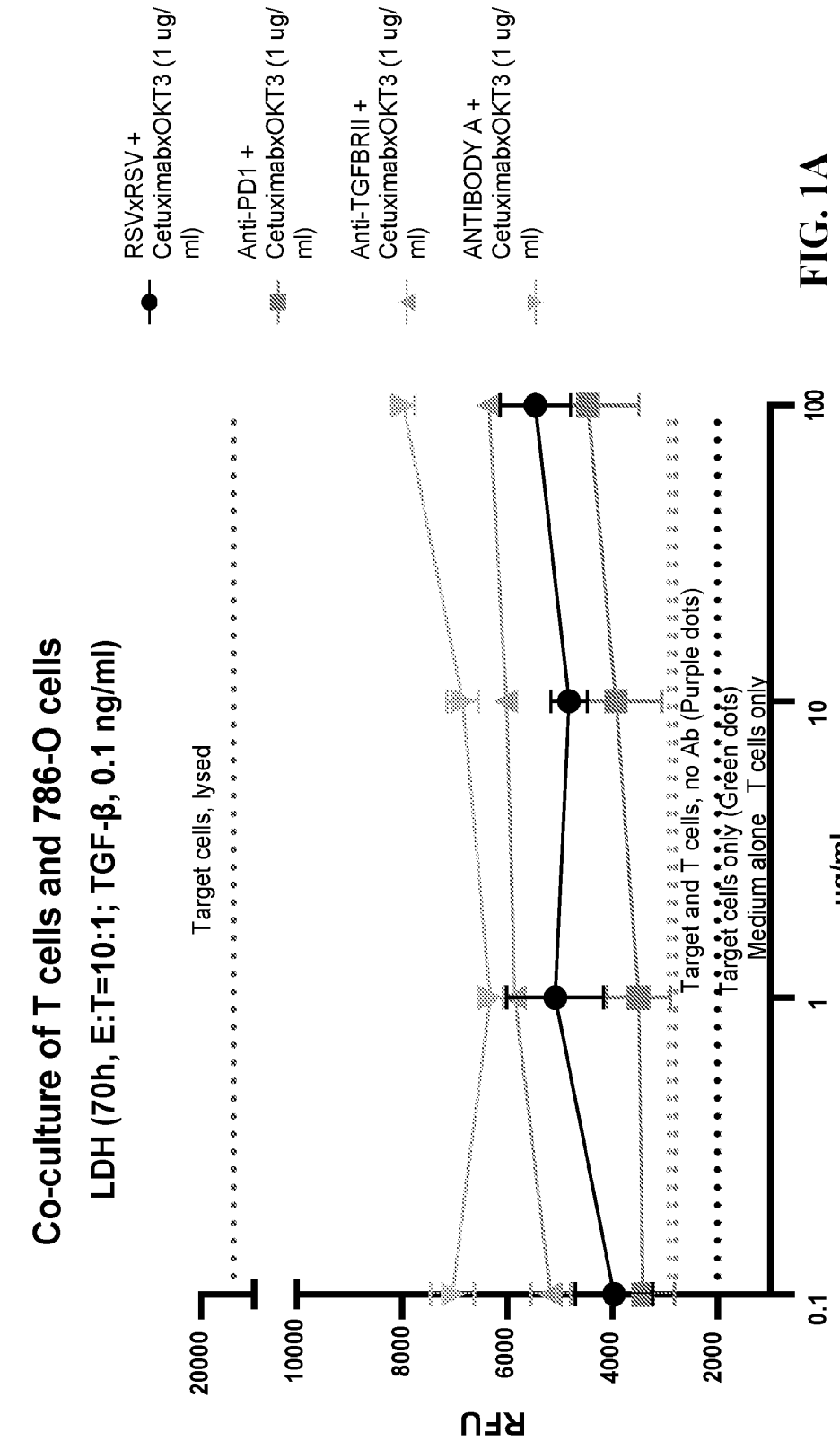
Co-culture of T cells and 786-O cells
LDH (70h, E:T=10:1; TGF-β, 0.1 ng/ml)
RSVxRSV + CetuximabxOKT3 (1 ug/ml)
Anti-PD1 + CetuximabxOKT3 (1 ug/ml)
Anti-TGFBRII + CetuximabxOKT3 (1 ug/ml)
ANTIBODY A + CetuximabxOKT3 (1 ug/ml)
Target cells, lysed
Target and T cells, no Ab (Purple dots)
Target cells only (Green dots)
Medium alone T cells only
RFU
20000
10000
8000
6000
4000
2000
0.1
1
10
100
µg/ml

FIG. 1A

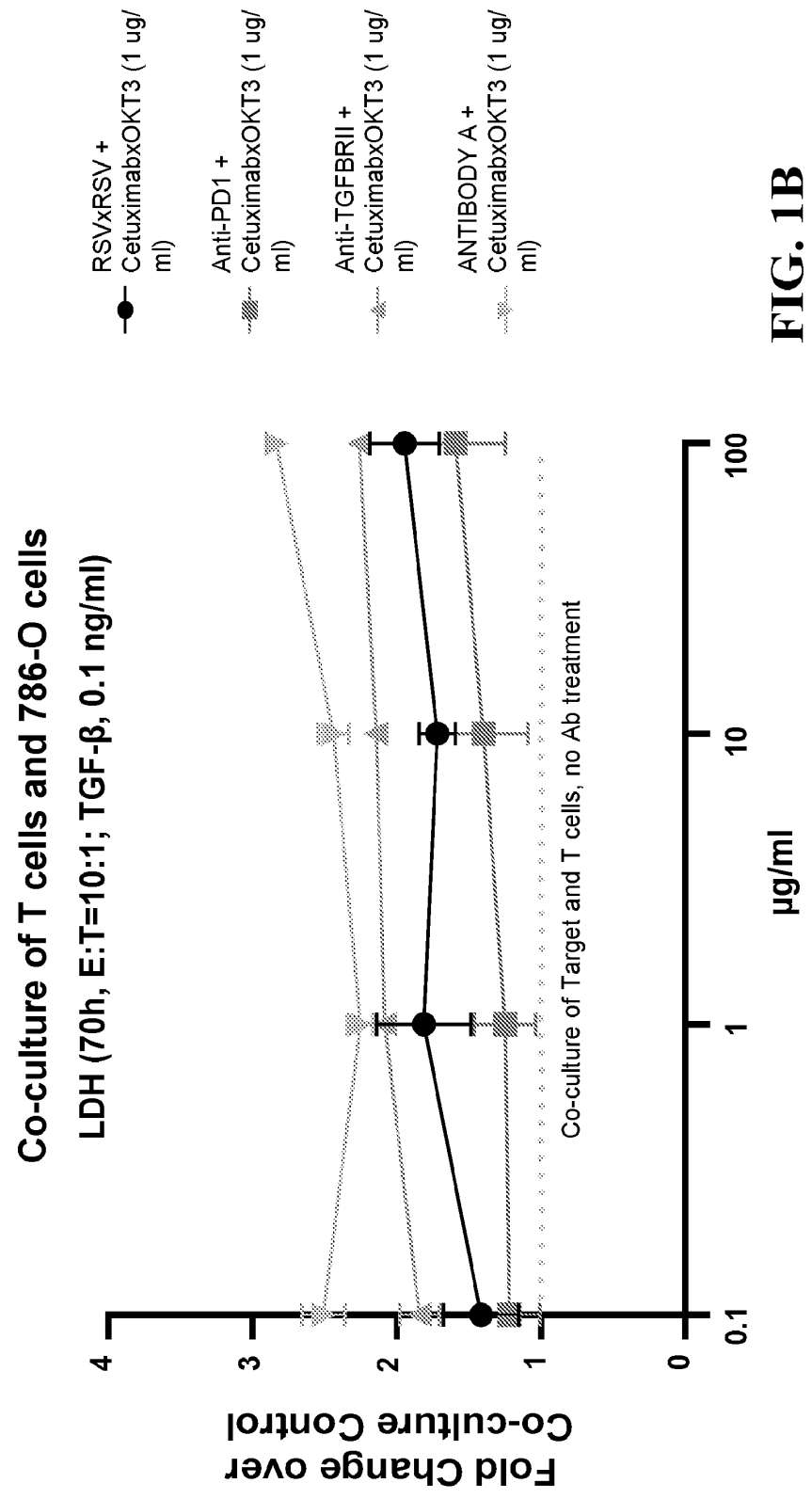
Co-culture of T cells and 786-O cells
LDH (70h, E:T=10:1; TGF-β, 0.1 ng/ml)
RSVxRSV + CetuximabxOKT3 (1 ug/ml)
Anti-PD1 + CetuximabxOKT3 (1 ug/ml)
Anti-TGFBRII + CetuximabxOKT3 (1 ug/ml)
ANTIBODY A + CetuximabxOKT3 (1 ug/ml)
Fold Change over Co-culture Control
Co-culture of Target and T cells, no Ab treatment
µg/ml
0.1
1
10
100
0
1
2
3
4

