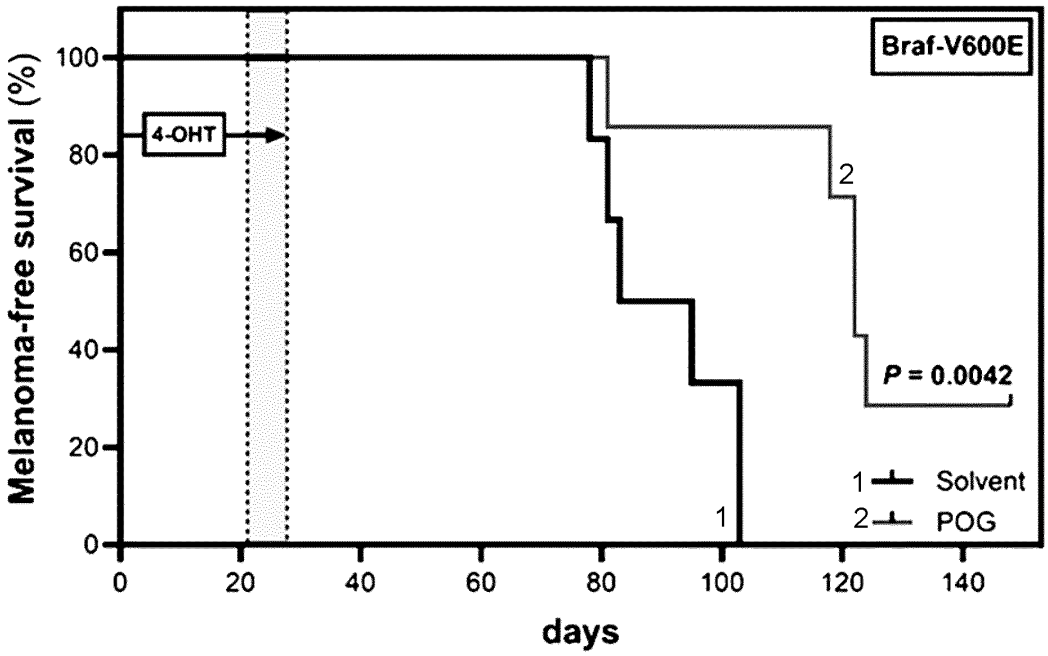


FIG 23B

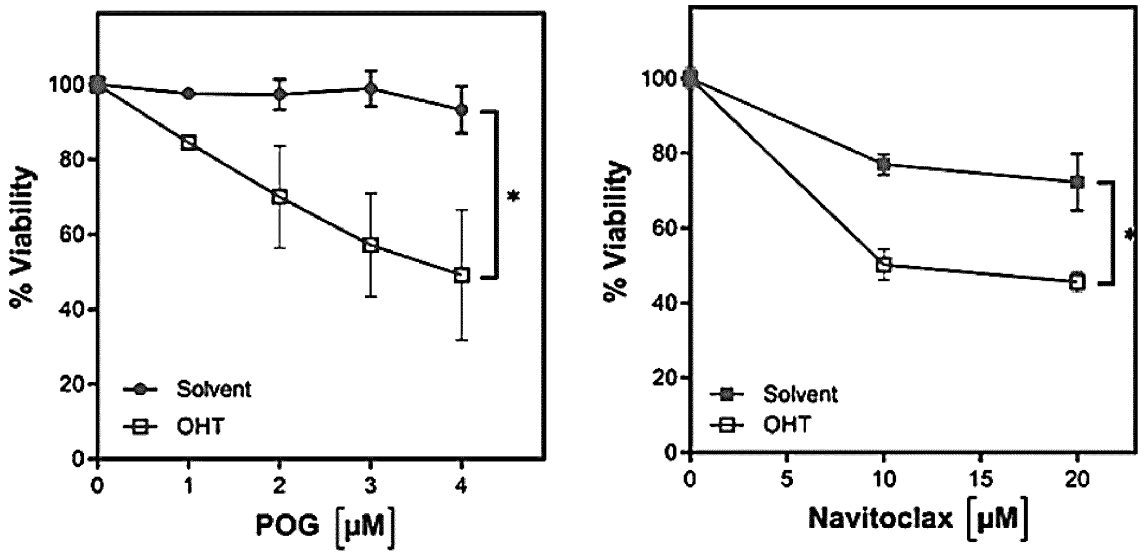


FIG 24

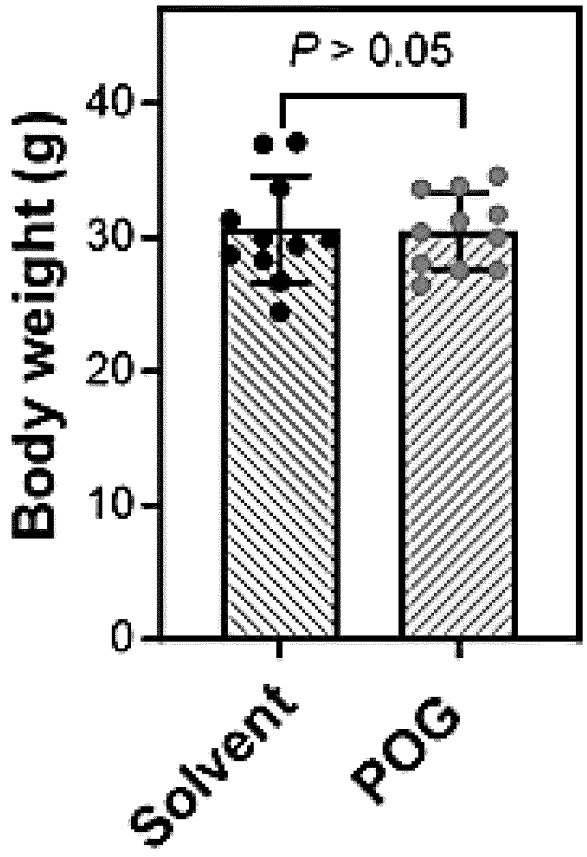


