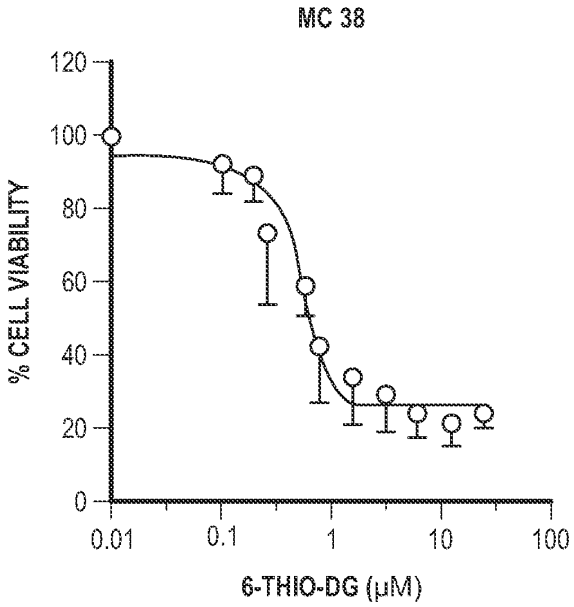

MC 38
% CELL VIABILITY
120
100
80
60
40
20
0
0.01
0.1
1
10
100
6-THIO-DG (μM)

FIG. 1A

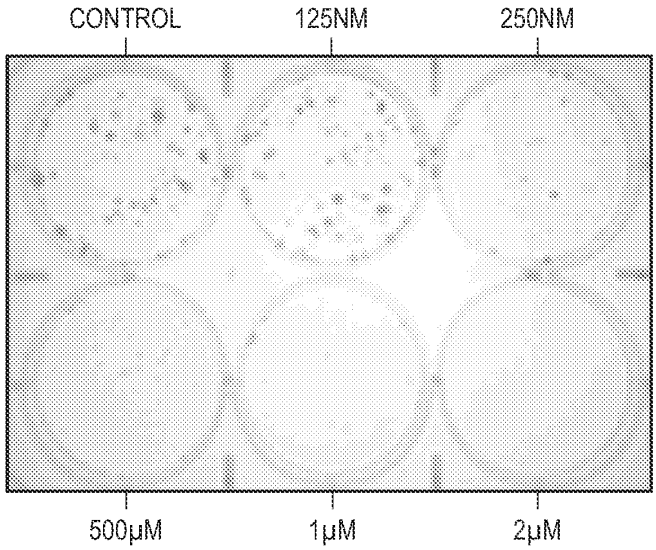

CONTROL
125NM
250NM
500μM
1μM
2μM

FIG. 1B

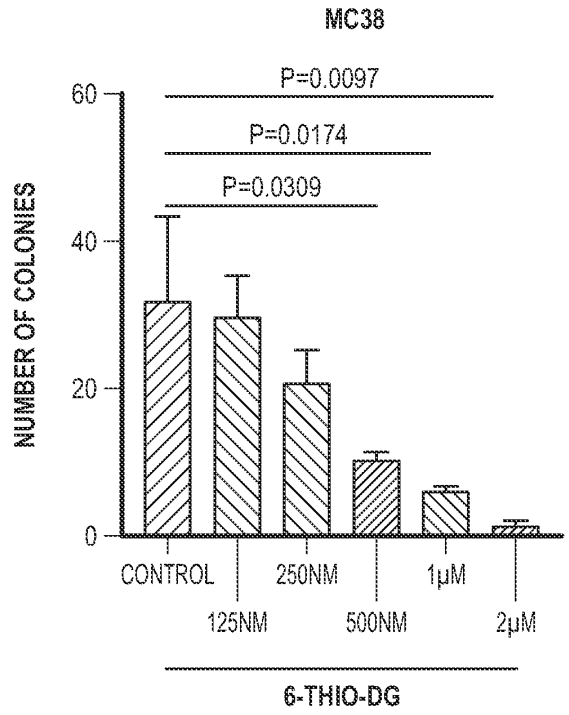

MC38
P=0.0097
P=0.0174
P=0.0309
NUMBER OF COLONIES
60
40
20
0
CONTROL
125NM
250NM
500NM
1μM
2μM
6-THIO-DG

FIG. 1C

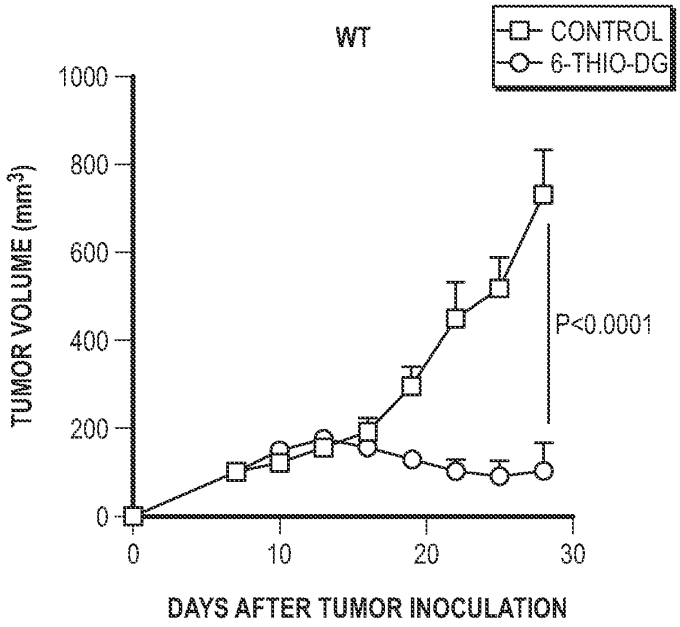

WT
CONTROL
6-THIO-DG
TUMOR VOLUME (mm3)
1000
800
600
400
200
0
P<0.0001
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 1D

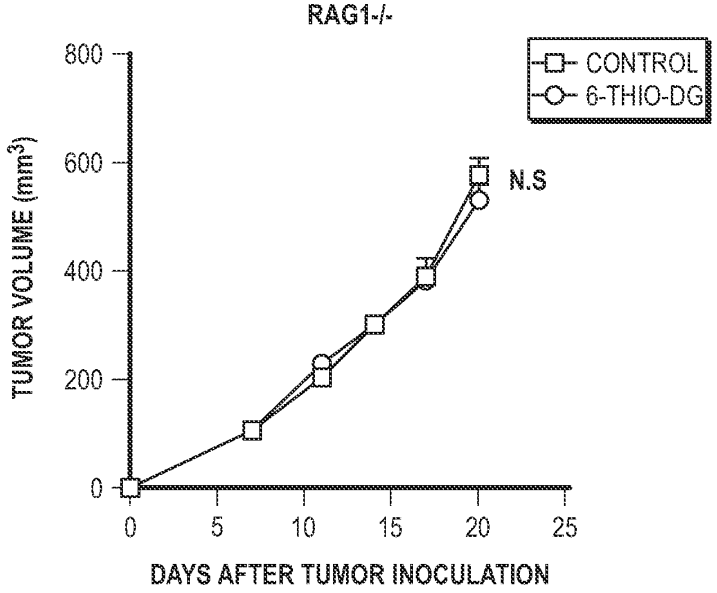

RAG1-/-
CONTROL
6-THIO-DG
N.S
TUMOR VOLUME (mm3)
800
600
400
200
0
0
5
10
15
20
25
DAYS AFTER TUMOR INOCULATION

FIG. 1E

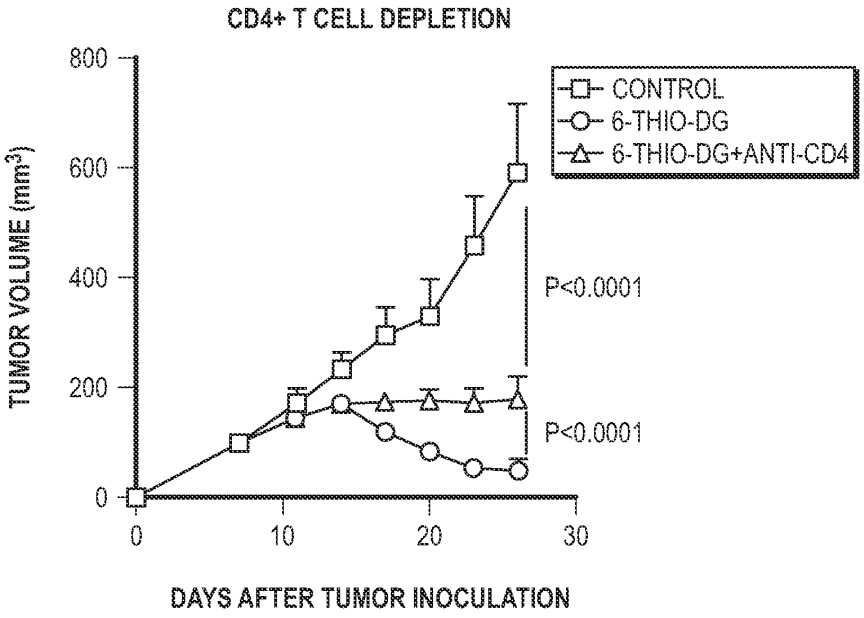

CD4+ T CELL DEPLETION
CONTROL
6-THIO-DG
6-THIO-DG+ANTI-CD4
P<0.0001
P<0.0001
TUMOR VOLUME (mm3)
800
600
400
200
0
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 1F

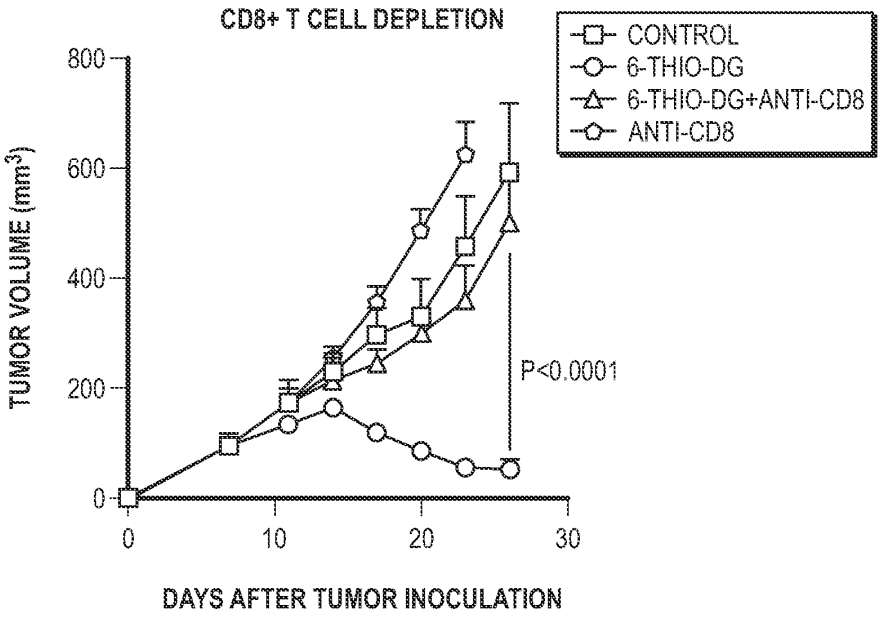

CD8+ T CELL DEPLETION
CONTROL
6-THIO-DG
6-THIO-DG+ANTI-CD8
ANTI-CD8
TUMOR VOLUME (mm3)
800
600
400
200
0
0
10
20
30
P<0.0001
DAYS AFTER TUMOR INOCULATION