FIG. 1B

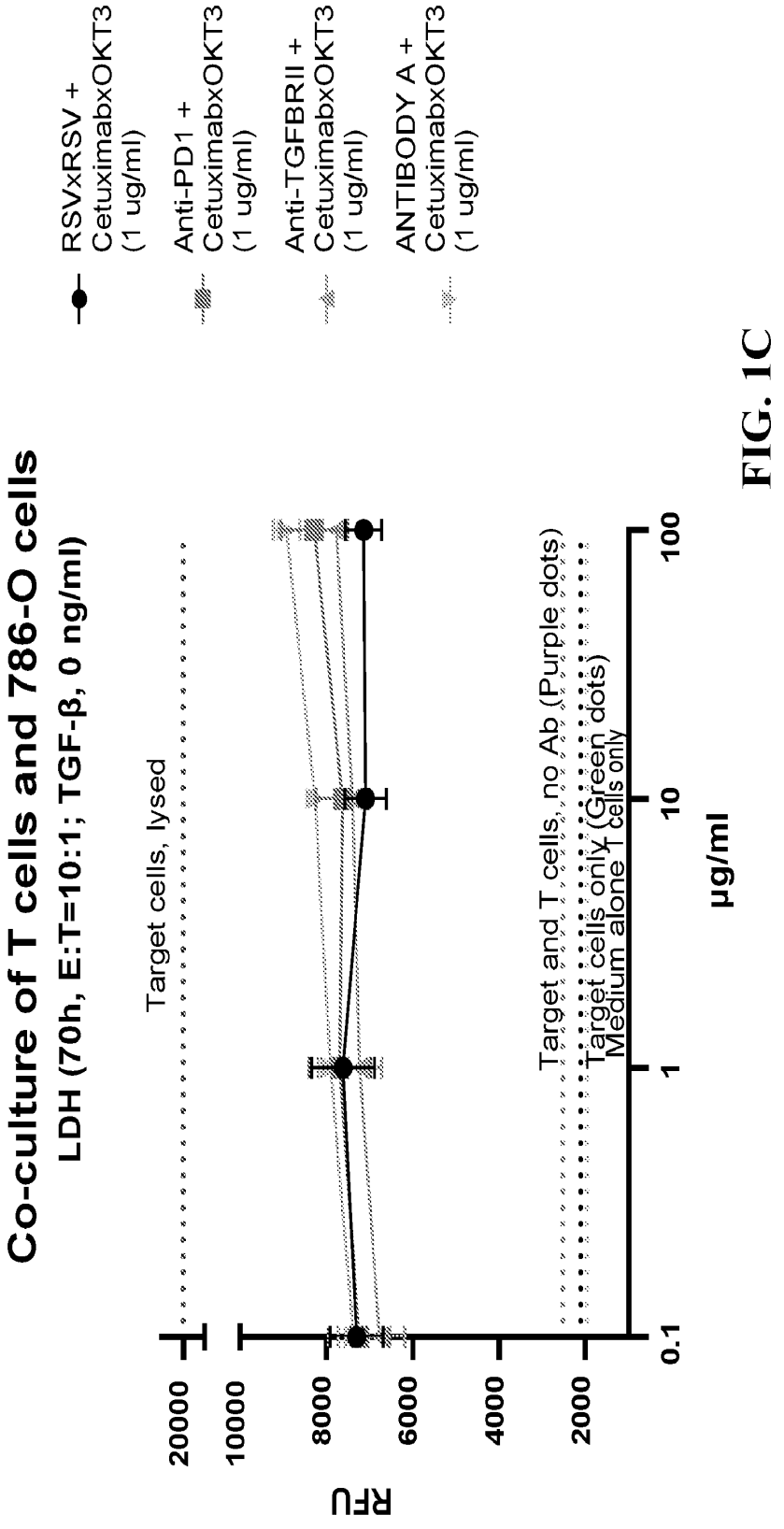
Co-culture of T cells and 786-O cells
LDH (70h, E:T=10:1; TGF-β, 0 ng/ml)
RSVxRSV + CetuximabxOKT3 (1 ug/ml)
Anti-PD1 + CetuximabxOKT3 (1 ug/ml)
Anti-TGFBRII + CetuximabxOKT3 (1 ug/ml)
ANTIBODY A + CetuximabxOKT3 (1 ug/ml)
Target cells, lysed
Target and T cells, no Ab (Purple dots)
Target cells only (Green dots)
Medium alone T cells only
RFU
20000
10000
8000
6000
4000
2000
0.1
1
10
100
µg/ml

FIG. 1C

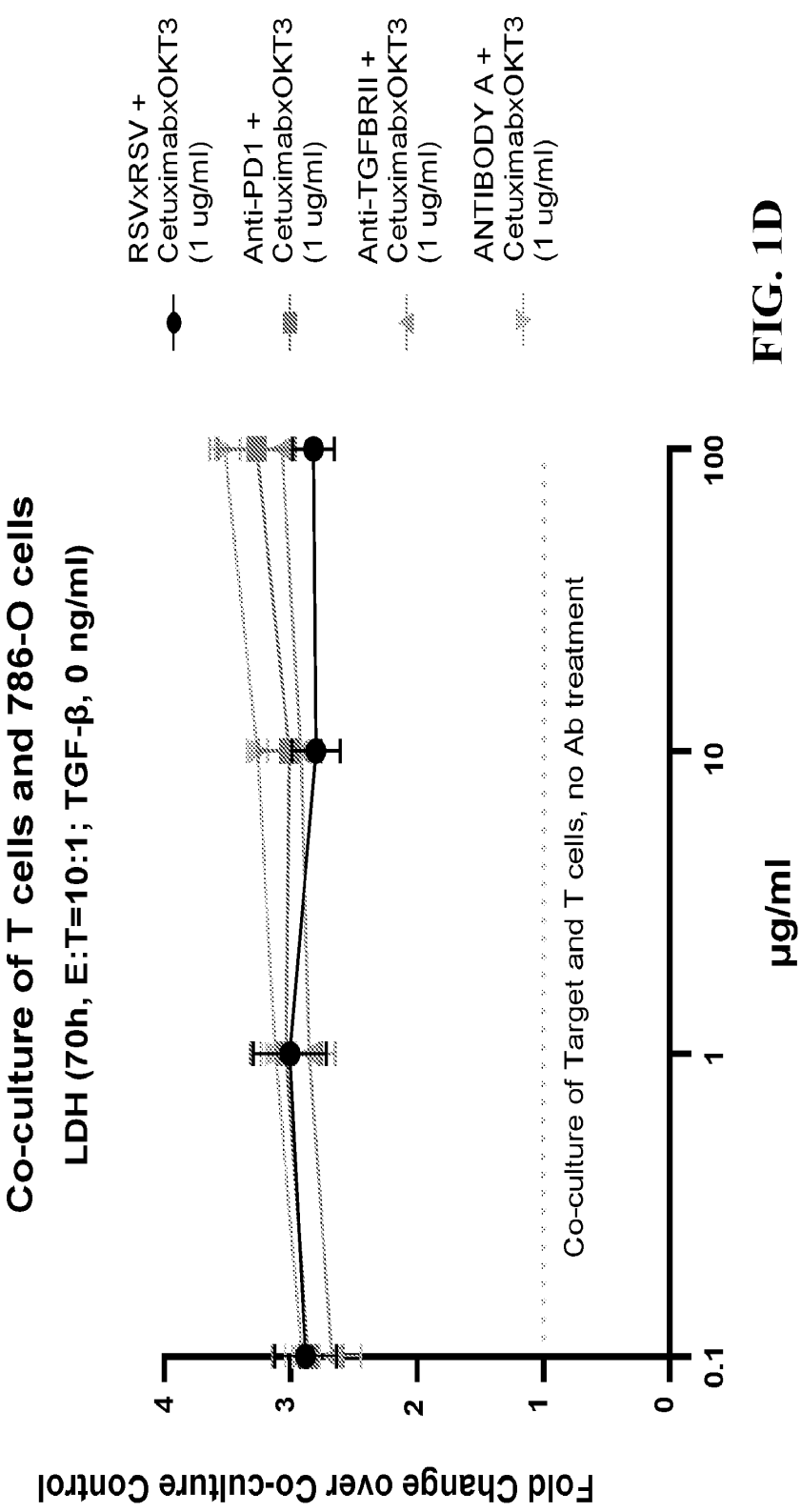
Co-culture of T cells and 786-O cells
LDH (70h, E:T=10:1; TGF-β, 0 ng/ml)
RSVxRSV + CetuximabxOKT3 (1 ug/ml)
Anti-PD1 + CetuximabxOKT3 (1 ug/ml)
Anti-TGFBRII + CetuximabxOKT3 (1 ug/ml)
ANTIBODY A + CetuximabxOKT3 (1 ug/ml)
Co-culture of Target and T cells, no Ab treatment
Fold Change over Co-culture Control
0
1
2
3
4
0.1
1
10
100
µg/ml