FIG 25A

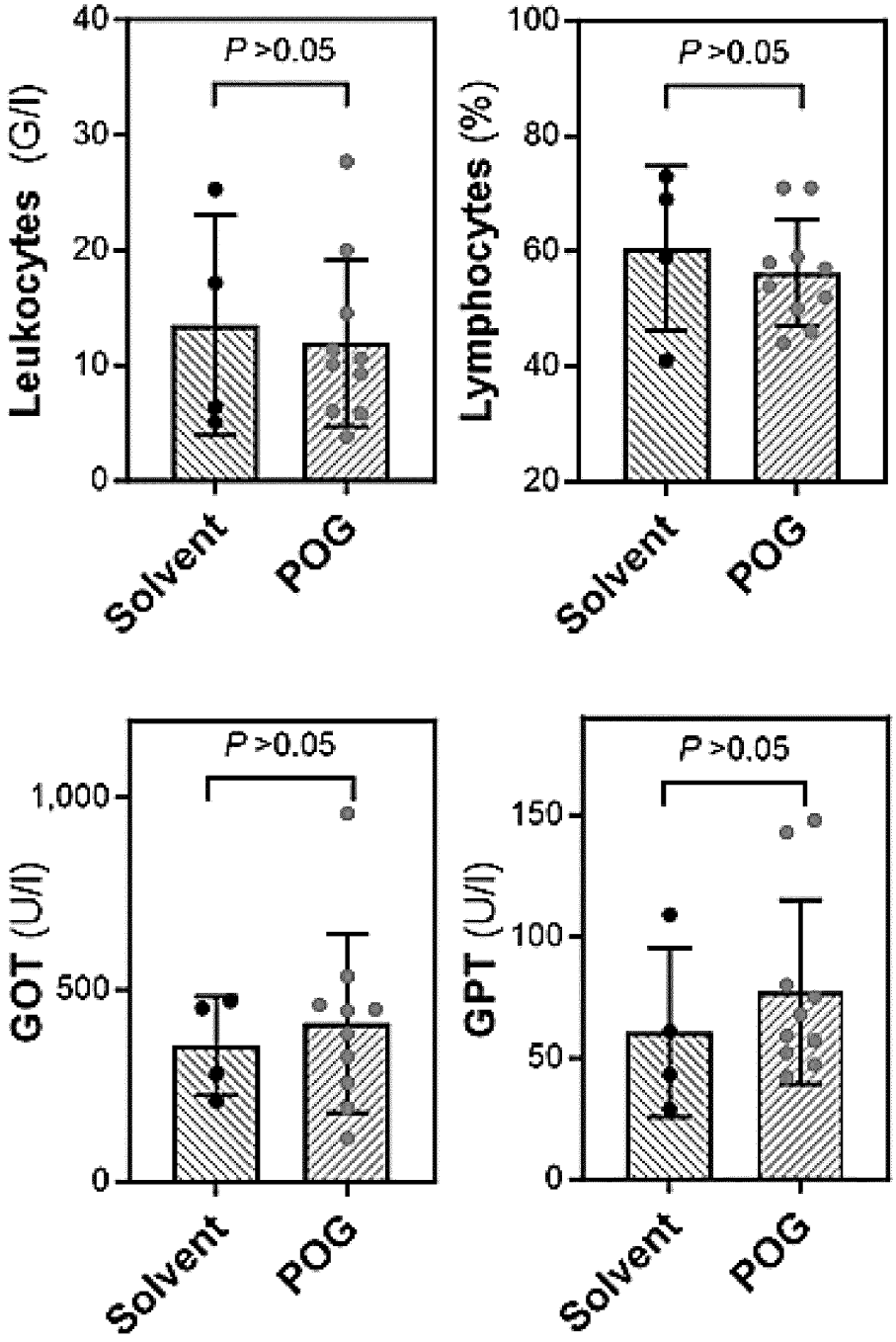

Leukocytes (G/l)
40
30
20
10
0
P >0.05
Solvent
POG
Lymphocytes (%)
100
80
60
40
20
P >0.05
Solvent
POG
GOT (U/l)
1,000
500
0
P >0.05
Solvent
POG
GPT (U/l)
150
100
50
0
P >0.05
Solvent
POG