FIG. 1G

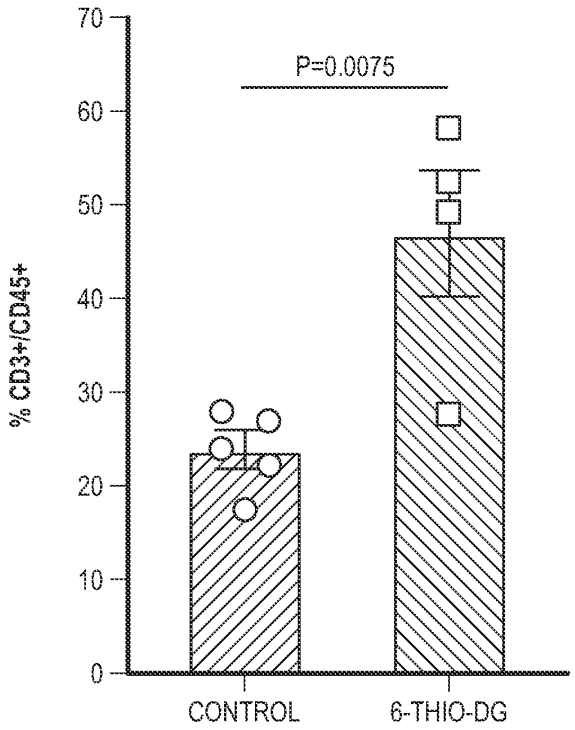

% CD3+/CD45+
70
60
50
40
30
20
10
0
P=0.0075
CONTROL
6-THIO-DG

FIG. 2A

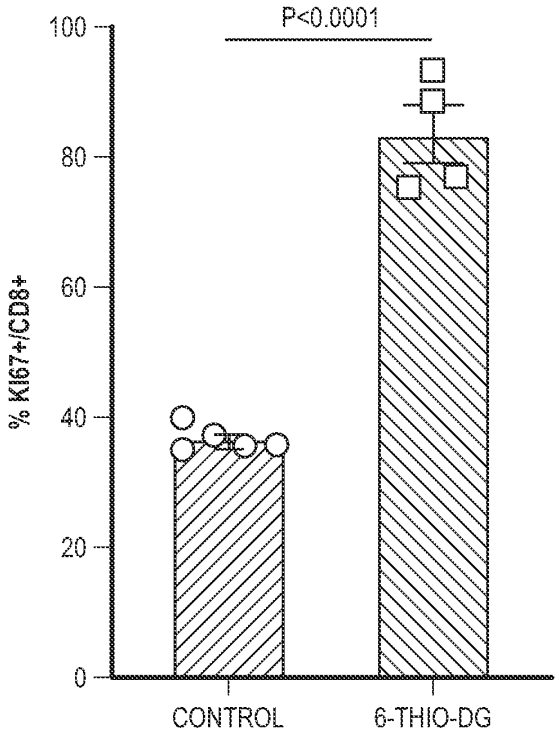

P<0.0001
100
80
60
40
20
0
% KI67+/CD8+
CONTROL
6-THIO-DG

FIG. 2B

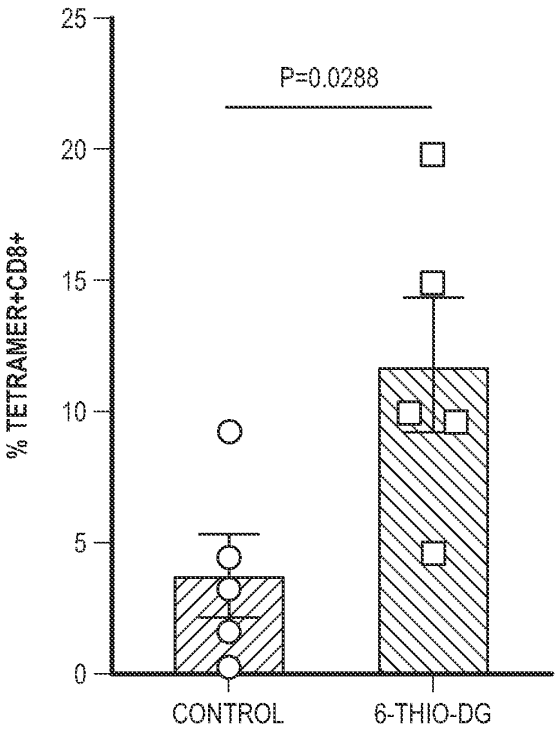

P=0.0288
25
20
15
10
5
0
% TETRAMER+CD8+
CONTROL
6-THIO-DG

FIG. 2C

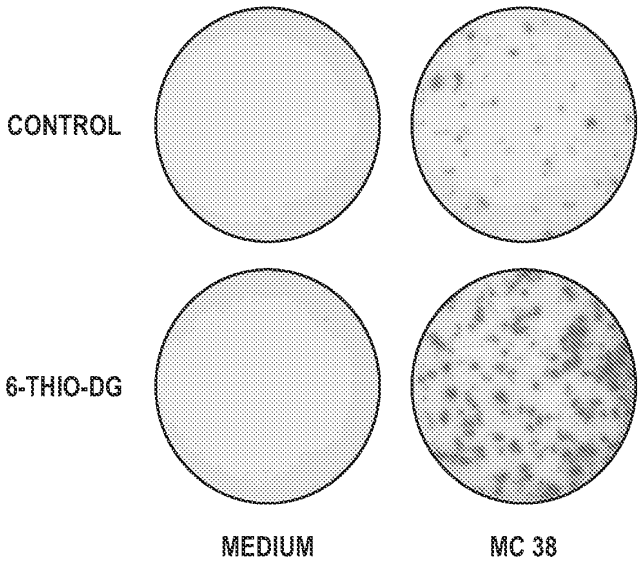

CONTROL
6-THIO-DG
MEDIUM
MC 38

FIG. 2D

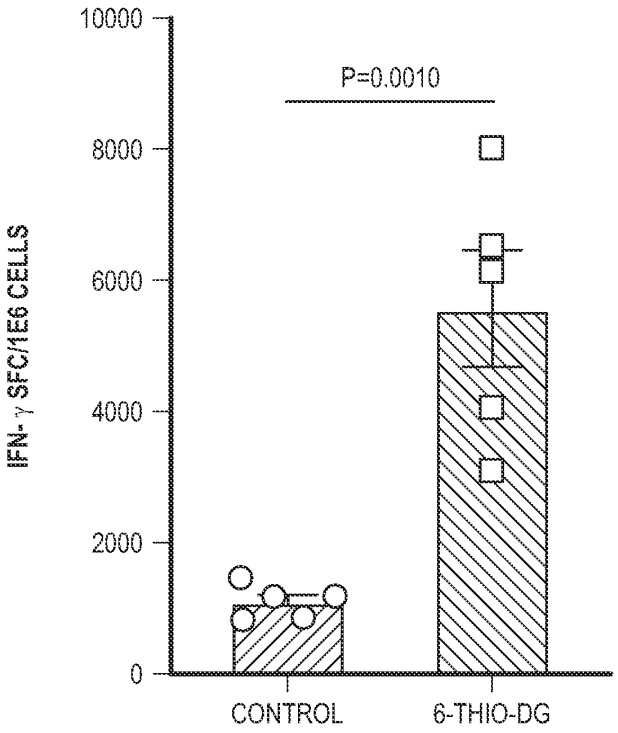

10000
8000
6000
4000
2000
0
P=0.0010
IFN-γ SFC/1E6 CELLS
CONTROL
6-THIO-DG

FIG. 2E

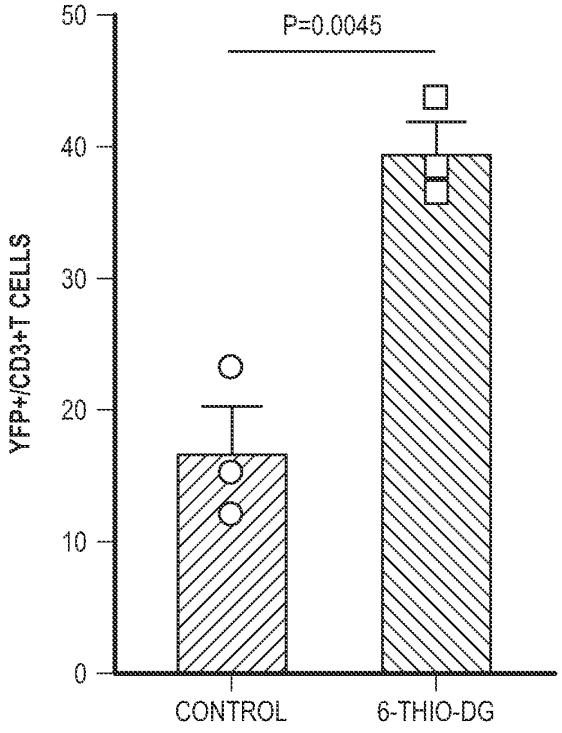

P=0.0045
YFP+/CD3+T CELLS
50
40
30
20
10
0
CONTROL
6-THIO-DG

FIG. 2F

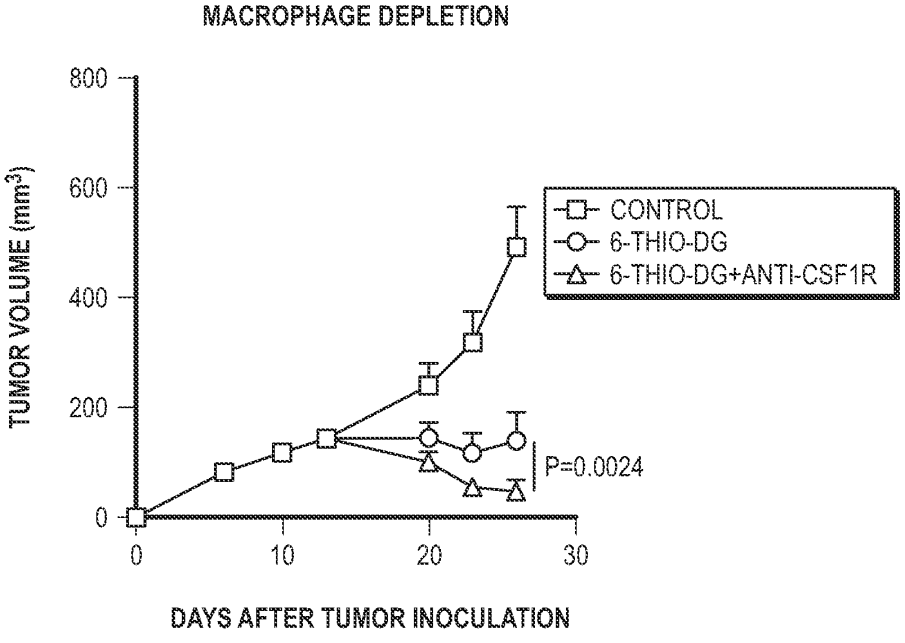

MACROPHAGE DEPLETION
TUMOR VOLUME (mm3)
800
600
400
200
0
0
10
20
30
DAYS AFTER TUMOR INOCULATION
CONTROL
6-THIO-DG
6-THIO-DG+ANTI-CSF1R
P=0.0024

FIG. 3A

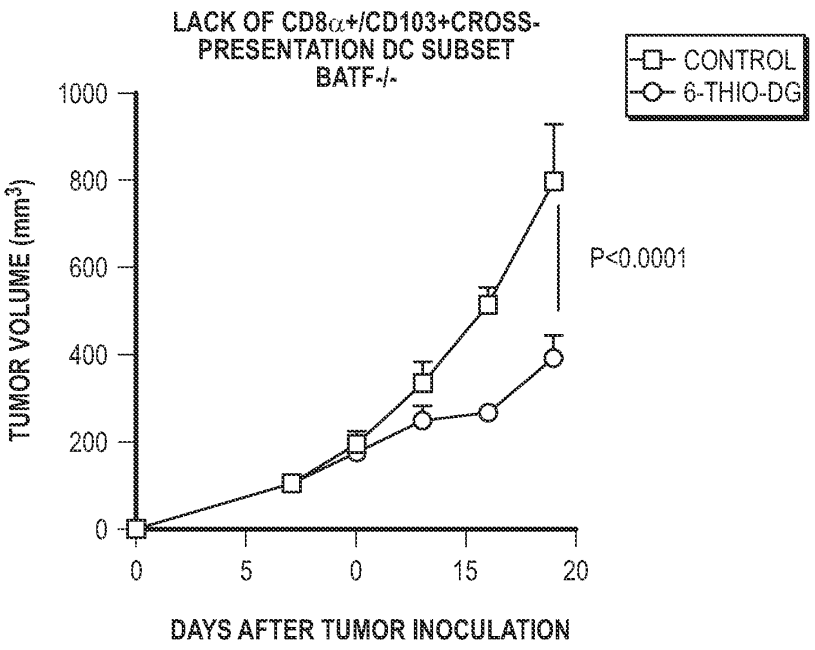

LACK OF CD8α+/CD103+CROSS-PRESENTATION DC SUBSET BATF-/-
CONTROL
6-THIO-DG
TUMOR VOLUME (mm3)
1000
800
600
400
200
0
P<0.0001
0
5
0
15
20
DAYS AFTER TUMOR INOCULATION

FIG. 3B

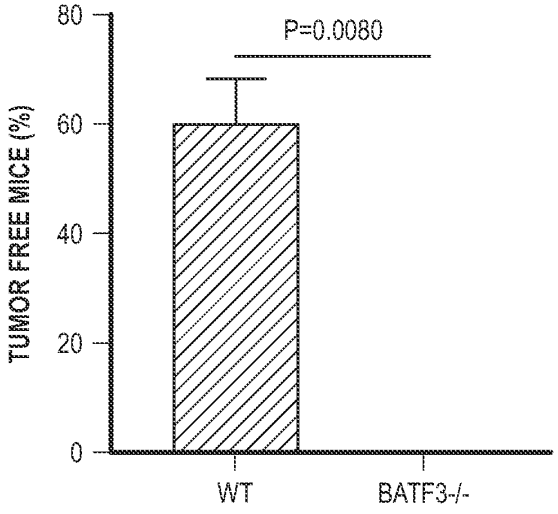

TUMOR FREE MICE (%)
80
60
40
20
0
P=0.0080
WT
BATF3-/-

FIG. 3C

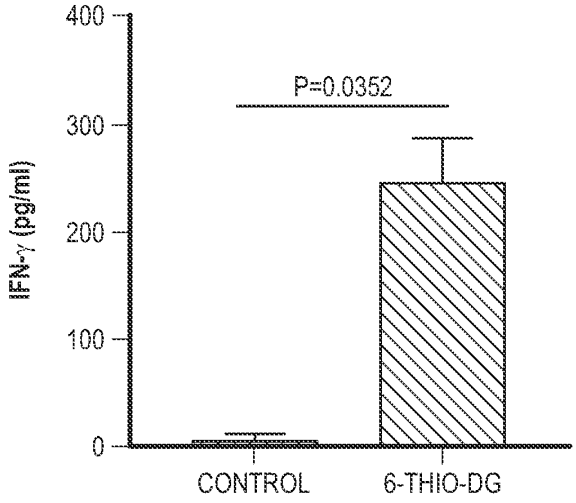

400
300
200
100
0
IFN-γ (pg/ml)
P=0.0352
CONTROL
6-THIO-DG

FIG. 3D

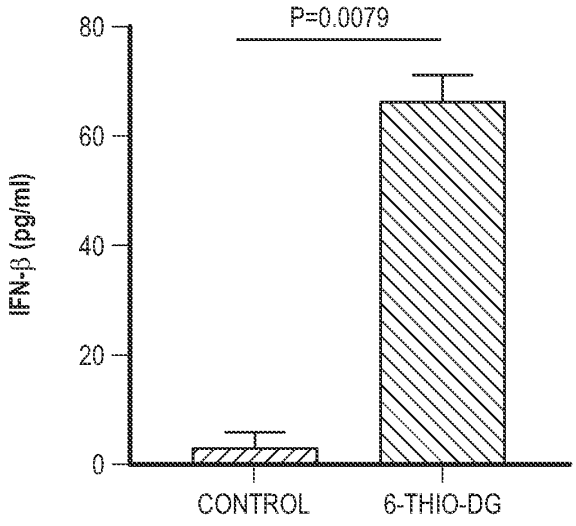

80
60
40
20
0
IFN-β (pg/ml)
P=0.0079
CONTROL
6-THIO-DG

FIG. 3E

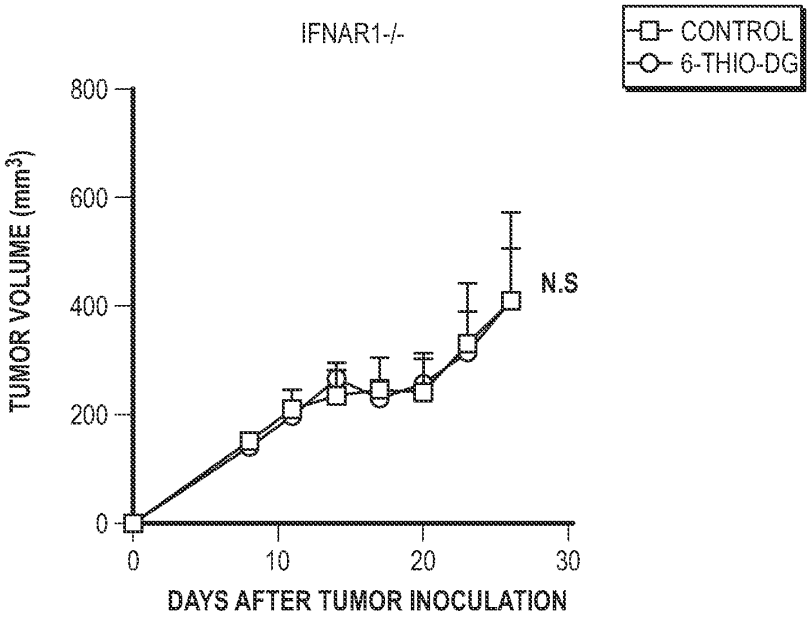

IFNAR1-/-
CONTROL
6-THIO-DG
TUMOR VOLUME (mm3)
800
600
400
200
0
N.S
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 3F

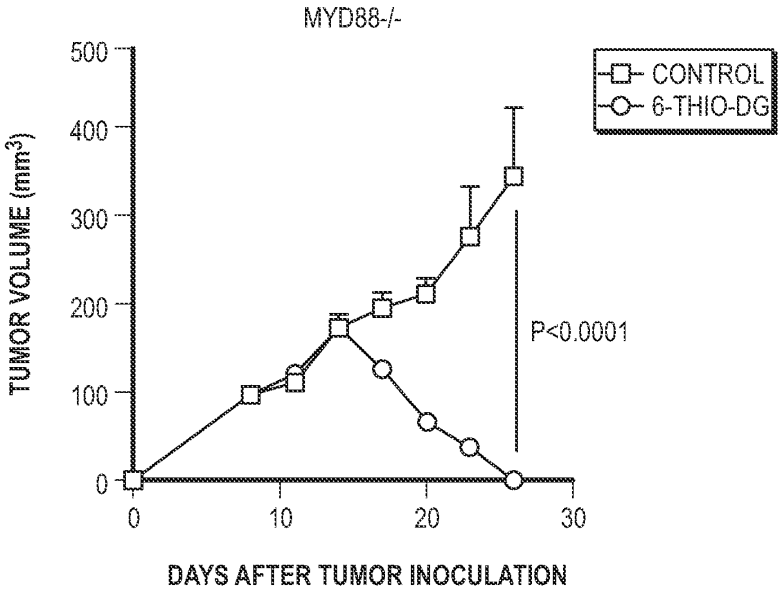

MYD88-/-
CONTROL
6-THIO-DG
TUMOR VOLUME (mm3)
500
400
300
200
100
0
P<0.0001
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG.4A