FIG. 1D

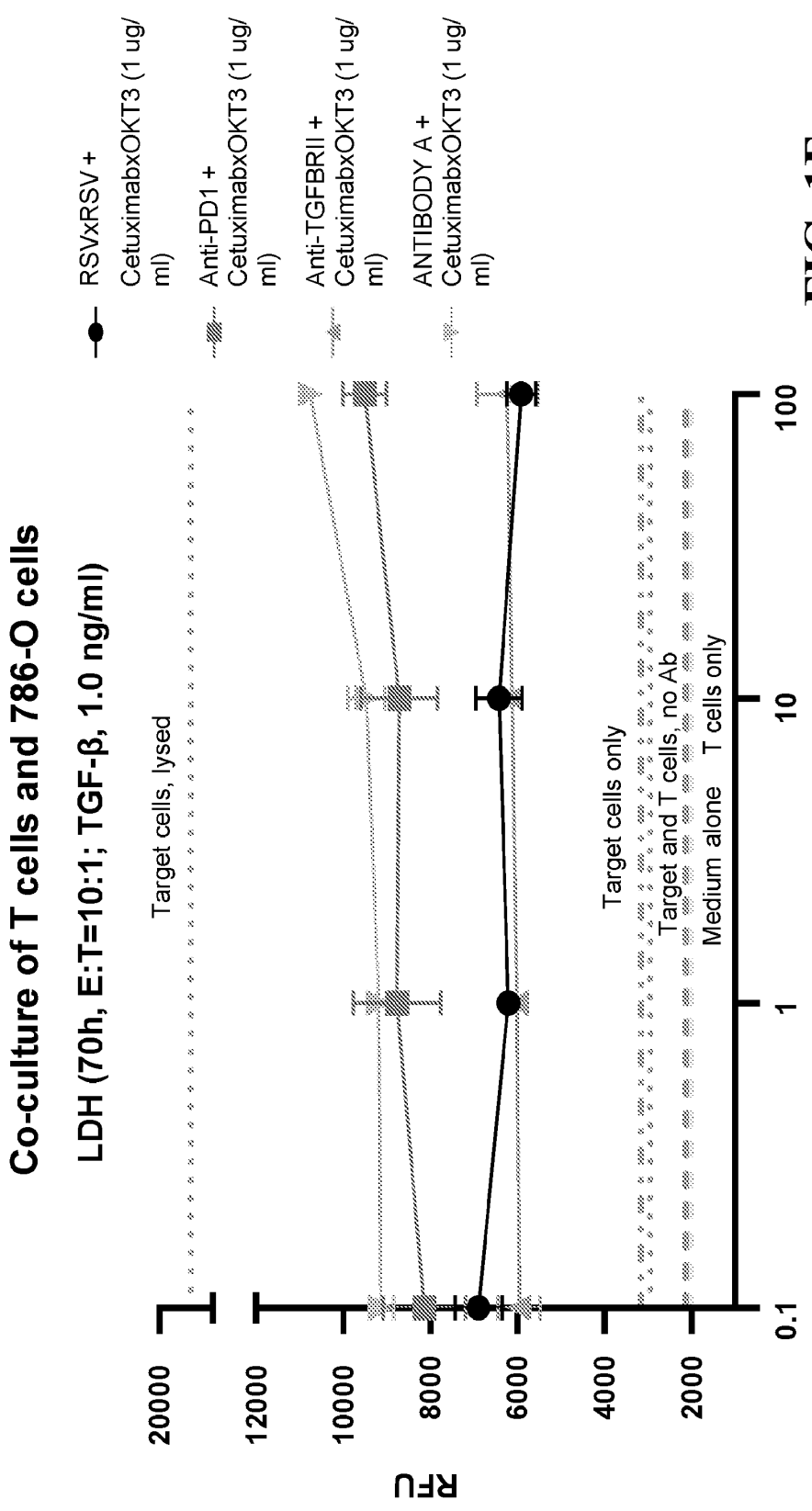
Co-culture of T cells and 786-O cells
LDH (70h, E:T=10:1; TGF-β, 1.0 ng/ml)
RSVxRSV + CetuximabxOKT3 (1 ug/ml)
Anti-PD1 + CetuximabxOKT3 (1 ug/ml)
Anti-TGFBRII + CetuximabxOKT3 (1 ug/ml)
ANTIBODY A + CetuximabxOKT3 (1 ug/ml)
Target cells, lysed
Target cells only
Target and T cells, no Ab
Medium alone T cells only
RFU
20000
12000
10000
8000
6000
4000
2000
0.1
1
10
100
µg/ml

FIG. 1E

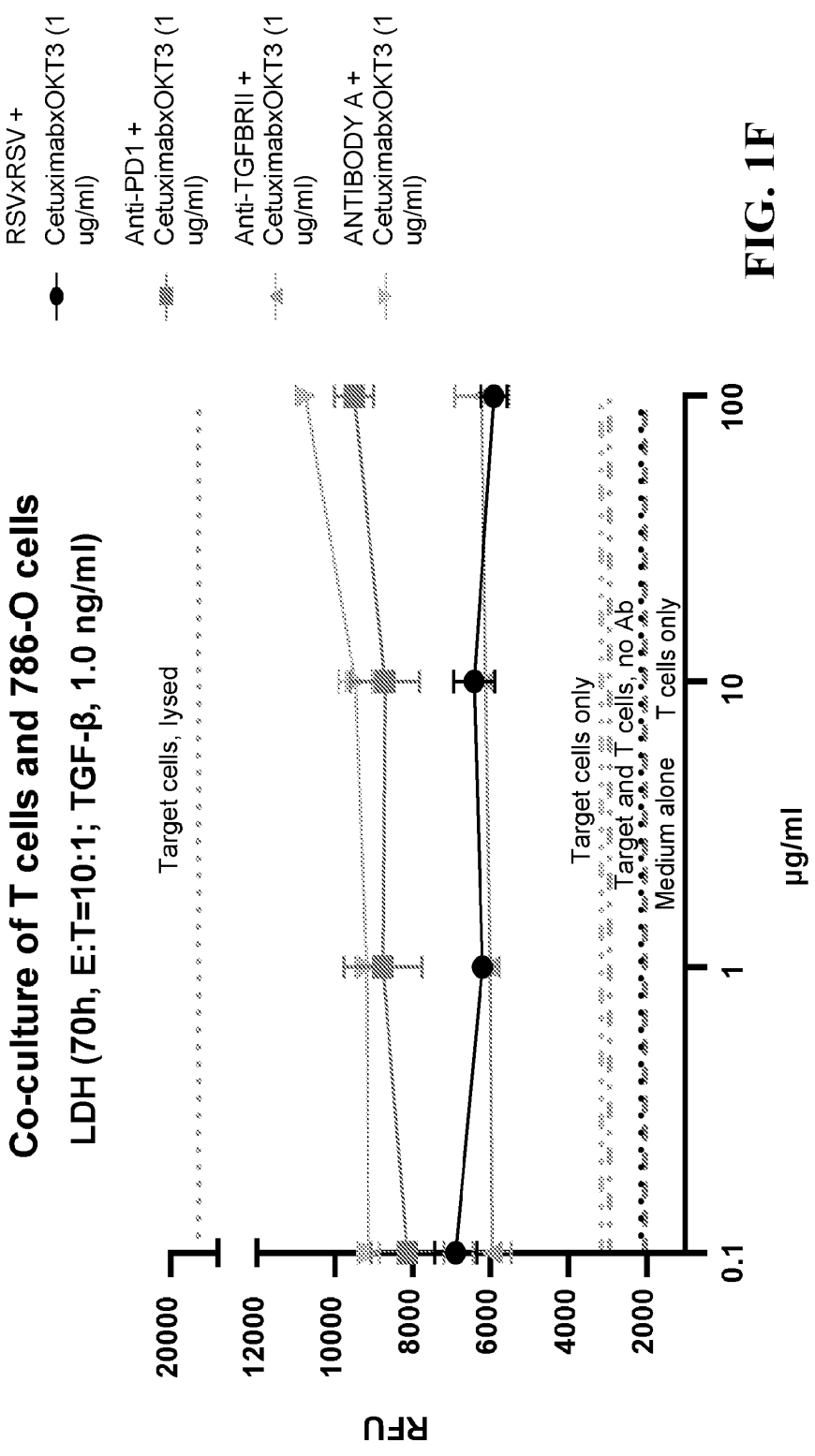
Co-culture of T cells and 786-O cells
LDH (70h, E:T=10:1; TGF-β, 1.0 ng/ml)
RSVxRSV + CetuximabxOKT3 (1 ug/ml)
Anti-PD1 + CetuximabxOKT3 (1 ug/ml)
Anti-TGFBRII + CetuximabxOKT3 (1 ug/ml)
ANTIBODY A + CetuximabxOKT3 (1 ug/ml)
Target cells, lysed
Target cells only
Target and T cells, no Ab
Medium alone T cells only
RFU
20000
12000
10000
8000
6000
4000
2000
0.1
1
10
100
µg/ml

FIG. 1F

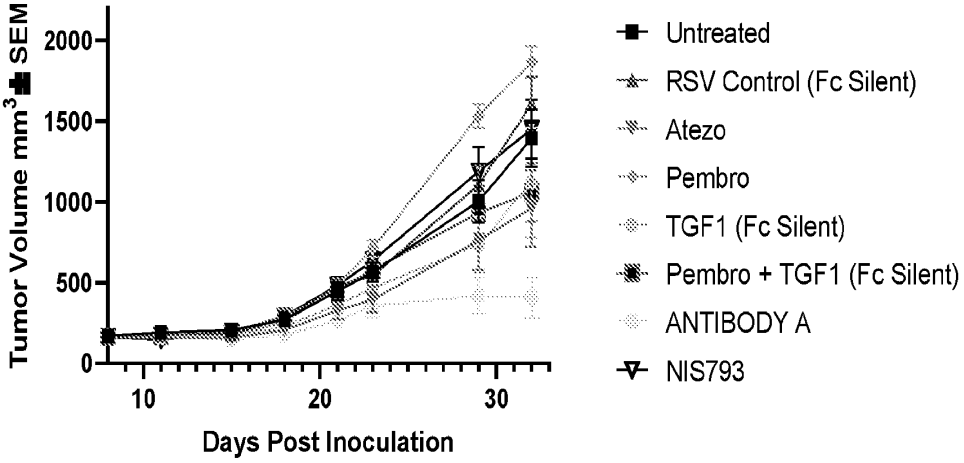
Tumor Volume mm3 ± SEM
2000
1500
1000
500
0
10
20
30
Days Post Inoculation
Untreated
RSV Control (Fc Silent)
Atezo
Pembro
TGF1 (Fc Silent)
Pembro + TGF1 (Fc Silent)
ANTIBODY A
NIS793