FIG 25B

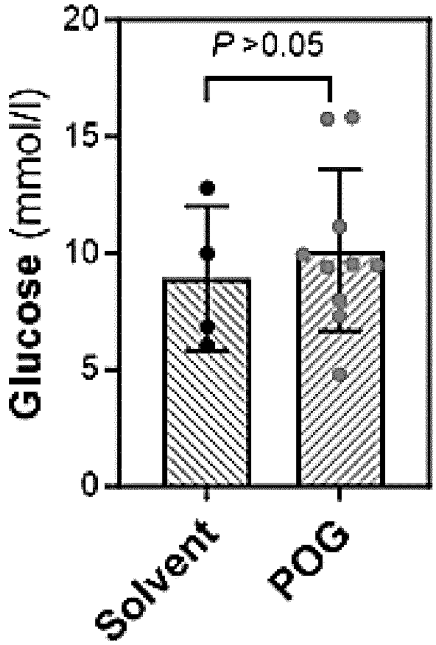


FIG 25B continued

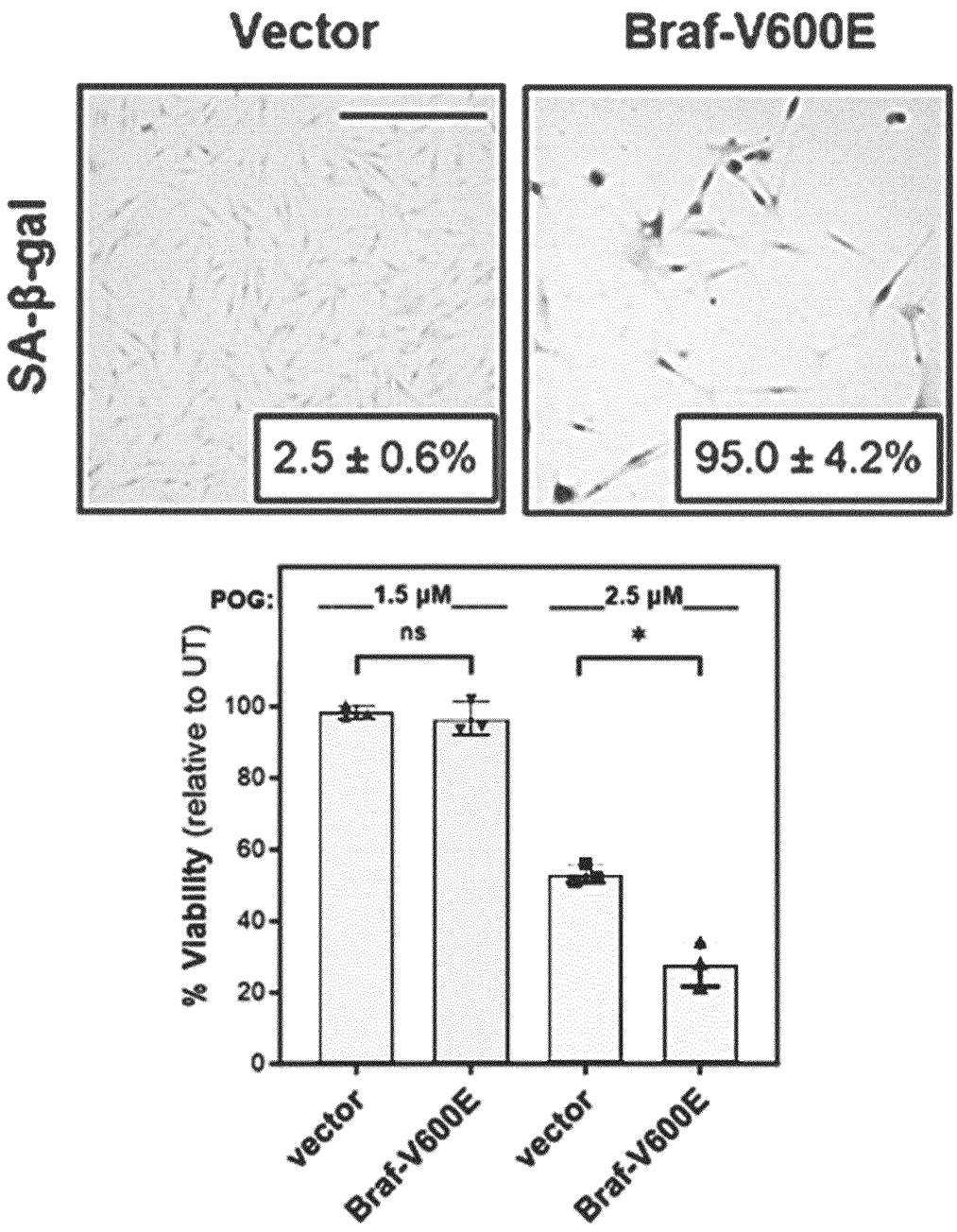

Vector
Braf-V600E
SA-β-gal
2.5 ± 0.6%
95.0 ± 4.2%
POG:
1.5 μM
2.5 μM
ns
*
% Viability (relative to UT)
100
80
60
40
20
0
vector
Braf-V600E
vector
Braf-V600E

FIG 26