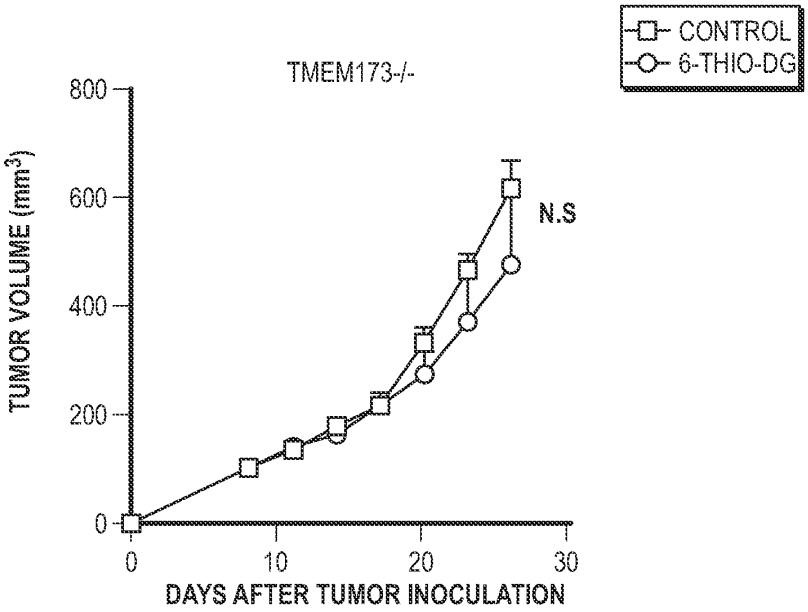

TMEM173-/-
CONTROL
6-THIO-DG
TUMOR VOLUME (mm3)
800
600
400
200
0
N.S
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 4B

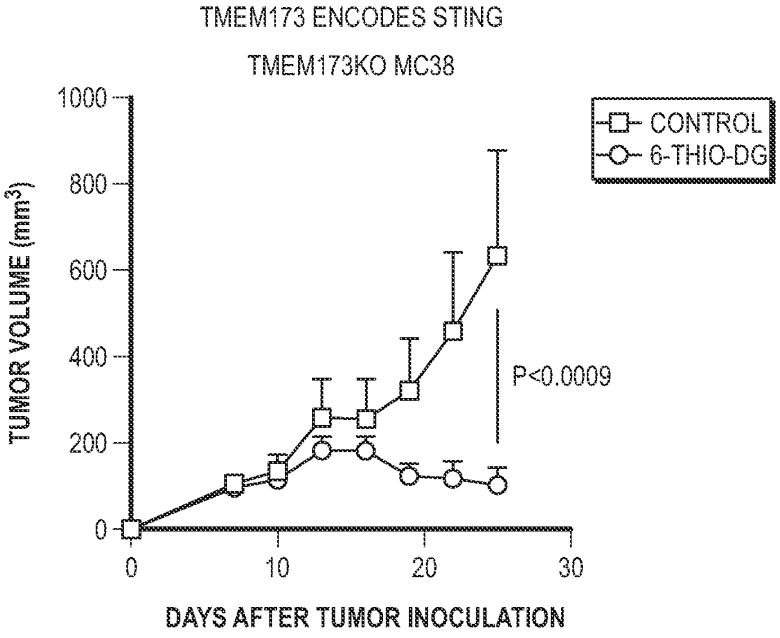

TMEM173 ENCODES STING
TMEM173KO MC38
CONTROL
6-THIO-DG
TUMOR VOLUME (mm3)
1000
800
600
400
200
0
P<0.0009
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG.4C

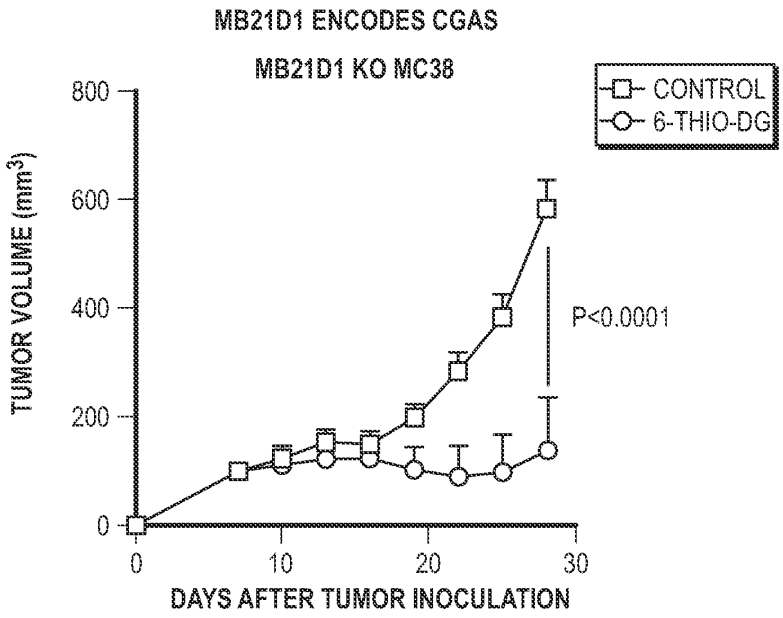

MB21D1 ENCODES CGAS
MB21D1 KO MC38
CONTROL
6-THIO-DG
TUMOR VOLUME (mm3)
800
600
400
200
0
P<0.0001
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 4D

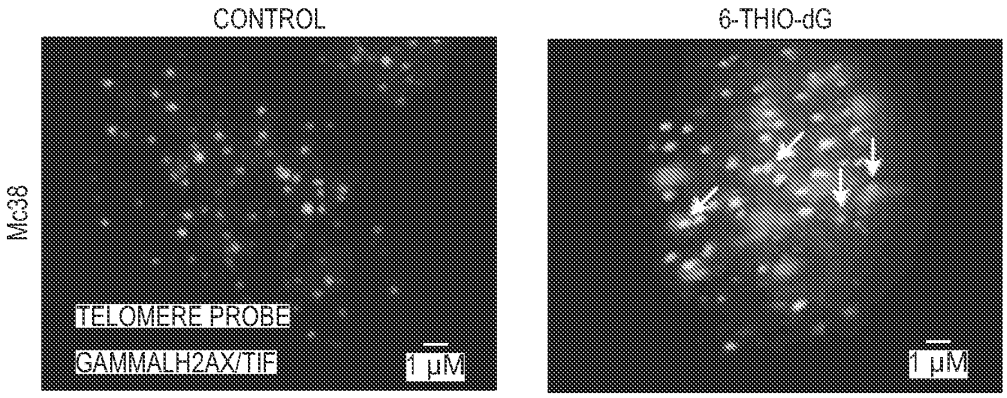

CONTROL
6-THIO-dG
Mc38
TELOMERE PROBE
GAMMALH2AX/TIF
1 μM
1 μM

FIG.4E

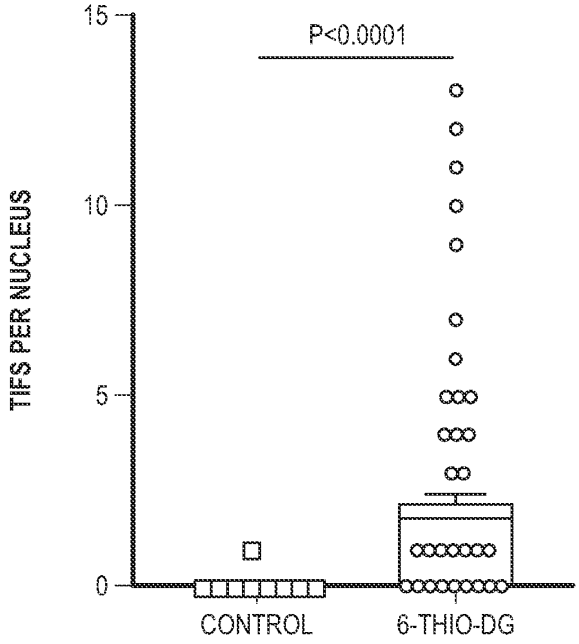

15
10
5
0
TIFS PER NUCLEUS
P<0.0001
CONTROL
6-THIO-DG

FIG. 4F

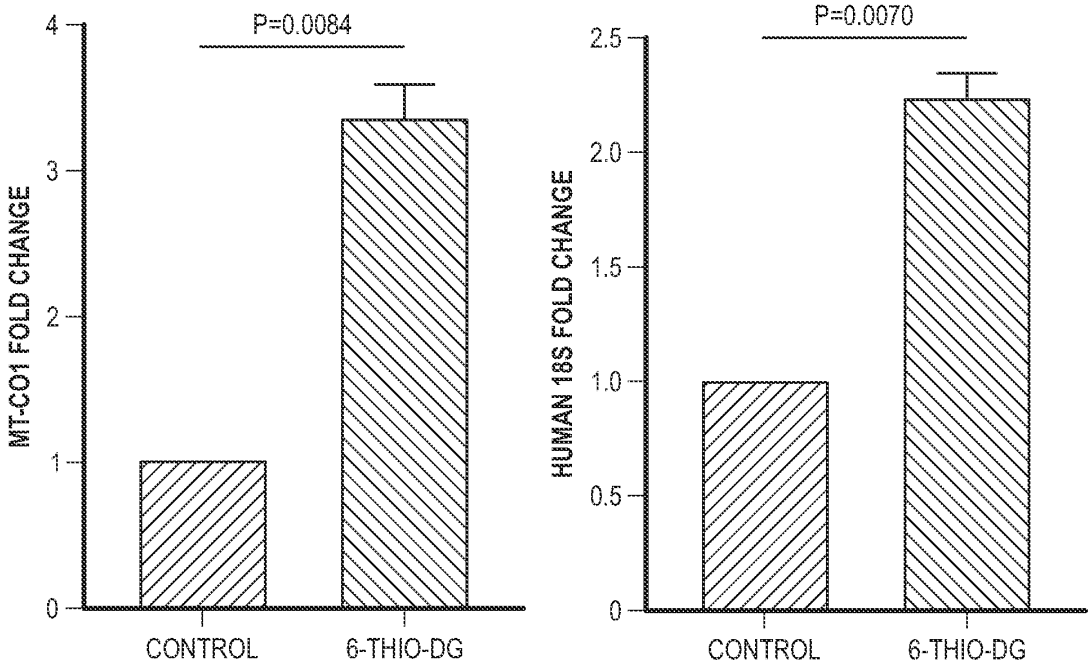

4
3
2
1
0
MT-CO1 FOLD CHANGE
P=0.0084
CONTROL
6-THIO-DG
2.5
2.0
1.5
1.0
0.5
0
HUMAN 18S FOLD CHANGE
P=0.0070
CONTROL
6-THIO-DG

FIG. 4G

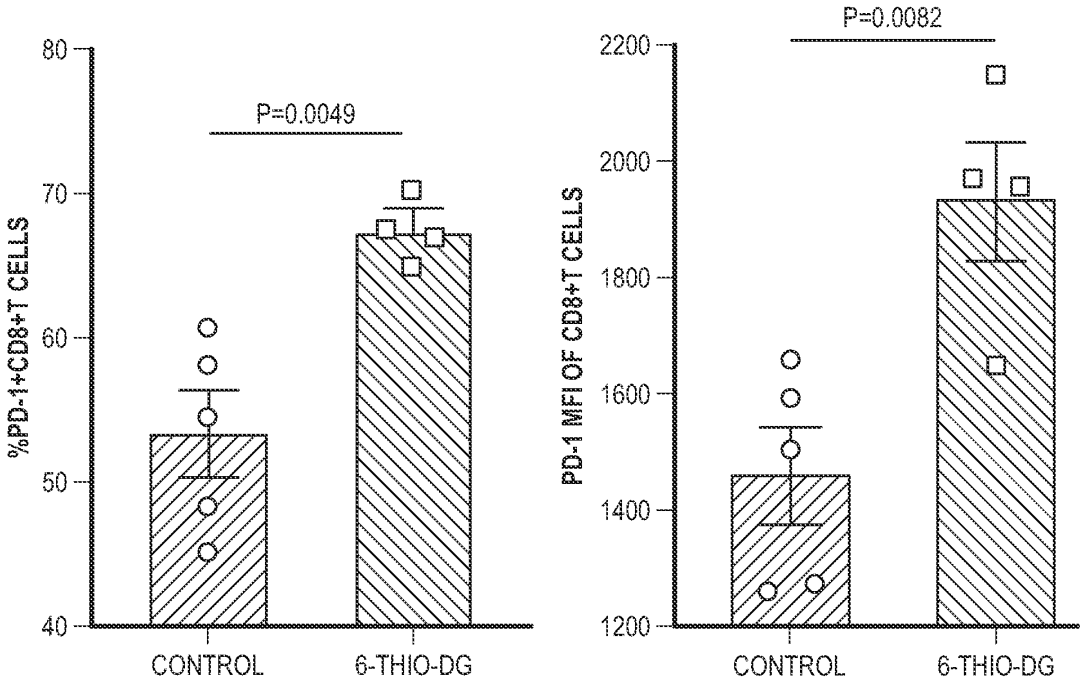

%PD-1+CD8+T CELLS
80
70
60
50
40
P=0.0049
CONTROL
6-THIO-DG
PD-1 MFI OF CD8+T CELLS
2200
2000
1800
1600
1400
1200
P=0.0082
CONTROL
6-THIO-DG

FIG. 5A

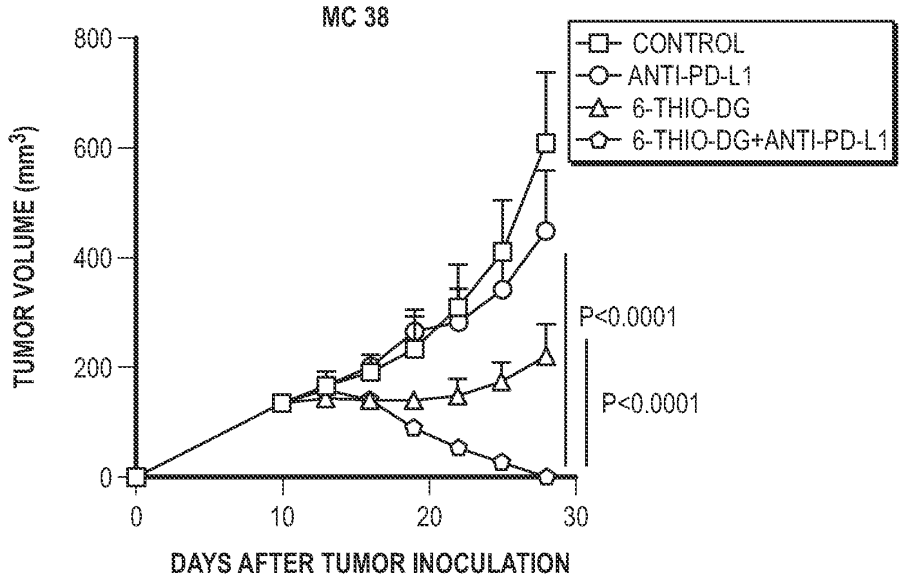

MC 38
TUMOR VOLUME (mm3)
800
600
400
200
0
0
10
20
30
DAYS AFTER TUMOR INOCULATION
CONTROL
ANTI-PD-L1
6-THIO-DG
6-THIO-DG+ANTI-PD-L1
P<0.0001
P<0.0001