FIG. 2A

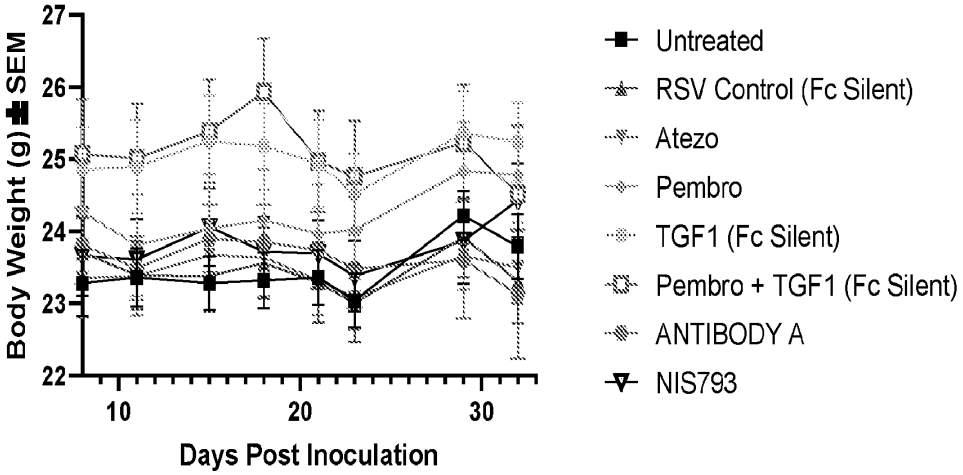
Body Weight (g) ± SEM
27
26
25
24
23
22
10
20
30
Days Post Inoculation
Untreated
RSV Control (Fc Silent)
Atezo
Pembro
TGF1 (Fc Silent)
Pembro + TGF1 (Fc Silent)
ANTIBODY A
NIS793

FIG. 2B

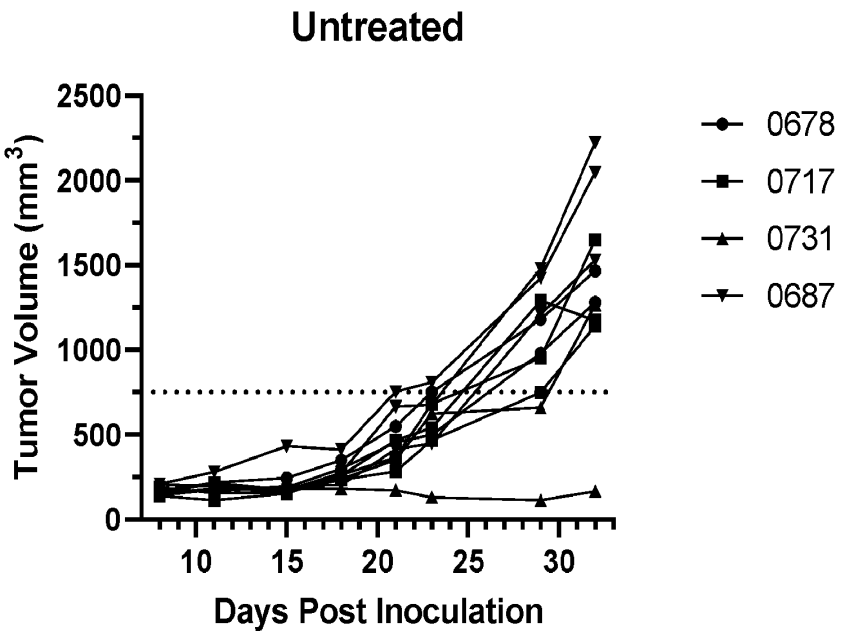
Untreated
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
15
20
25
30
Days Post Inoculation
0678
0717
0731
0687

FIG. 3A

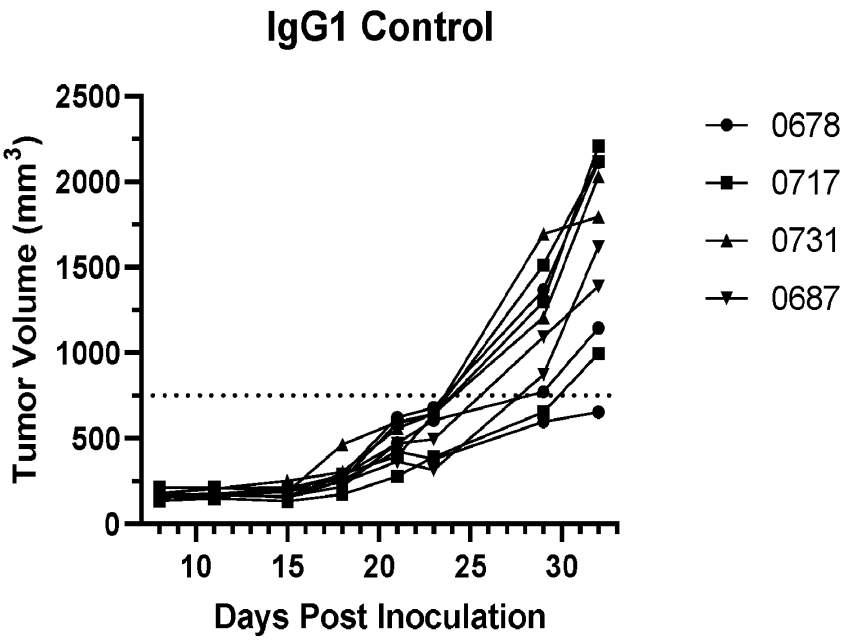
IgG1 Control
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
15
20
25
30
Days Post Inoculation
0678
0717
0731
0687

FIG. 3B

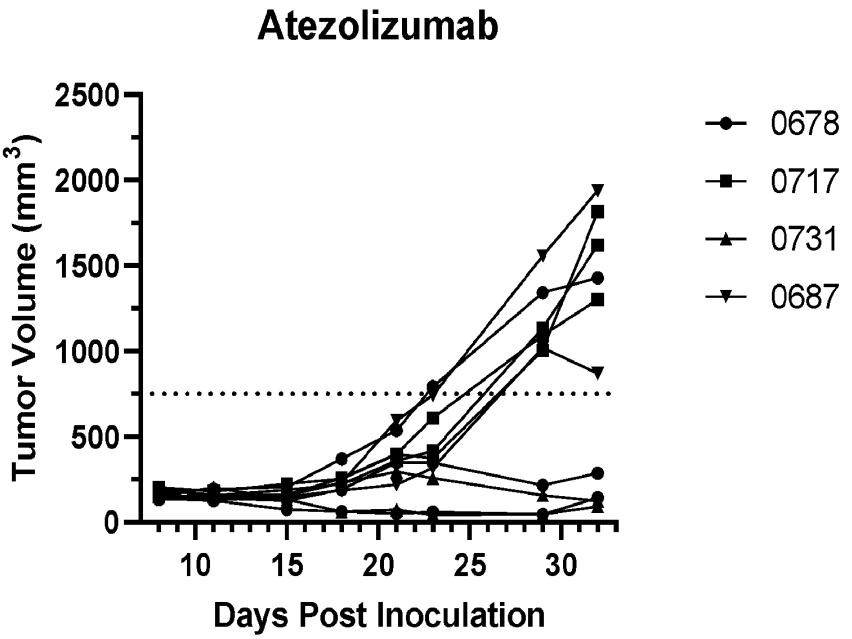
Atezolizumab
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
15
20
25
30
Days Post Inoculation
0678
0717
0731
0687

FIG. 3C

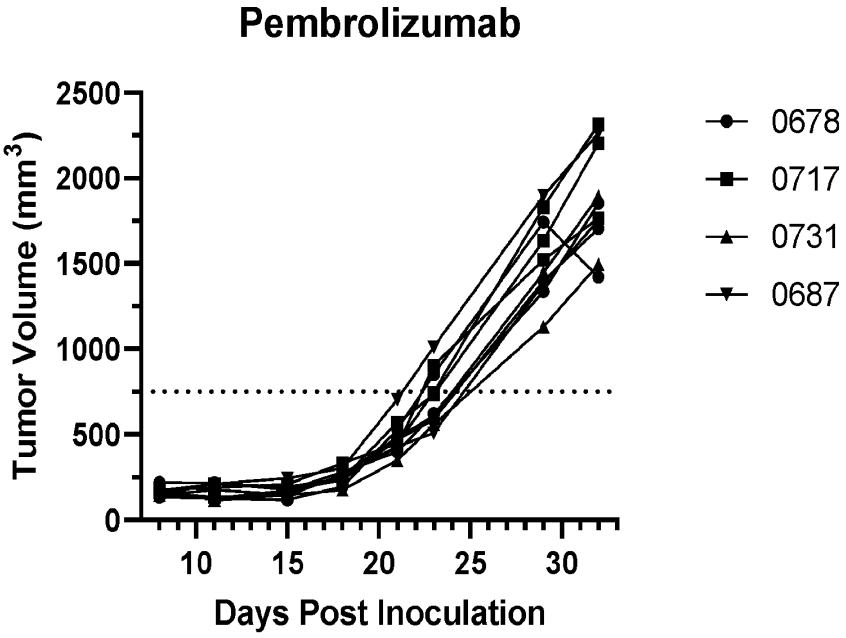
Pembrolizumab
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
15
20
25
30
Days Post Inoculation
0678
0717
0731
0687