FIG. 5B

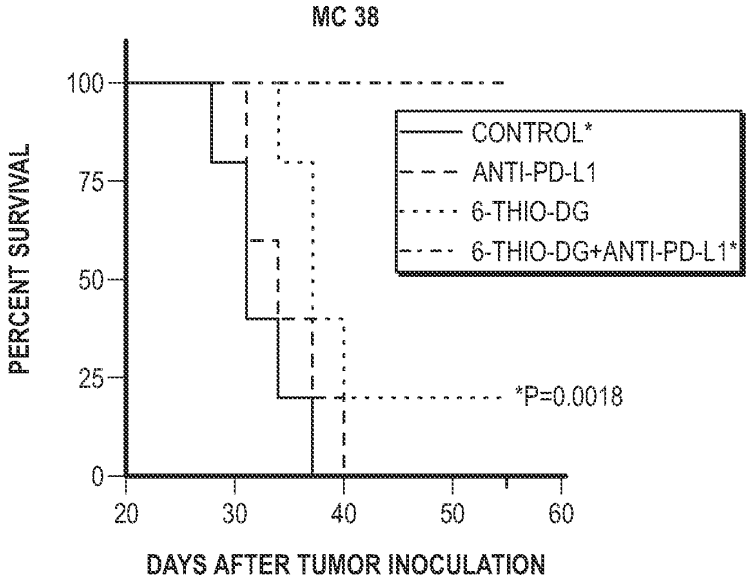

MC 38
PERCENT SURVIVAL
100
75
50
25
0
20
30
40
50
60
DAYS AFTER TUMOR INOCULATION
CONTROL*
ANTI-PD-L1
6-THIO-DG
6-THIO-DG+ANTI-PD-L1*
*P=0.0018

FIG. 5C

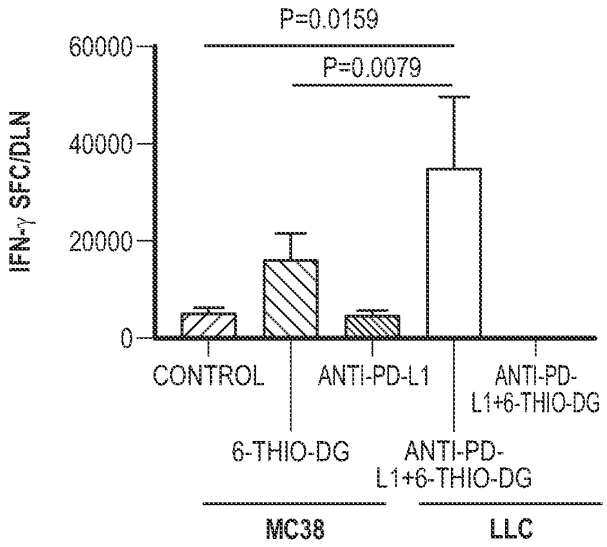

P=0.0159
P=0.0079
IFN-γ SFC/DLN
60000
40000
20000
0
CONTROL
ANTI-PD-L1
ANTI-PD-L1+6-THIO-DG
6-THIO-DG
ANTI-PD-L1+6-THIO-DG
MC38
LLC

FIG. 5D

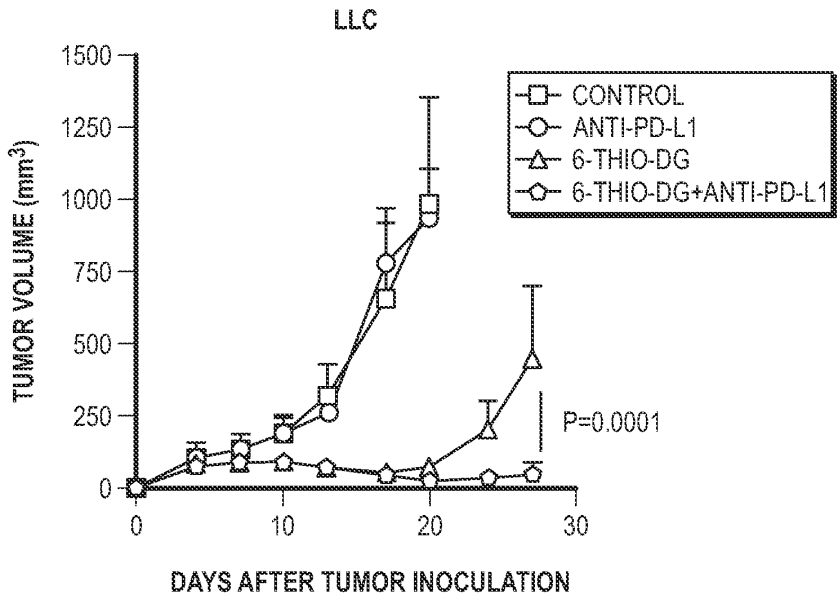

LLC
CONTROL
ANTI-PD-L1
6-THIO-DG
6-THIO-DG+ANTI-PD-L1
TUMOR VOLUME (mm3)
1500
1250
1000
750
500
250
0
P=0.0001
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 5E

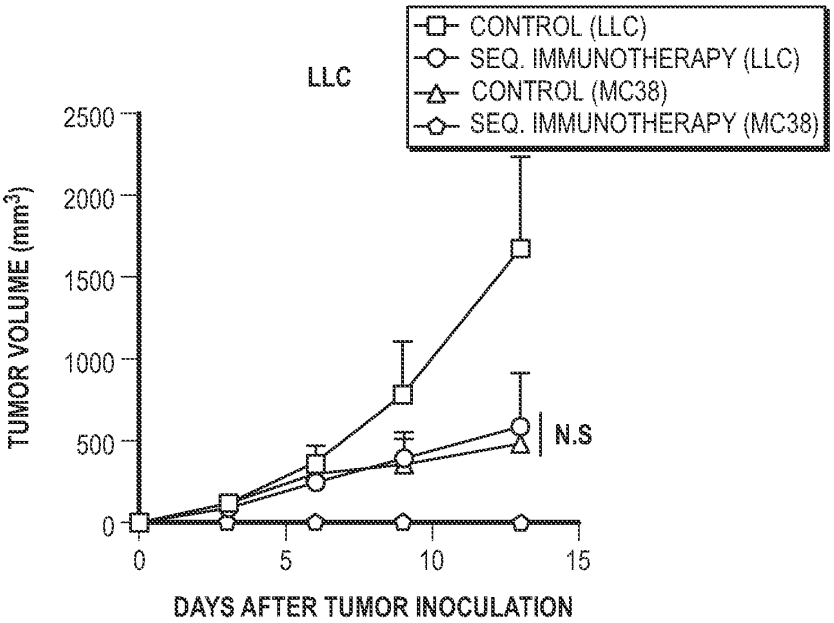

LLC
CONTROL (LLC)
SEQ. IMMUNOTHERAPY (LLC)
CONTROL (MC38)
SEQ. IMMUNOTHERAPY (MC38)
TUMOR VOLUME (mm3)
2500
2000
1500
1000
500
0
N.S
0
5
10
15
DAYS AFTER TUMOR INOCULATION

FIG. 5F

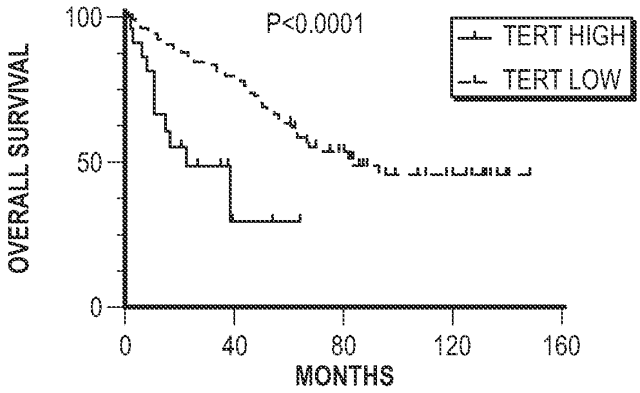

P<0.0001
TERT HIGH
TERT LOW
OVERALL SURVIVAL
100
50
0
0
40
80
120
160
MONTHS

FIG. 6A

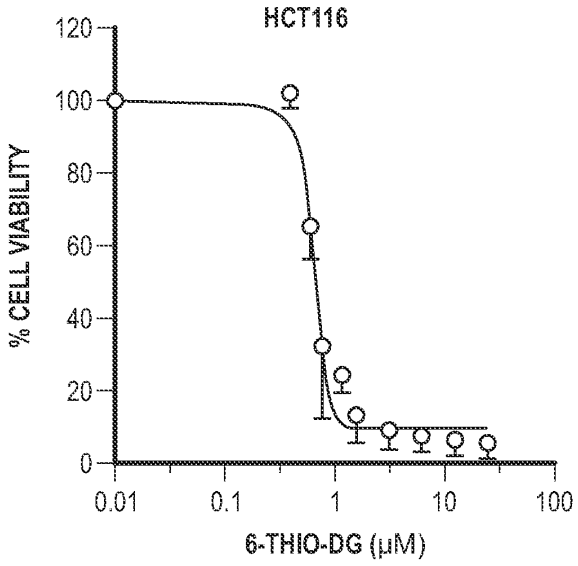

HCT116
% CELL VIABILITY
120
100
80
60
40
20
0
0.01
0.1
1
10
100
6-THIO-DG (μM)

FIG. 6B

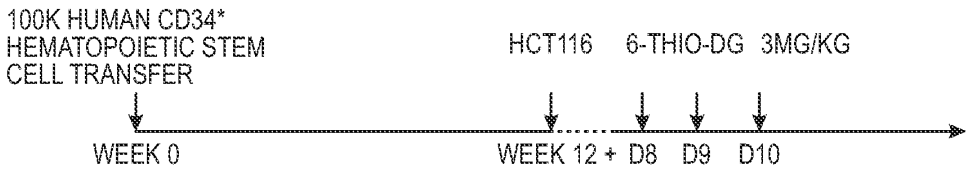

100K HUMAN CD34*
HEMATOPOIETIC STEM
CELL TRANSFER
HCT116 6-THIO-DG 3MG/KG
WEEK 0
WEEK 12 + D8 D9 D10

FIG. 6C

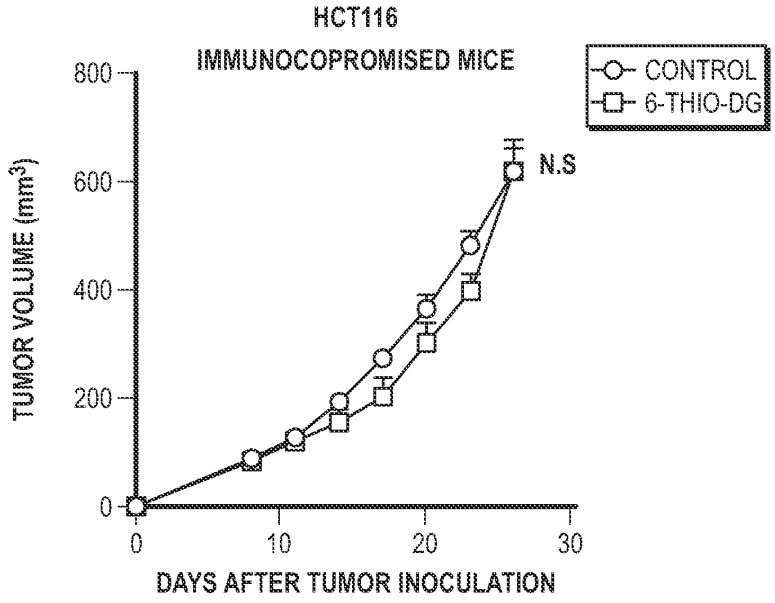

HCT116
IMMUNOCOPROMISED MICE
CONTROL
6-THIO-DG
N.S
TUMOR VOLUME (mm3)
800
600
400
200
0
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 6D

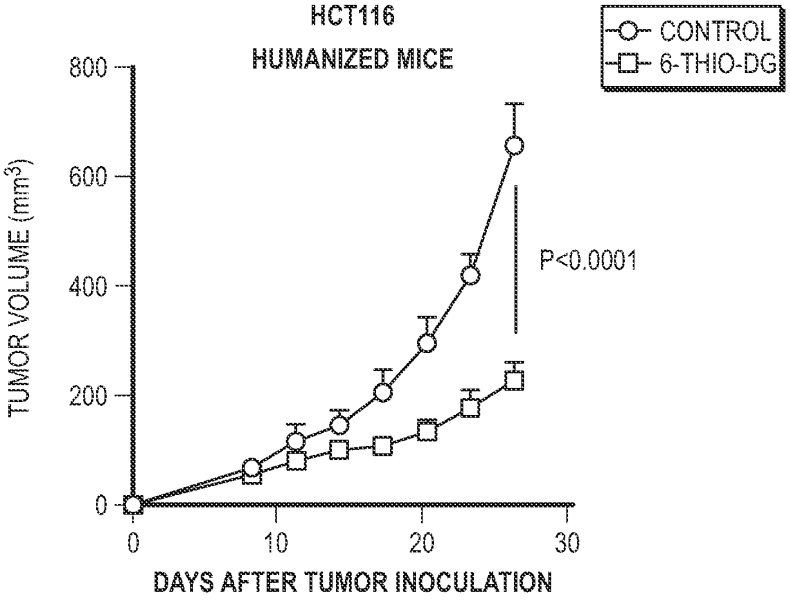

HCT116
HUMANIZED MICE
CONTROL
6-THIO-DG
TUMOR VOLUME (mm3)
800
600
400
200
0
P<0.0001
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 6E