FIG. 3D

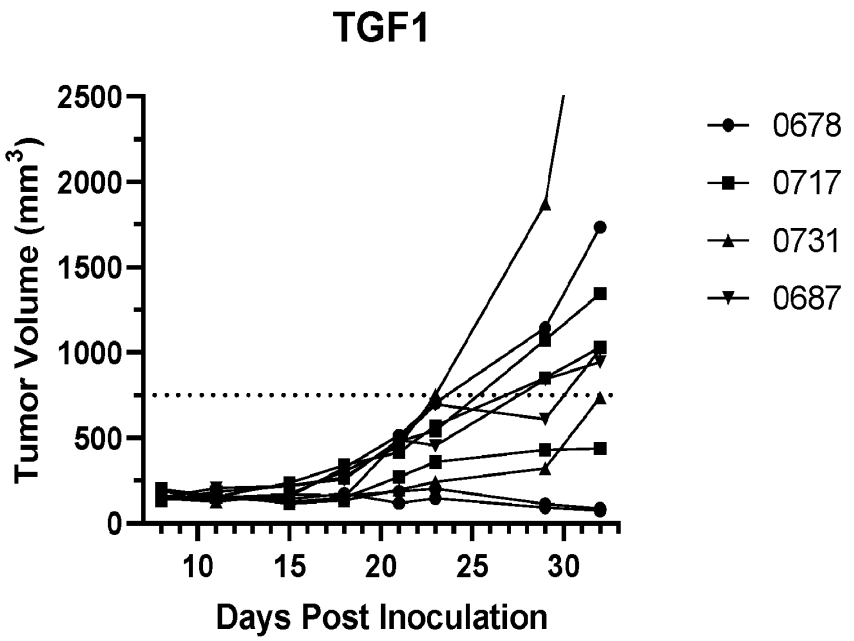
TGF1
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
15
20
25
30
Days Post Inoculation
0678
0717
0731
0687

FIG. 3E

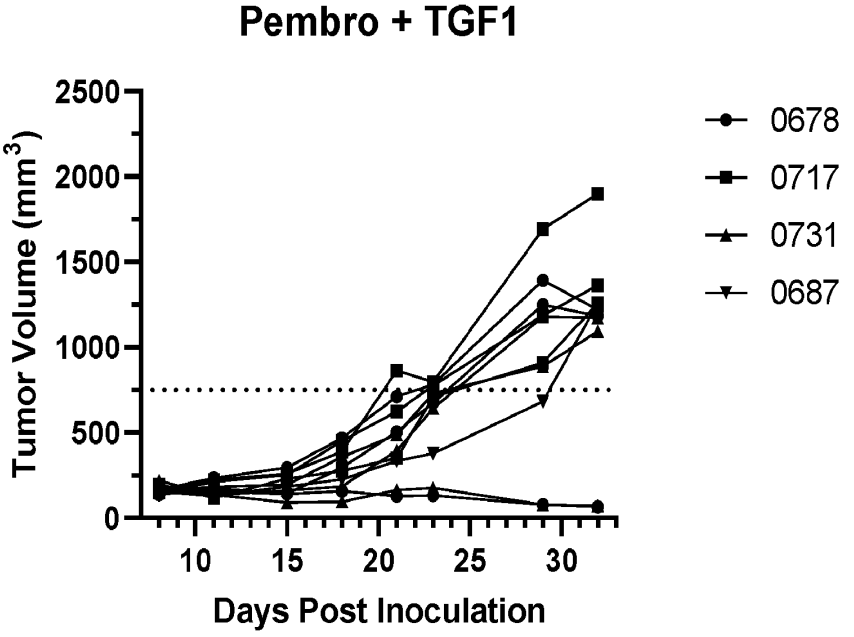
Pembro + TGF1
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
15
20
25
30
Days Post Inoculation
0678
0717
0731
0687

FIG. 3F

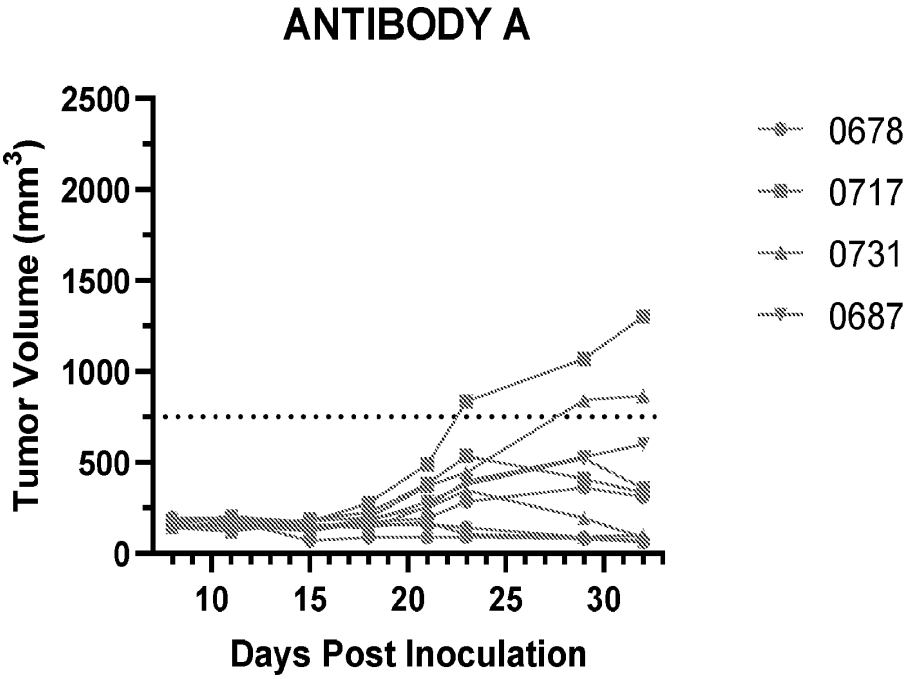
ANTIBODY A
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
15
20
25
30
Days Post Inoculation
0678
0717
0731
0687

FIG. 3G

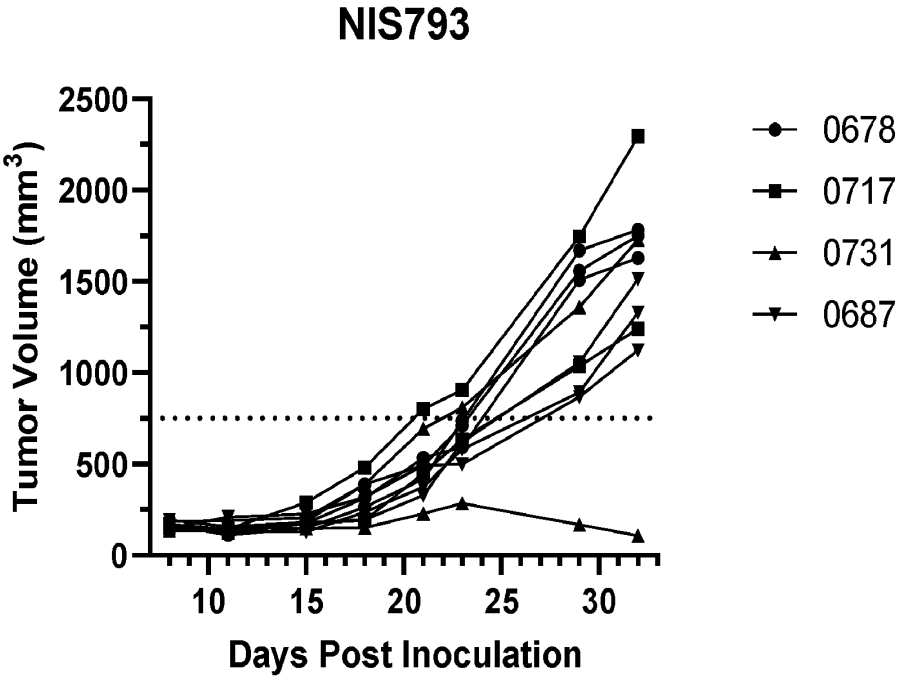
NIS793
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
15
20
25
30
Days Post Inoculation
0678
0717
0731
0687

FIG. 3H

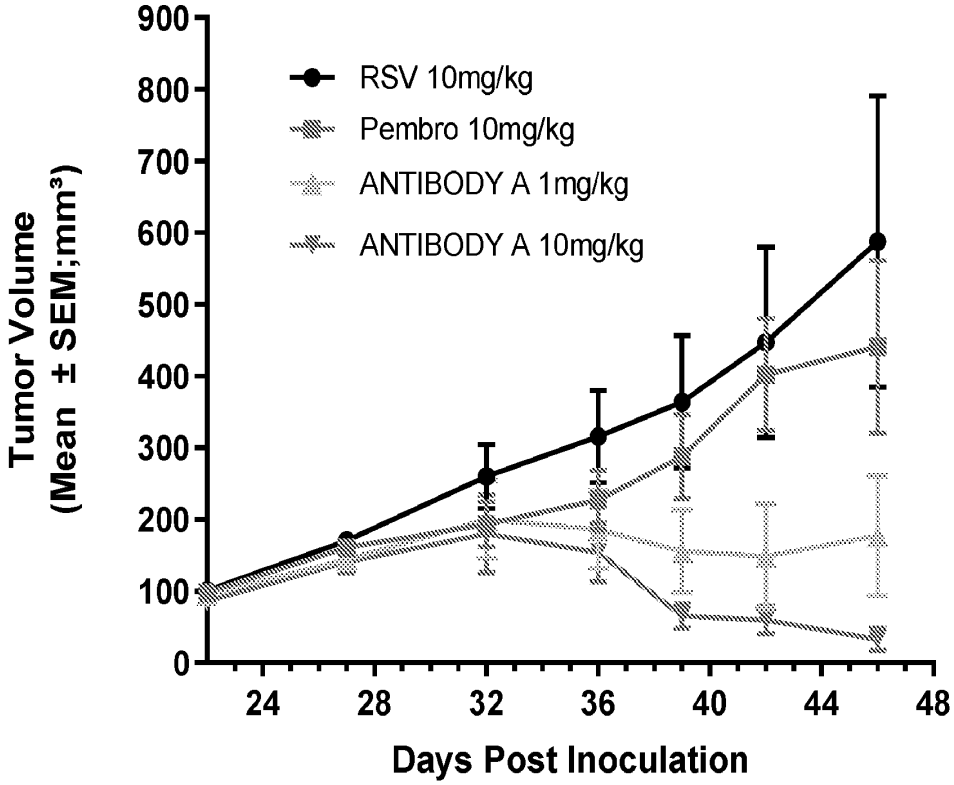
900
800
700
600
500
400
300
200
100
0
Tumor Volume
(Mean ± SEM;mm³)
RSV 10mg/kg
Pembro 10mg/kg
ANTIBODY A 1mg/kg
ANTIBODY A 10mg/kg
24
28
32
36
40
44
48
Days Post Inoculation

FIG. 4

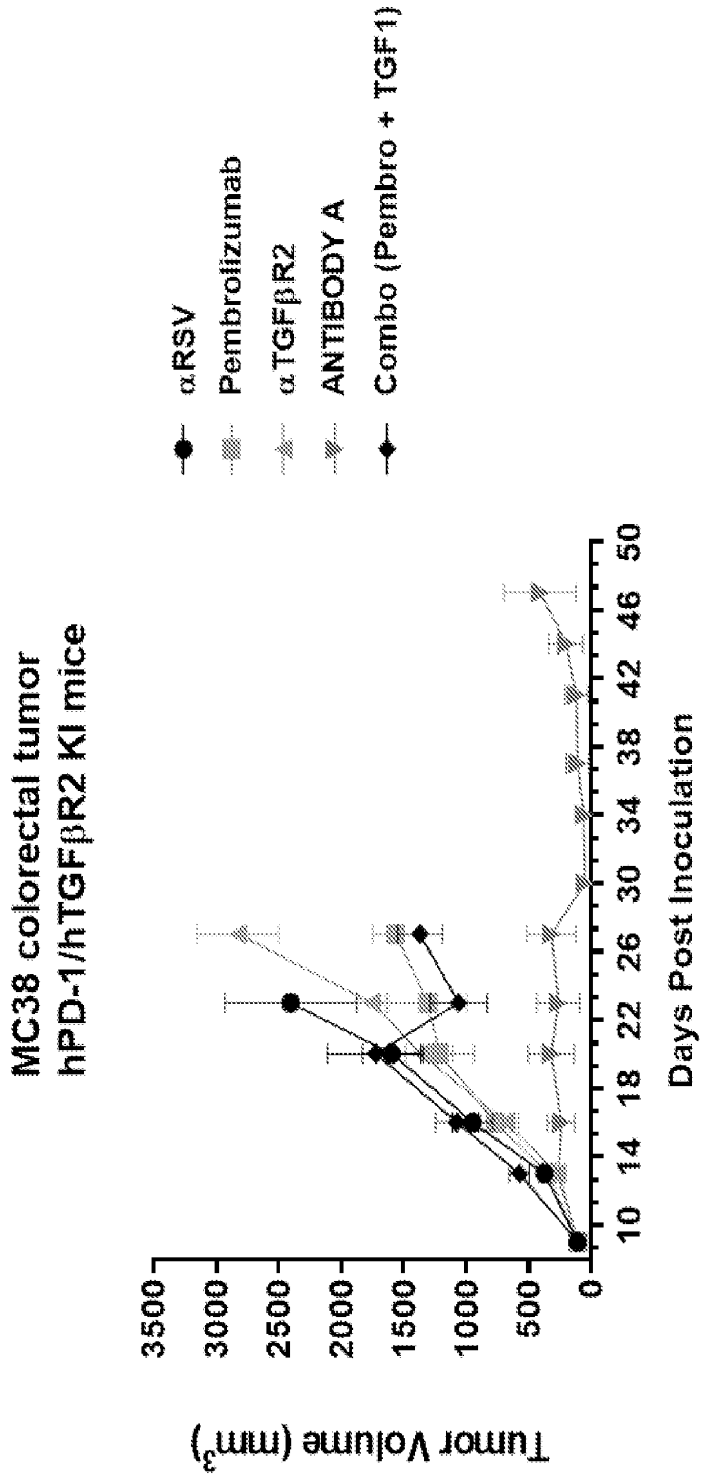
MC38 colorectal tumor
hPD-1/hTGFβR2 KI mice
αRSV
Pembrolizumab
αTGFβR2
ANTIBODY A
Combo (Pembro + TGF1)
Tumor Volume (mm³)
3500
3000
2500
2000
1500
1000
500
0
10 14 18 22 26 30 34 38 42 46 50
Days Post Inoculation

FIG. 5A

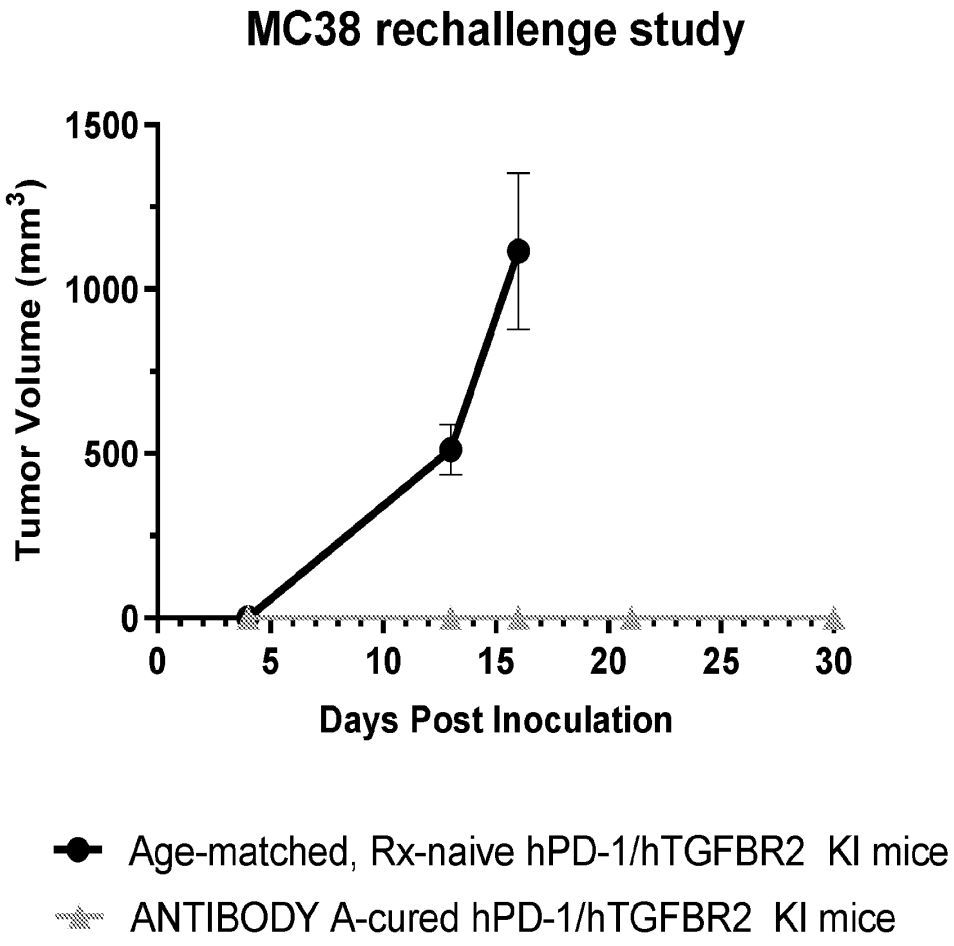
MC38 rechallenge study
Tumor Volume (mm3)
1500
1000
500
0
0
5
10
15
20
25
30
Days Post Inoculation
Age-matched, Rx-naive hPD-1/hTGFBR2 KI mice
ANTIBODY A-cured hPD-1/hTGFBR2 KI mice

FIG. 5B

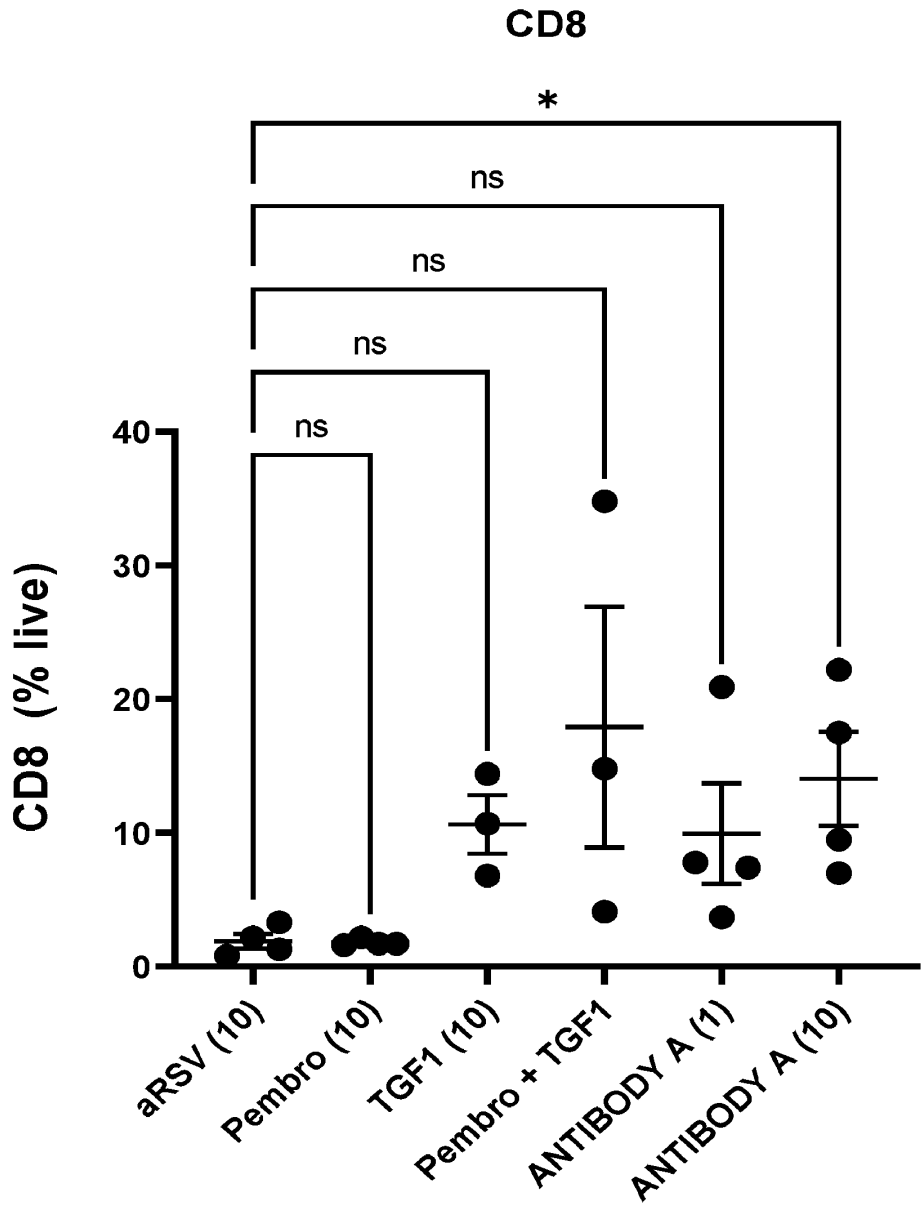
CD8
*
ns
ns
ns
ns
CD8 (% live)
40
30
20
10
0
aRSV (10)
Pembro (10)
TGF1 (10)
Pembro + TGF1
ANTIBODY A (1)
ANTIBODY A (10)