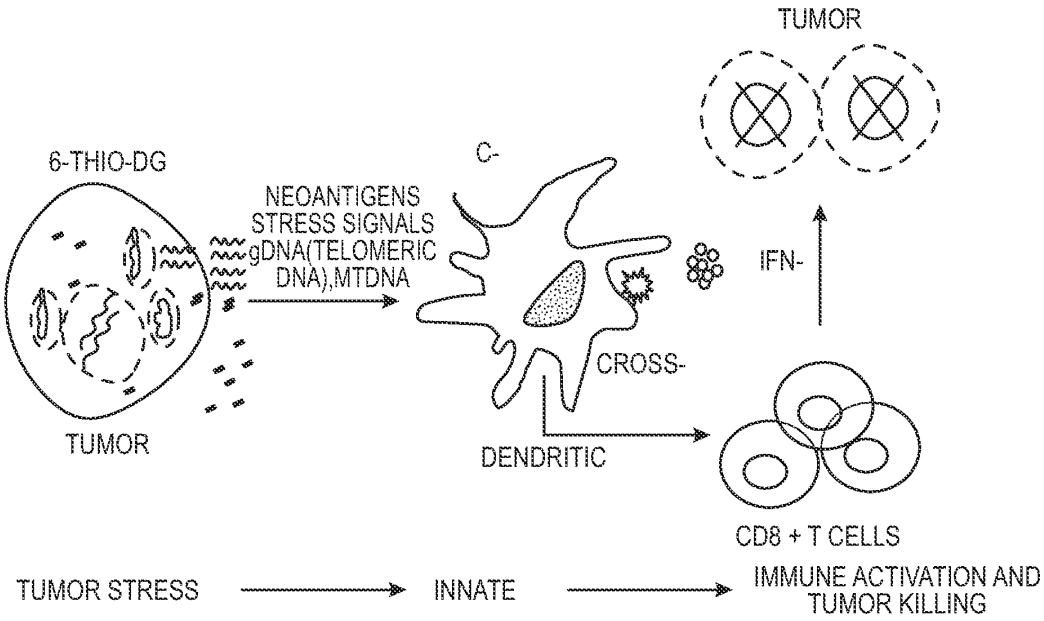

TUMOR
6-THIO-DG
NEOANTIGENS
STRESS SIGNALS
gDNA(TELOMERIC
DNA),MTDNA
C-
IFN-
CROSS-
TUMOR
DENDRITIC
CD8 + T CELLS
TUMOR STRESS
INNATE
IMMUNE ACTIVATION AND
TUMOR KILLING

FIG. 7

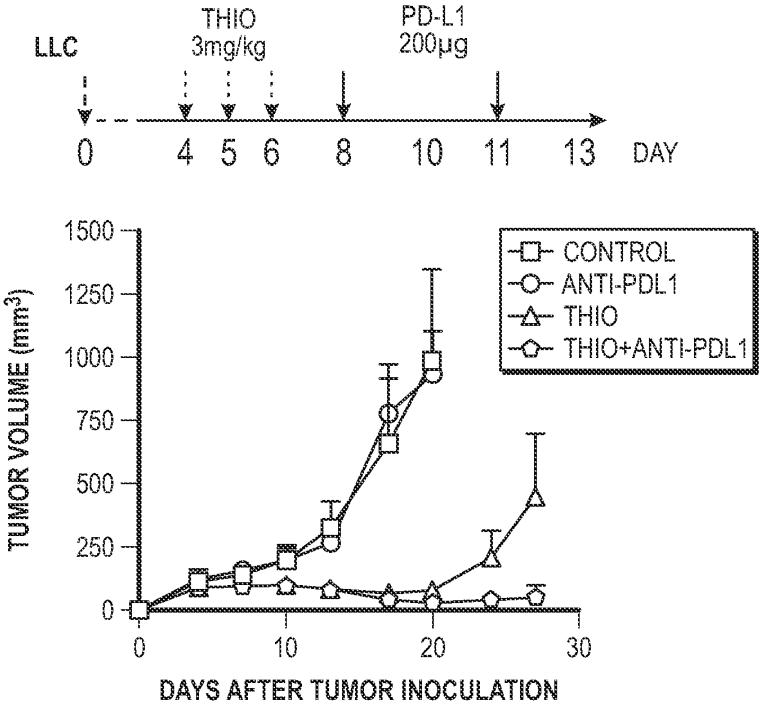

LLC
THIO
3mg/kg
PD-L1
200µg
0
4
5
6
8
10
11
13
DAY
TUMOR VOLUME (mm3)
1500
1250
1000
750
500
250
0
0
10
20
30
DAYS AFTER TUMOR INOCULATION
CONTROL
ANTI-PDL1
THIO
THIO+ANTI-PDL1

FIG. 8A

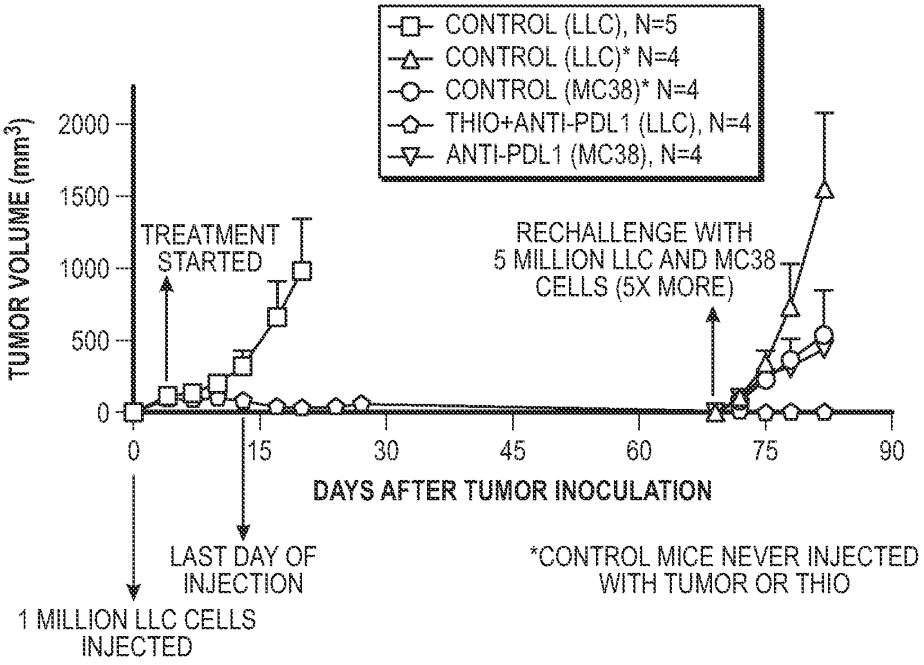

CONTROL (LLC), N=5
CONTROL (LLC)* N=4
CONTROL (MC38)* N=4
THIO+ANTI-PDL1 (LLC), N=4
ANTI-PDL1 (MC38), N=4
TUMOR VOLUME (mm3)
2000
1500
1000
500
0
TREATMENT STARTED
RECHALLENGE WITH 5 MILLION LLC AND MC38 CELLS (5X MORE)
0
15
30
45
60
75
90
DAYS AFTER TUMOR INOCULATION
LAST DAY OF INJECTION
1 MILLION LLC CELLS INJECTED
*CONTROL MICE NEVER INJECTED WITH TUMOR OR THIO

FIG. 8B

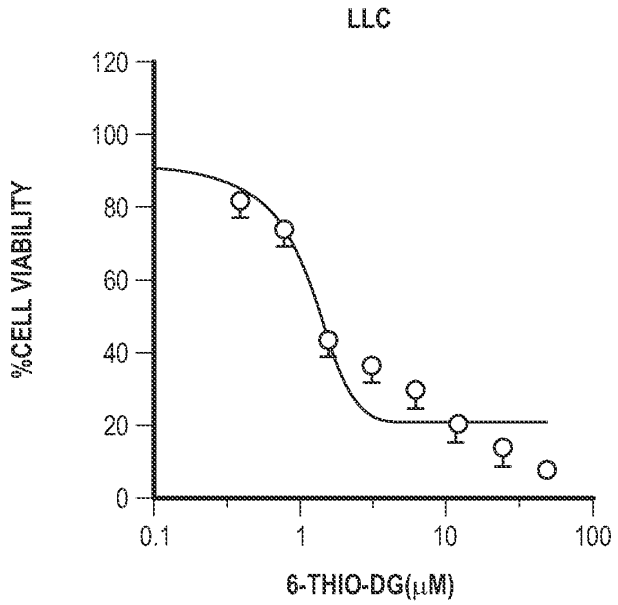

LLC
%CELL VIABILITY
120
100
80
60
40
20
0
0.1
1
10
100
6-THIO-DG(μM)

FIG. 9A

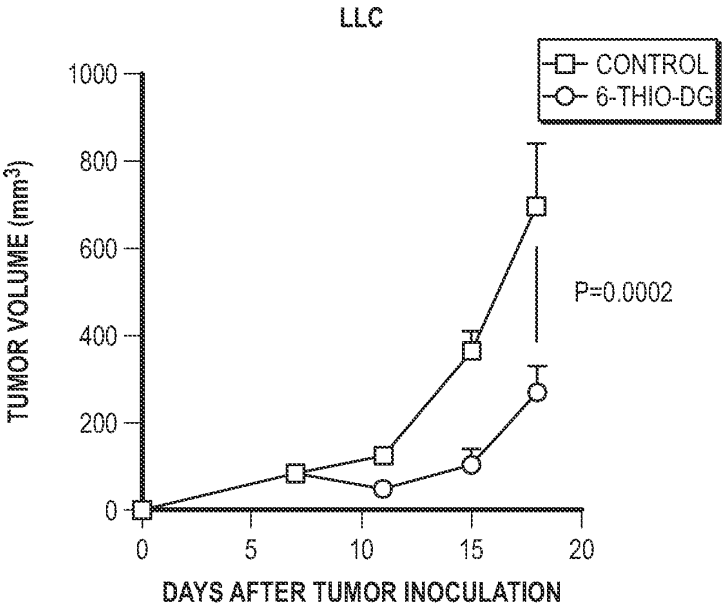

LLC
CONTROL
6-THIO-DG
TUMOR VOLUME (mm3)
1000
800
600
400
200
0
P=0.0002
0
5
10
15
20
DAYS AFTER TUMOR INOCULATION

FIG. 9B

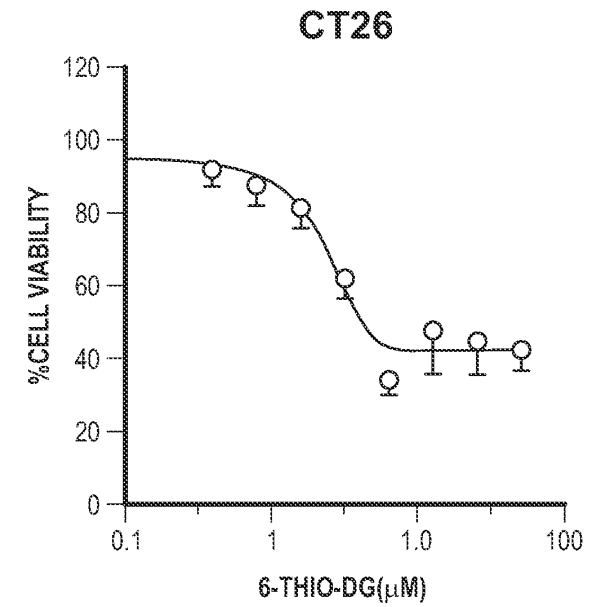

CT26
120
100
80
60
40
20
0
%CELL VIABILITY
0.1
1
1.0
100
6-THIO-DG(μM)

FIG. 9C

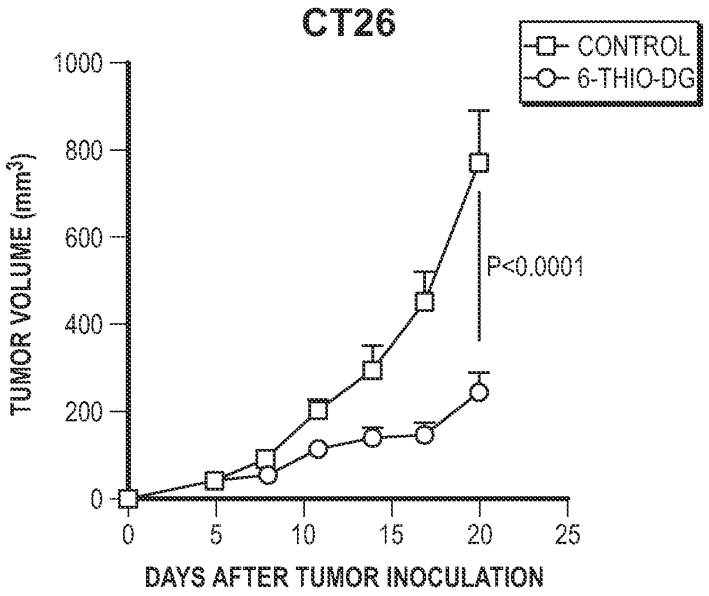

CT26
CONTROL
6-THIO-DG
1000
800
600
400
200
0
TUMOR VOLUME (mm3)
P<0.0001
0
5
10
15
20
25
DAYS AFTER TUMOR INOCULATION

FIG. 9D

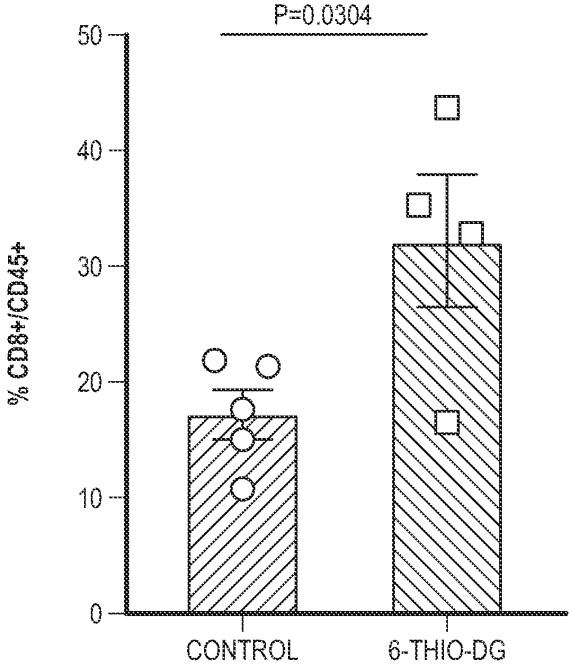


FIG. 10A

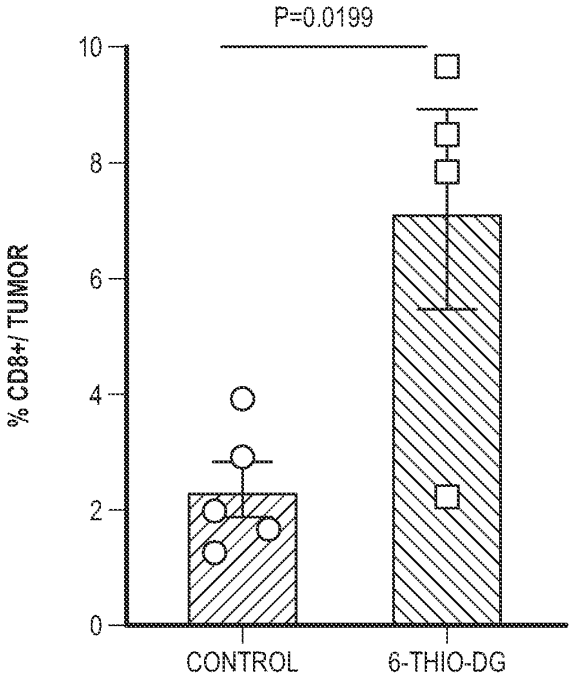


FIG. 10B

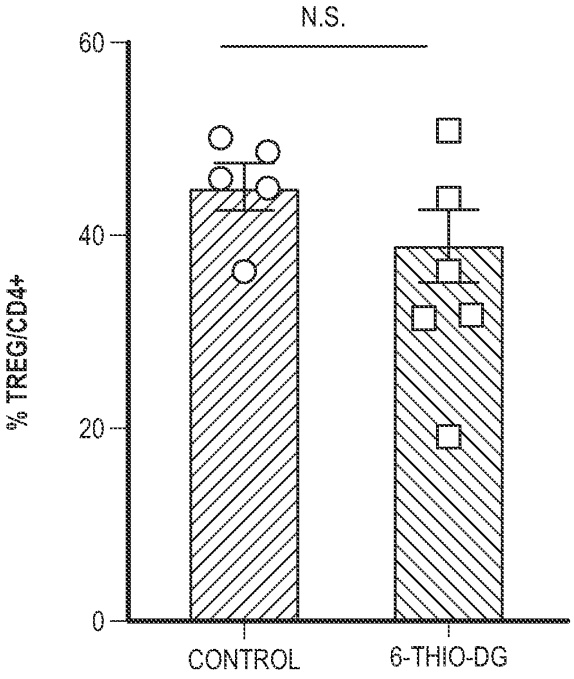


FIG. 10C

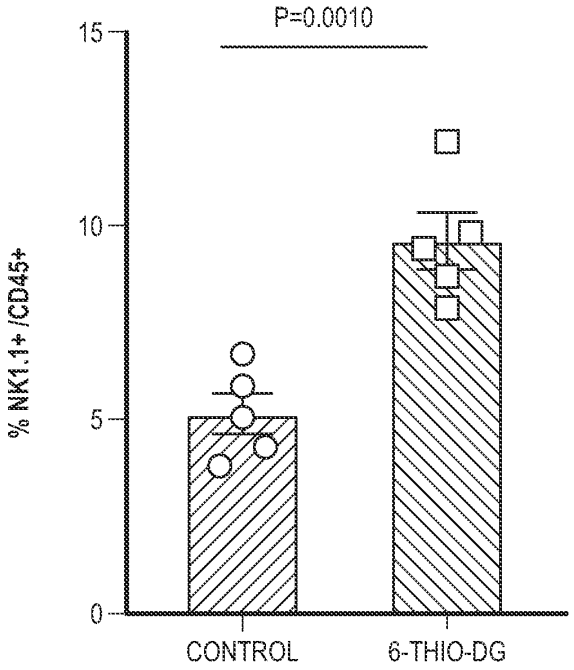


FIG. 10D

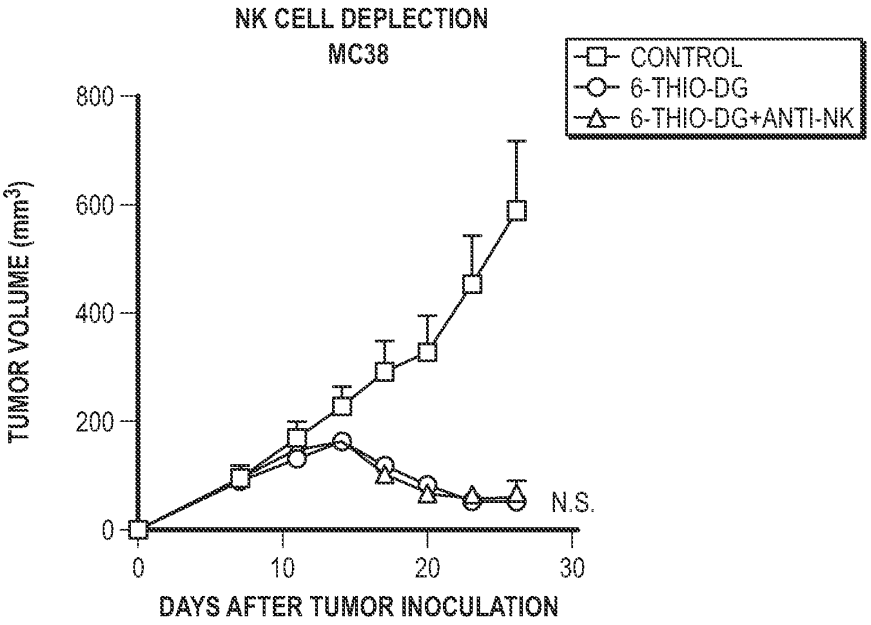

NK CELL DEPLECTION
MC38
CONTROL
6-THIO-DG
6-THIO-DG+ANTI-NK
TUMOR VOLUME (mm3)
800
600
400
200
0
N.S.
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 10E