FIG. 6A

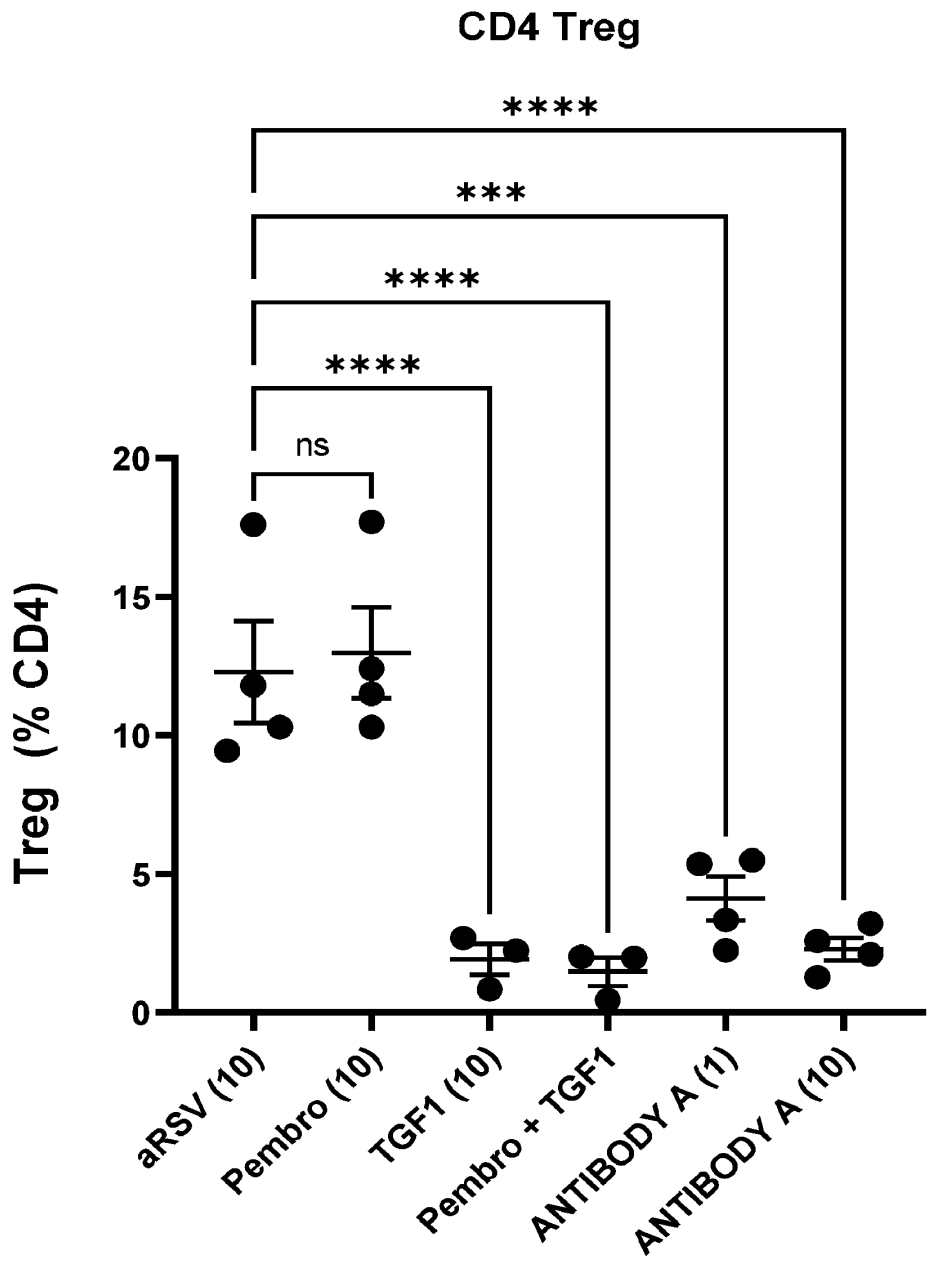
CD4 Treg
****
***
****
****
ns
20
15
10
5
0
Treg (% CD4)
aRSV (10)
Pembro (10)
TGF1 (10)
Pembro + TGF1
ANTIBODY A (1)
ANTIBODY A (10)

FIG. 6B

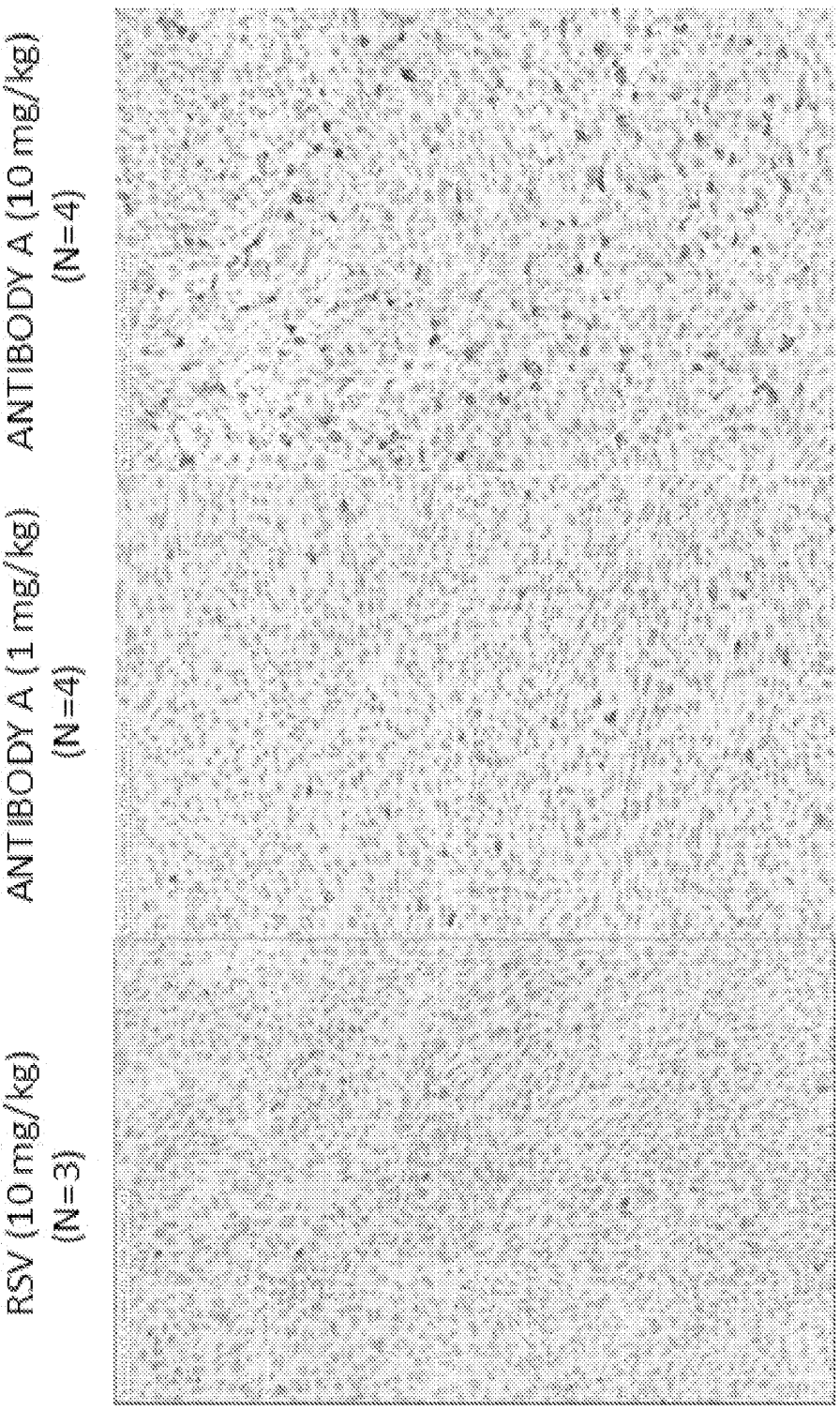

FIG. 7A

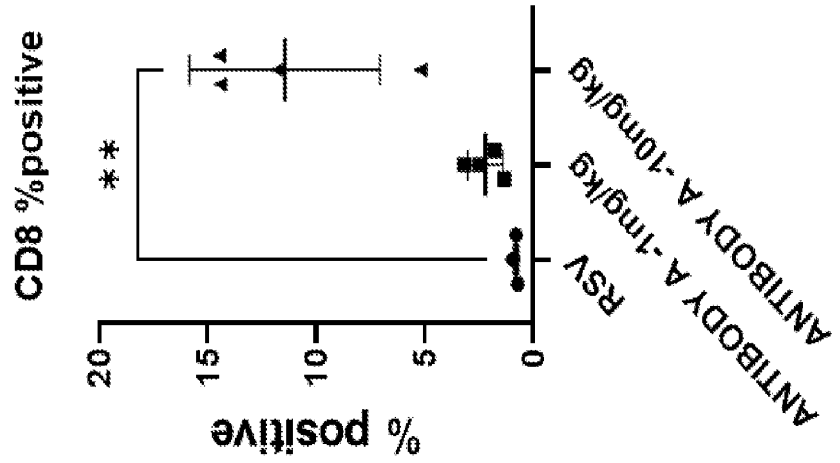
CD8 %positive
**
% positive
20
15
10
5
0
RSV
ANTIBODY A -1mg/kg
ANTIBODY A -10mg/kg