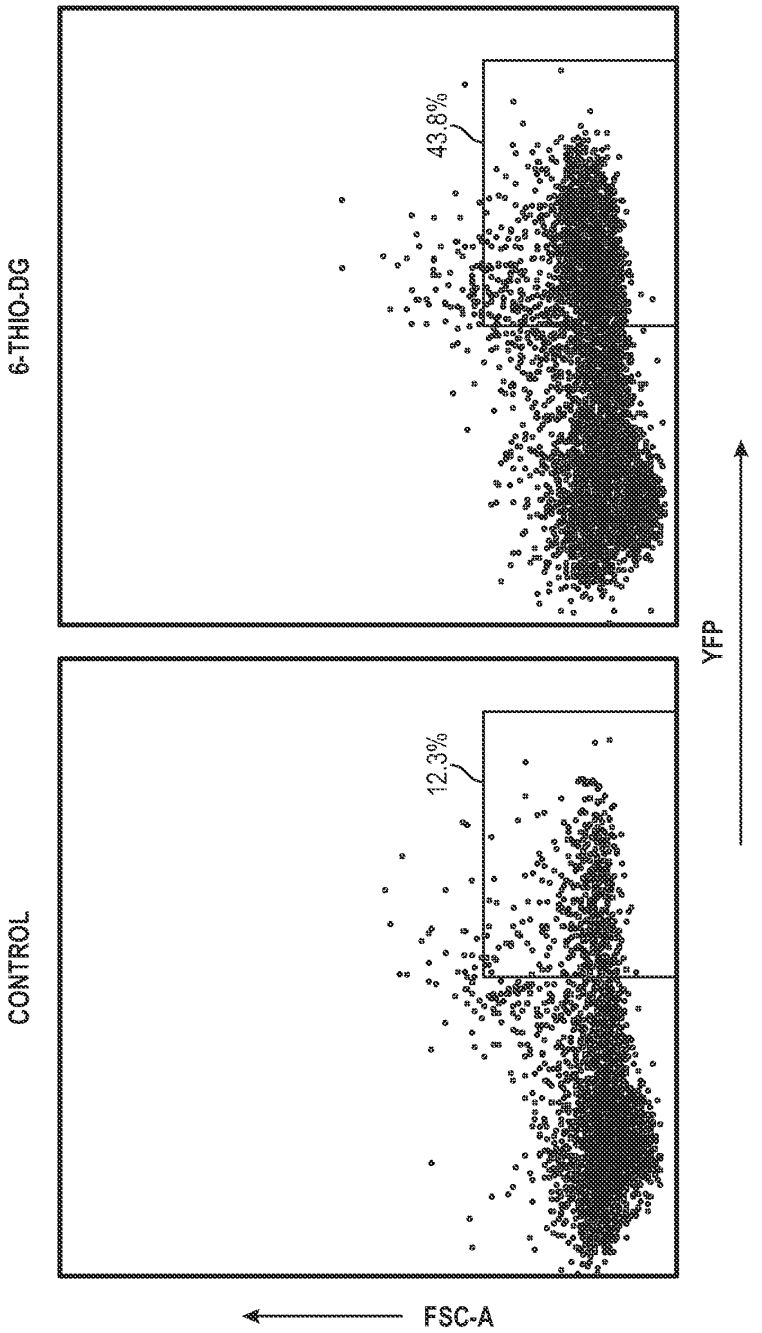


FIG. 10F

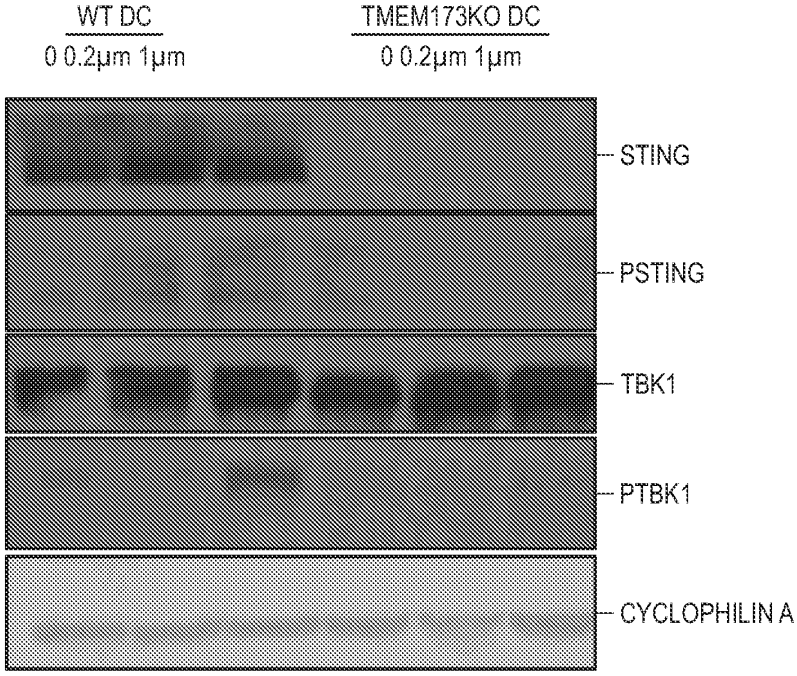


FIG. 11A

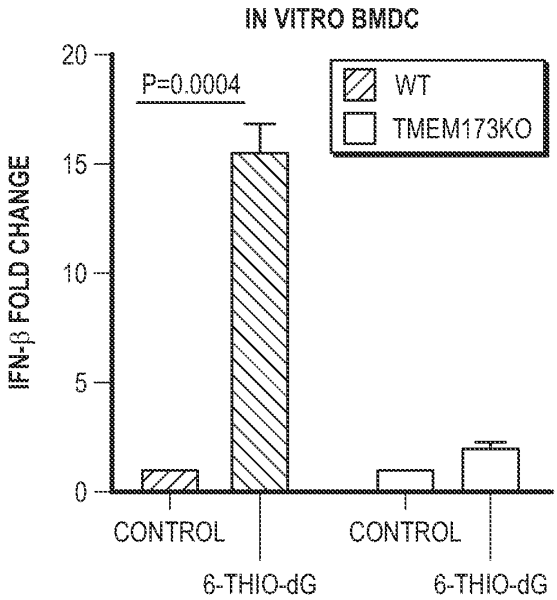


FIG. 11B

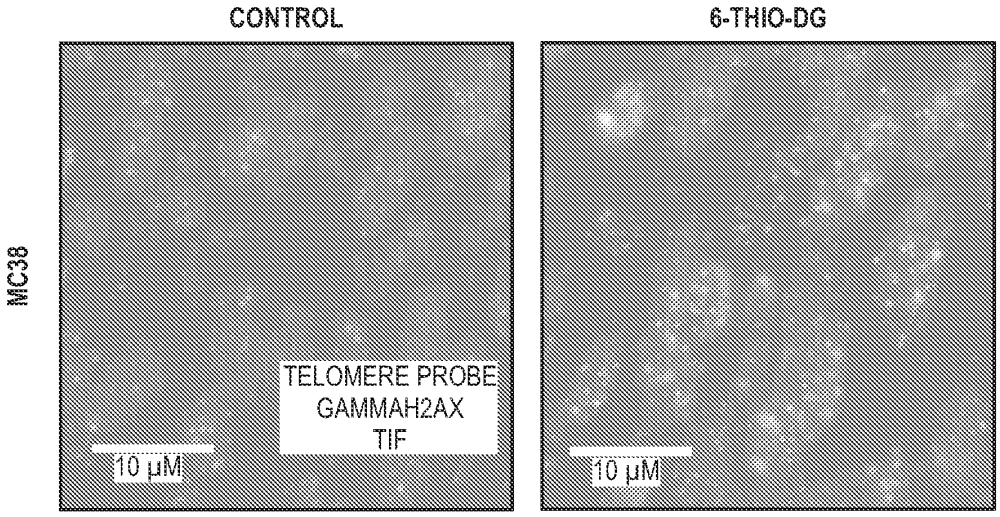


FIG. 11C

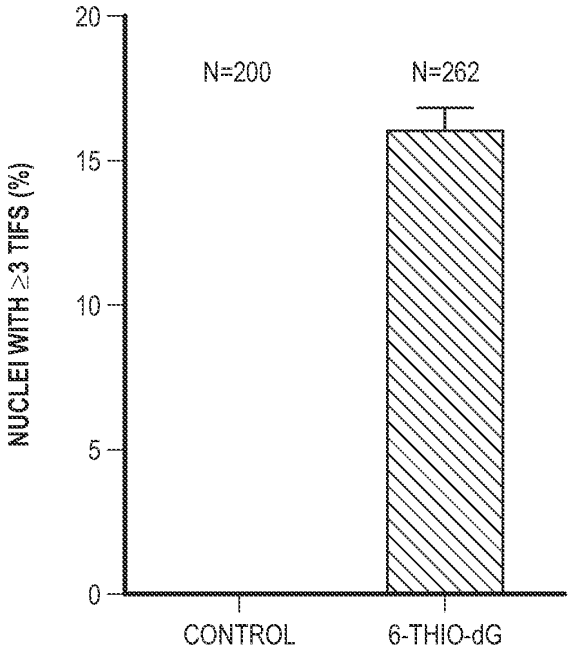


FIG. 11D

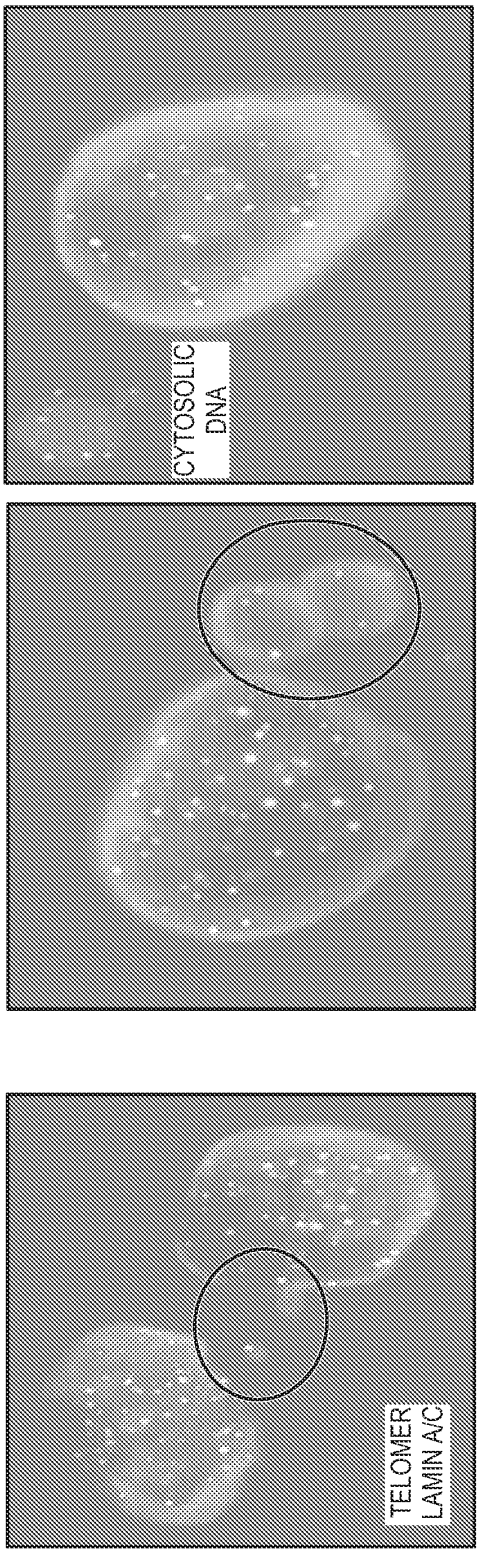


FIG. 11E

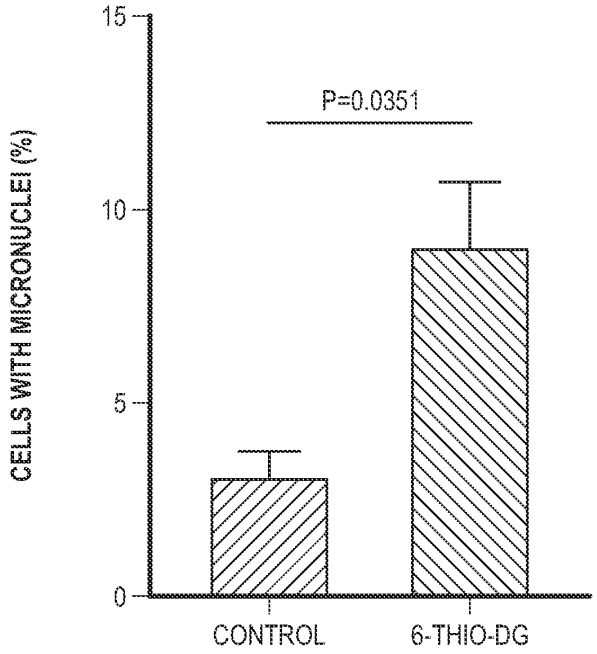


FIG. 11F

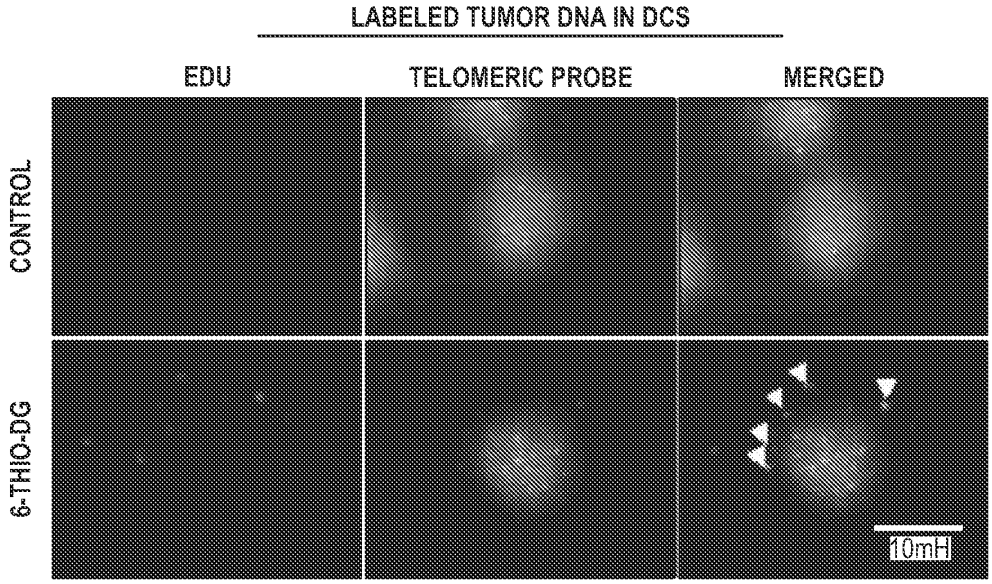


FIG. 11G

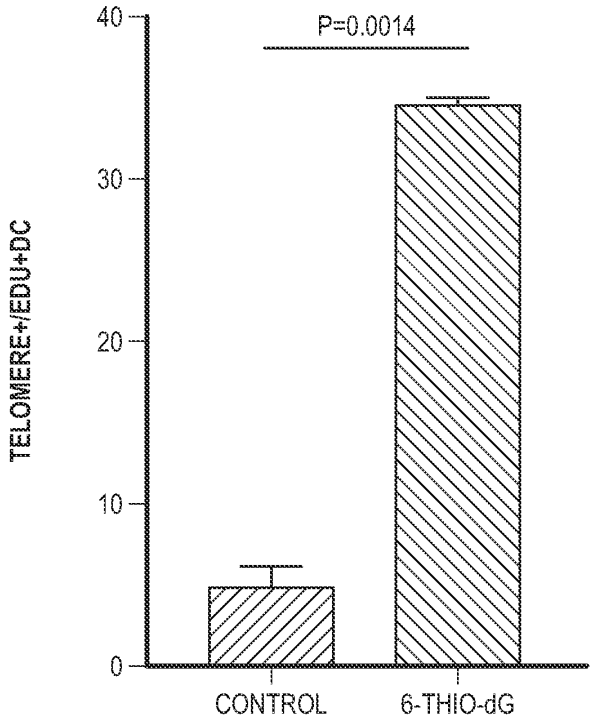


FIG. 11H

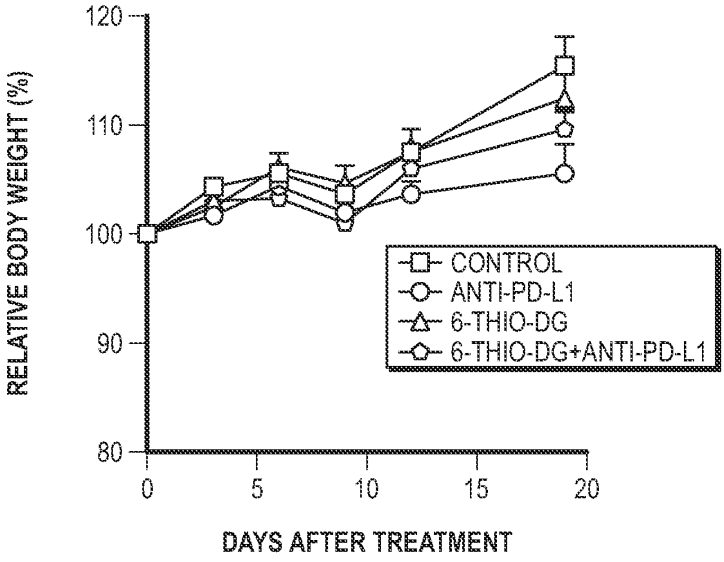


FIG. 12

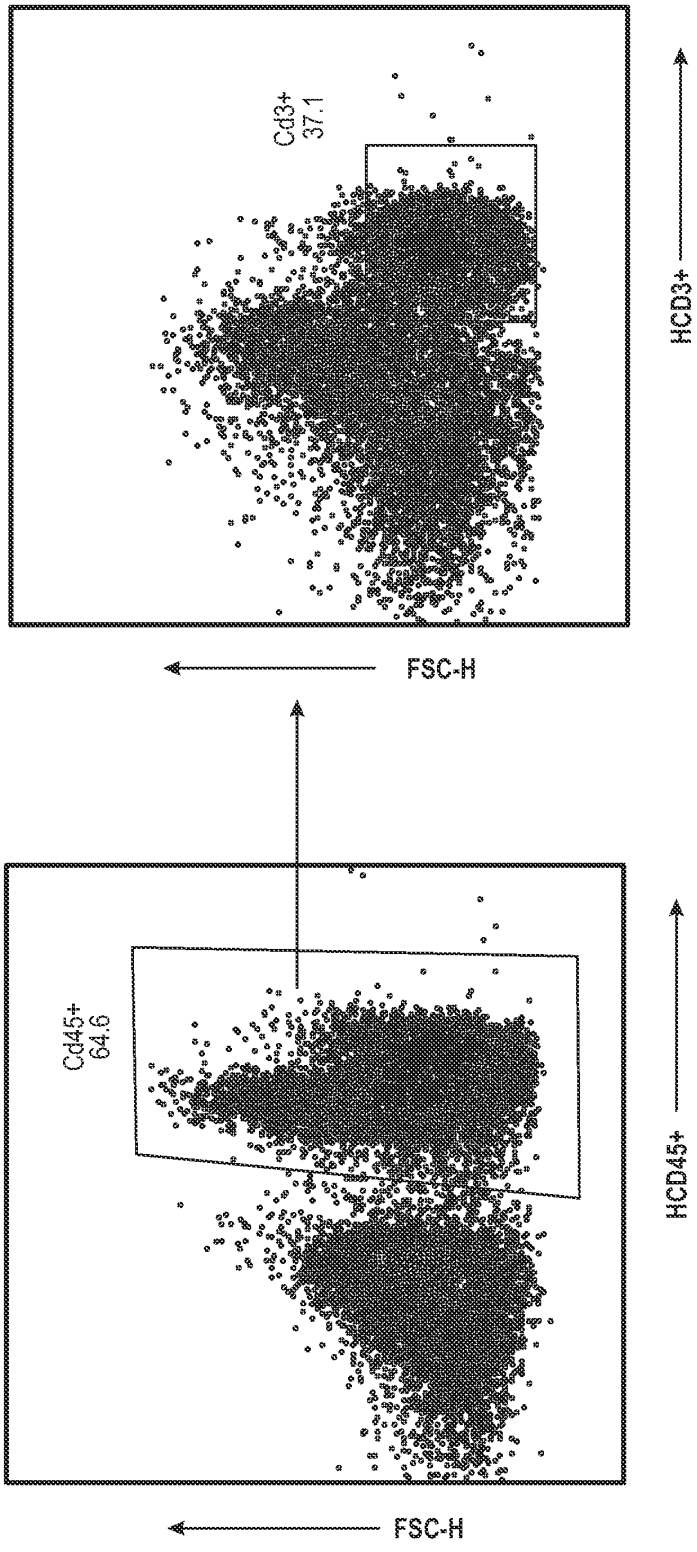


FIG. 13A

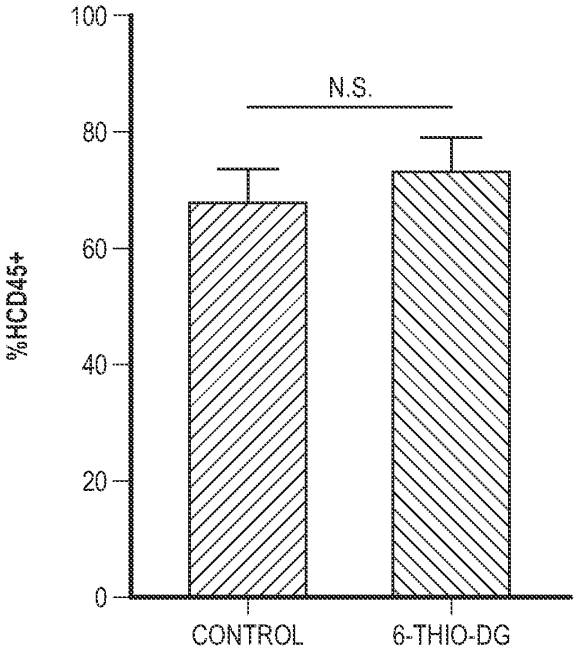


FIG. 13B

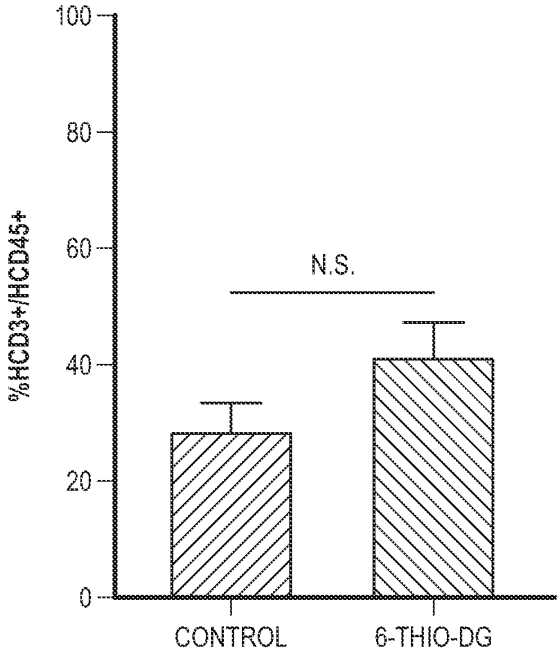


FIG. 13C

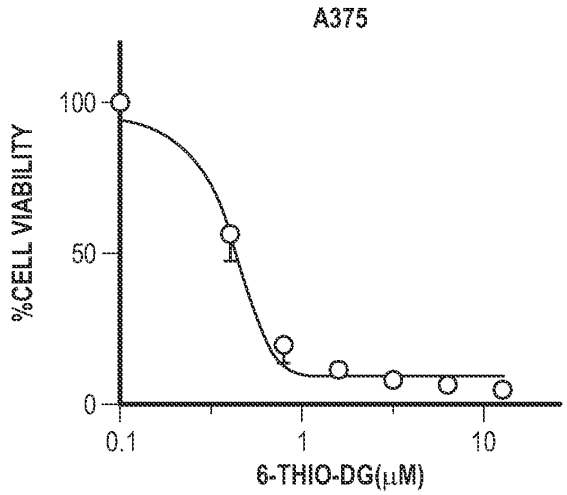


FIG. 13D

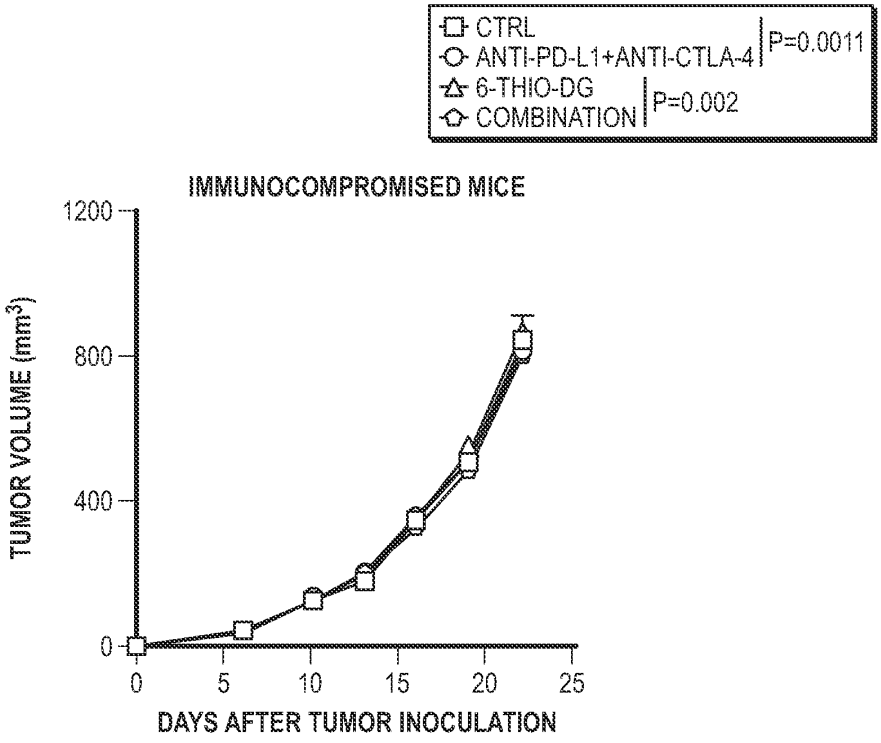


FIG. 13E

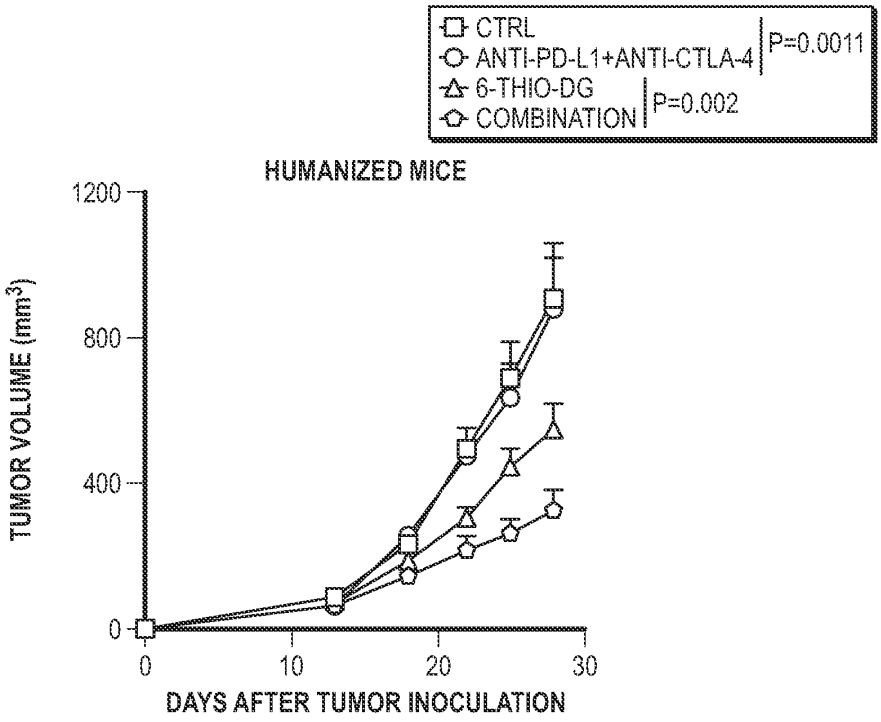

CTRL
ANTI-PD-L1+ANTI-CTLA-4
P=0.0011
6-THIO-DG
COMBINATION
P=0.002
HUMANIZED MICE
TUMOR VOLUME (mm3)
1200
800
400
0
0
10
20
30
DAYS AFTER TUMOR INOCULATION

FIG. 13F

COMBINATION OF 6-THIO-DG WITH ANTI-PD-1 AGENT CEMIPLIMAB (LIBTAYO)

	GROUP NAME	DAY 13	DAY 14	DAY 15	DAY 16	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21	DAY 22	DAY 23	DAY 24	DAY 25	DAY 26
GROUP 1	CONTROL														
GROUP 7	THIO	THIO	THIO	THIO				THIO	THIO	THIO					
GROUP 2	THIO+LIBTAYO	THIO	THIO	THIO		LIBTAYO		THIO	THIO	THIO		LIBTAYO			LIBTAYO

		DAY 11	DAY 12	DAY 13	DAY 14	DAY 15	DAY 16	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21	DAY 22	DAY 23	DAY 24	DAY 25	DAY 26
GROUP 3	THIO	THIO	THIO				THIO	THIO				THIO	THIO				
GROUP 4	LIBTAYO	LIBTAYO				LIBTAYO				LIBTAYO			LIBTAYO			LIBTAYO	
GROUP 5	THIO/LIBTAYO	THIO	THIO/LIBTAYO				THIO	THIO/LIBTAYO				THIO	THIO/LIBTAYO				