FIG. 7C

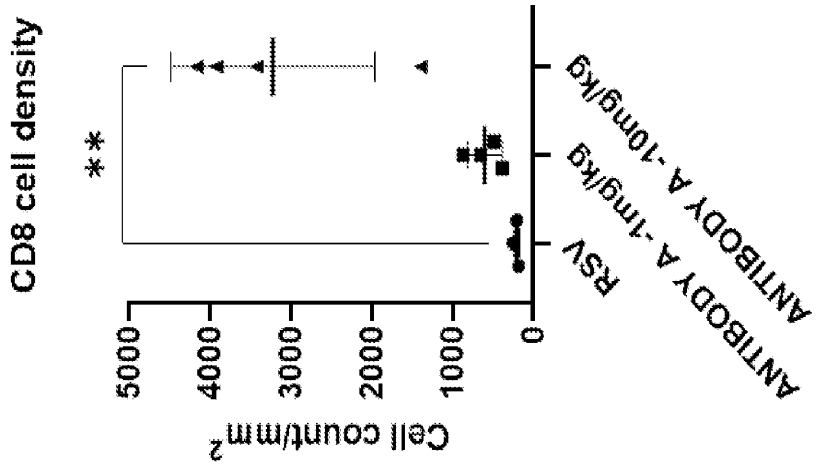
CD8 cell density
**
Cell count/mm²
5000
4000
3000
2000
1000
0
RSV
ANTIBODY A -1mg/kg
ANTIBODY A -10mg/kg

FIG. 7B

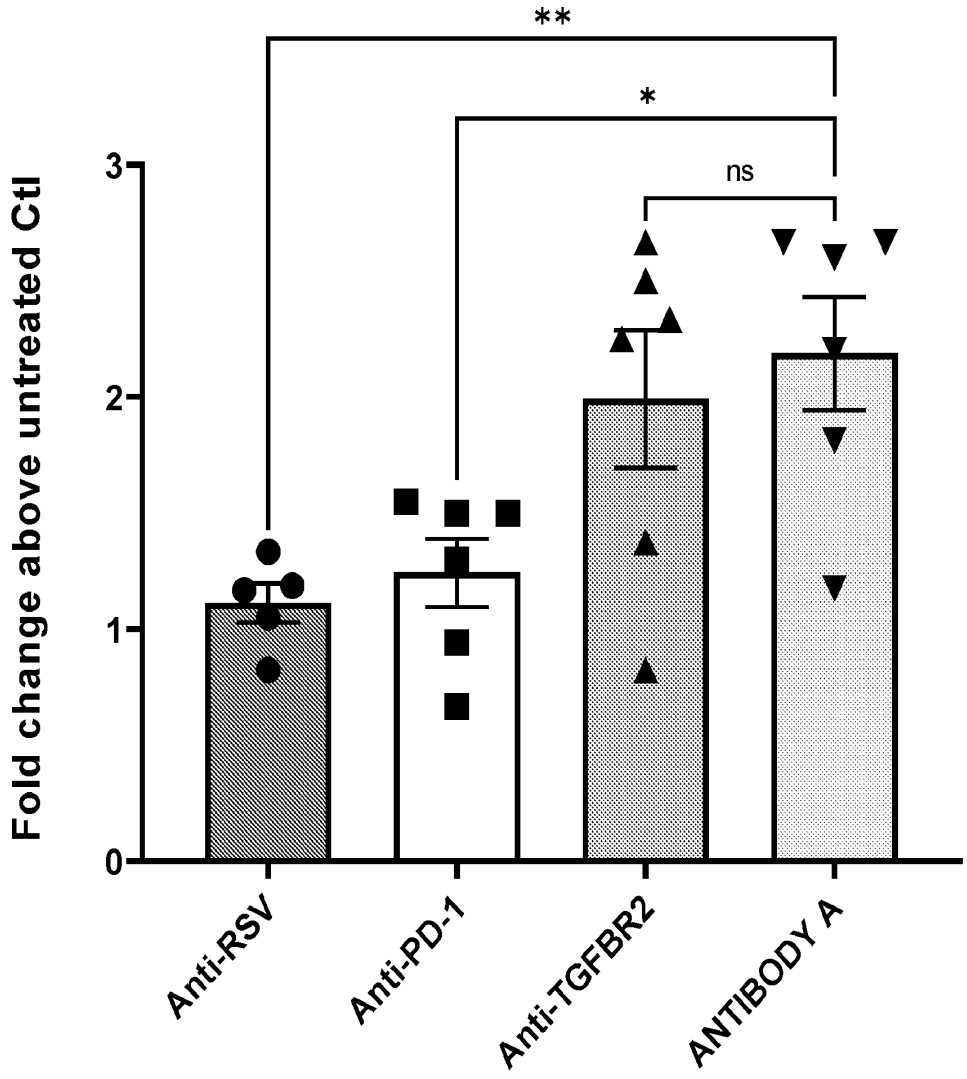
**
*
ns
Fold change above untreated Ctl
3
2
1
0
Anti-RSV
Anti-PD-1
Anti-TGFBR2
ANTIBODY A

FIG. 8

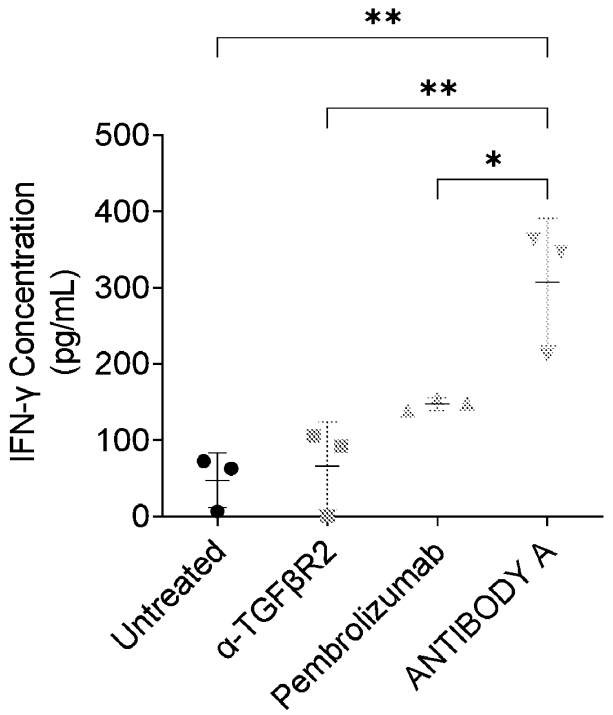
**
**
*
500
400
300
200
100
0
IFN-γ Concentration (pg/mL)
Untreated
α-TGFβR2
Pembrolizumab
ANTIBODY A

FIG. 9A

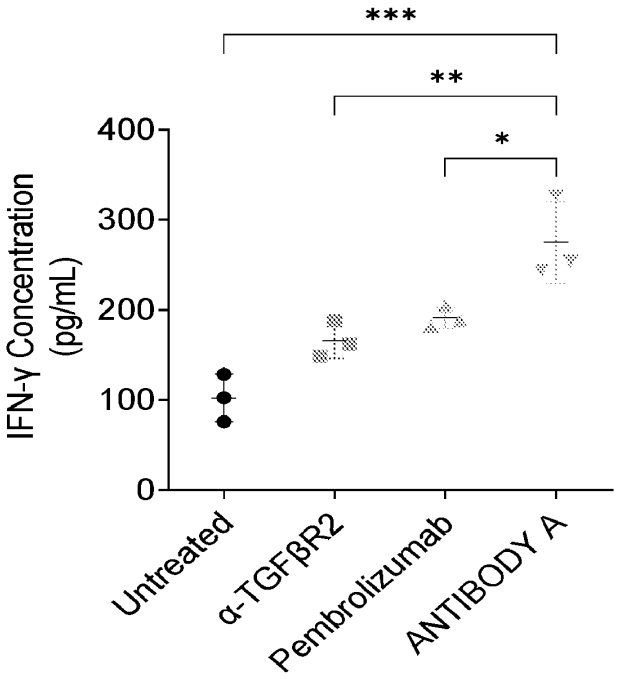
***
**
*
400
300
200
100
0
IFN-γ Concentration (pg/mL)
Untreated
α-TGFβR2
Pembrolizumab
ANTIBODY A

FIG. 9B