GROUP 6	THIO+LIBTAYO	THIO	THIO		LIBTAYO		THIO	THIO		LIBTAYO		THIO	THIO		LIBTAYO		

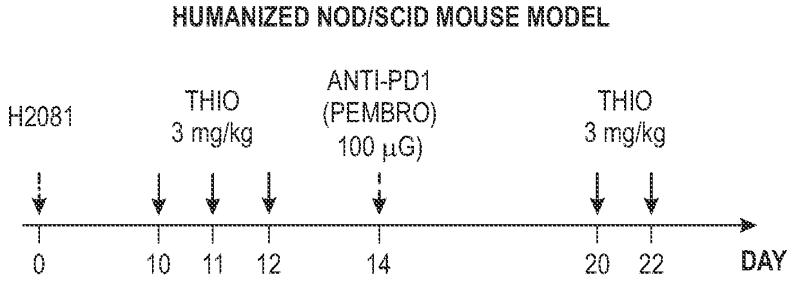
FIG. 14

COMBINATION OF 6-THIO-DG WITH ANTI-PD-1 AGENT CEMIPLIMAB (LIBTAYO)

	GROUP NAME	DAY 13	DAY 14	DAY 15	DAY 16	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21	DAY 22	DAY 23	DAY 24	DAY 25	DAY 26
GROUP 1	CONTROL														
GROUP 7	THIO	THIO	THIO	THIO				THIO	THIO	THIO					
GROUP 2	THIO+LIBTAYO	THIO	THIO	THIO		LIBTAYO		THIO	THIO	THIO		LIBTAYO			LIBTAYO

		DAY 11	DAY 12	DAY 13	DAY 14	DAY 15	DAY 16	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21	DAY 22	DAY 23	DAY 24	DAY 25	DAY 26
GROUP 3	THIO	THIO	THIO				THIO	THIO				THIO	THIO				
GROUP 4	LIBTAYO	LIBTAYO				LIBTAYO				LIBTAYO			LIBTAYO			LIBTAYO	
GROUP 5	THIO/LIBTAYO	THIO	THIO/LIBTAYO				THIO	THIO/LIBTAYO				THIO	THIO/LIBTAYO				
GROUP 6	THIO+LIBTAYO	THIO	THIO		LIBTAYO		THIO	THIO		LIBTAYO		THIO	THIO		LIBTAYO		

FIG. 15


HUMANIZED NOD/SCID MOUSE MODEL
H2081
THIO
3 mg/kg
ANTI-PD1
(PEMBRO)
100 μG)
THIO
3 mg/kg
0
10
11
12
14
20
22
DAY

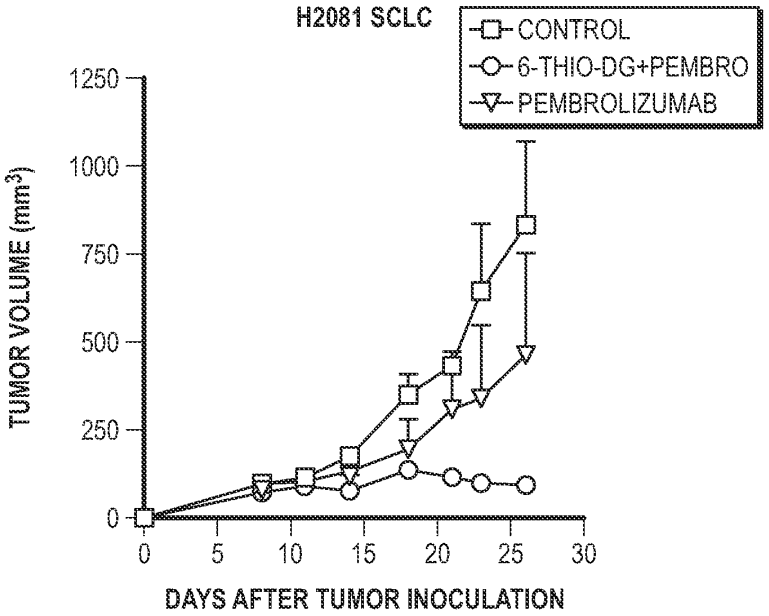

H2081 SCLC
CONTROL
6-THIO-DG+PEMBRO
PEMBROLIZUMAB
TUMOR VOLUME (mm3)
1250
1000
750
500
250
0
0
5
10
15
20
25
30
DAYS AFTER TUMOR INOCULATION

FIG. 16

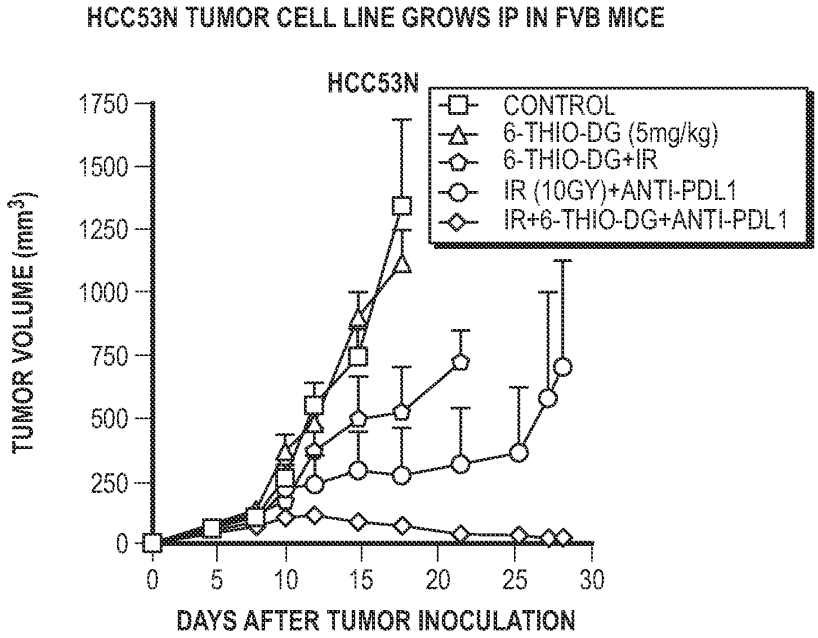

HCC53N TUMOR CELL LINE GROWS IP IN FVB MICE
HCC53N
CONTROL
6-THIO-DG (5mg/kg)
6-THIO-DG+IR
IR (10GY)+ANTI-PDL1
IR+6-THIO-DG+ANTI-PDL1
TUMOR VOLUME (mm3)
1750
1500
1250
1000
750
500
250
0
0
5
10
15
20
25
30
DAYS AFTER TUMOR INOCULATION

FIG. 17

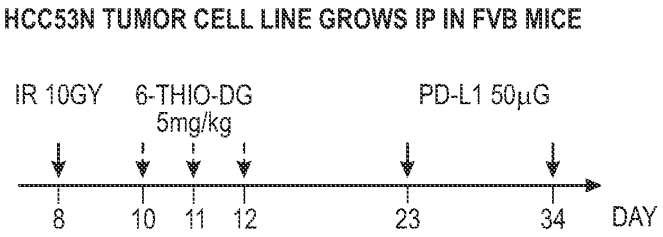


FIG. 18A

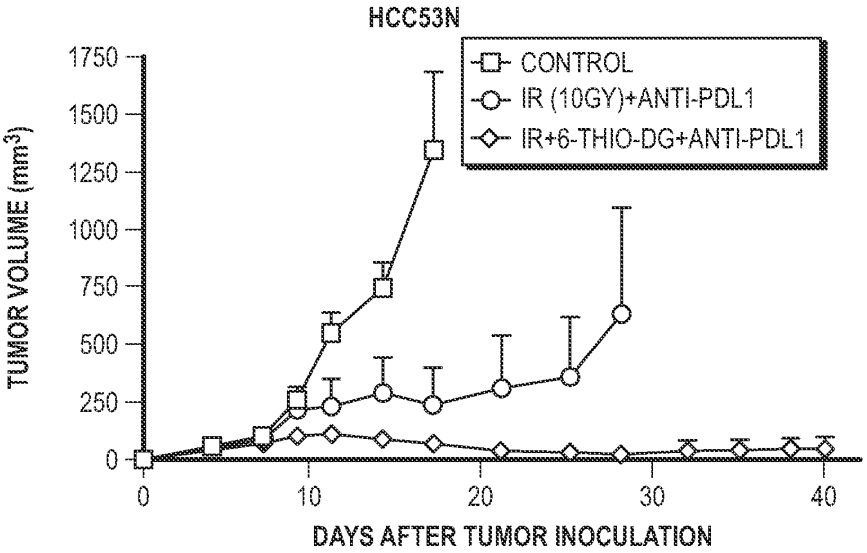


FIG. 18B

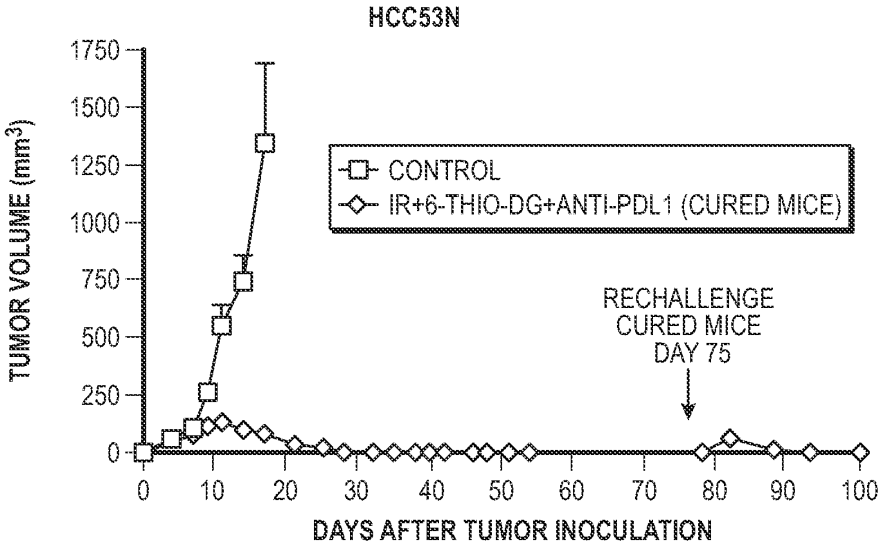


FIG. 18C

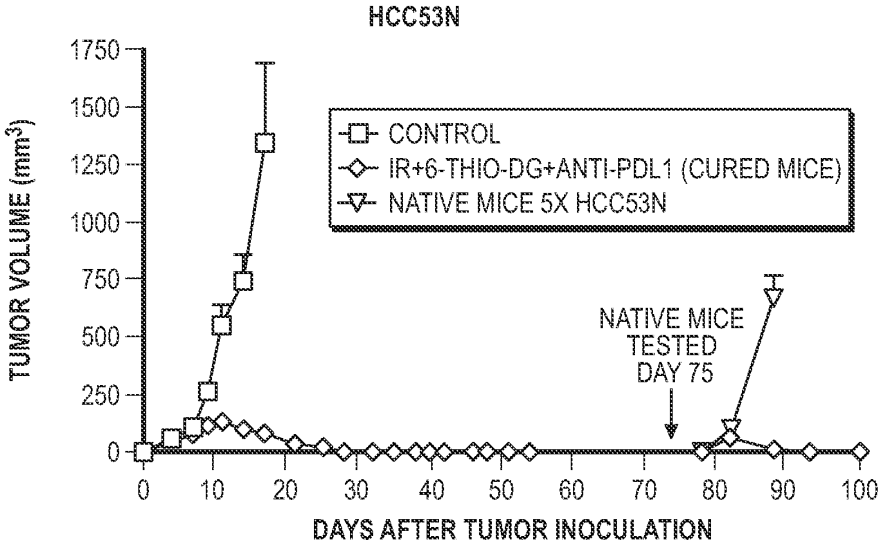


FIG. 18D