FIG. 1

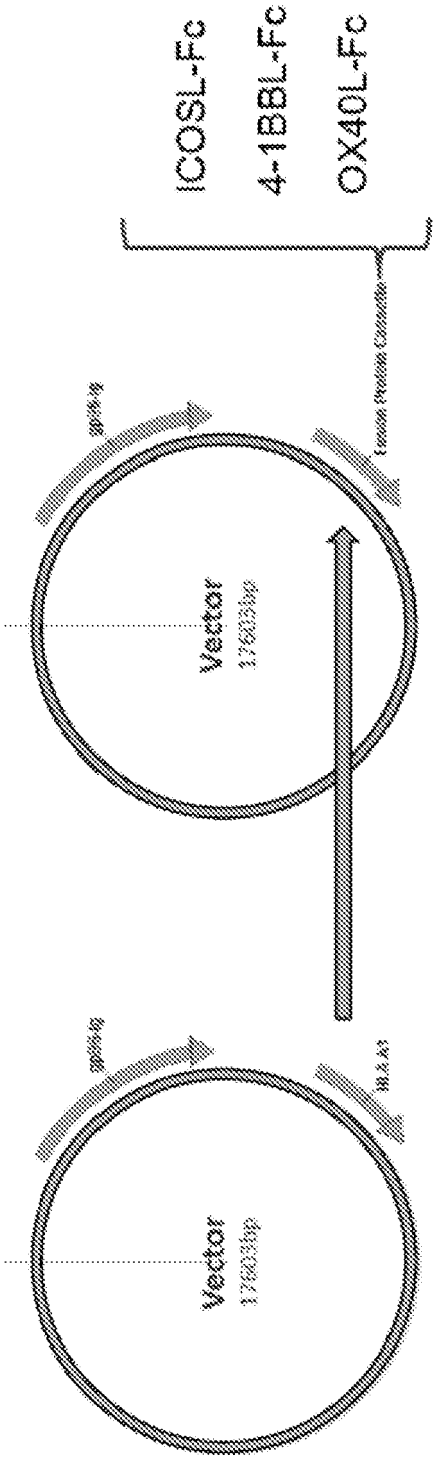


FIG. 2

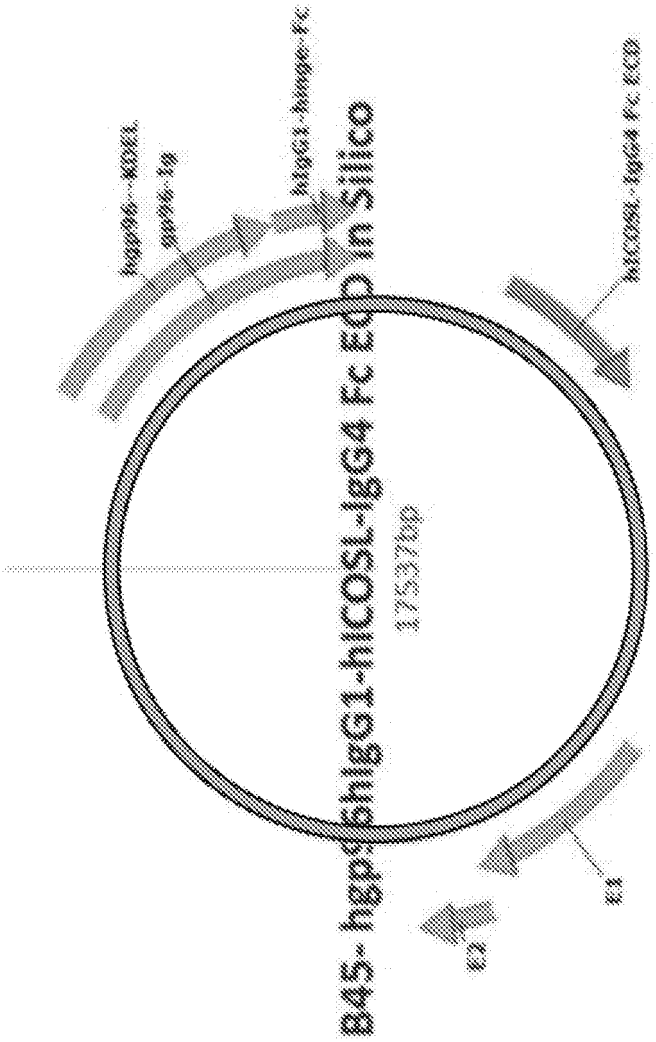
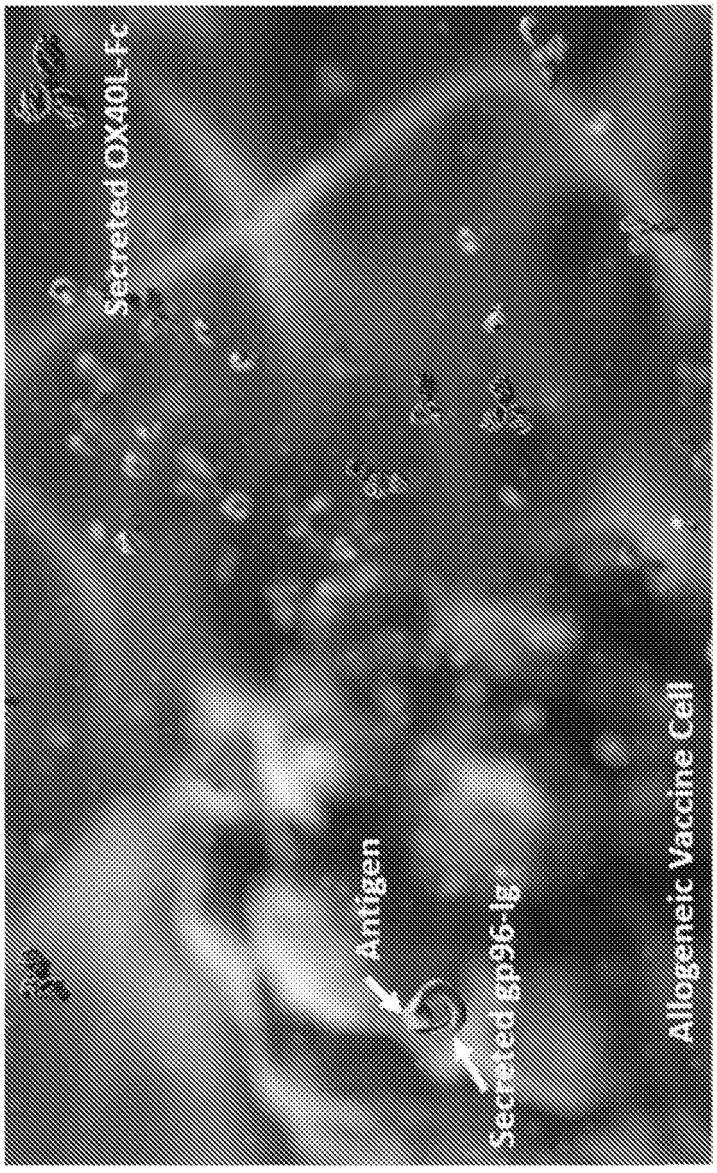

B45- hgpsbhIgG1-hICOSL-IgG4 Fc EdD in Silico
17537bp
hIgG1-hinge-Fc
hICOSL-IgG4 Fc ECD
E1
E2

FIG. 3


Secreted OX40L-Fc
Antigen
Secreted sp96-Ig
Allogeneic Vaccine Cell

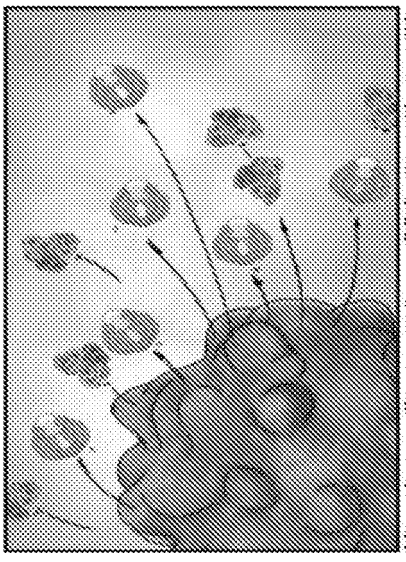


FIG. 4A

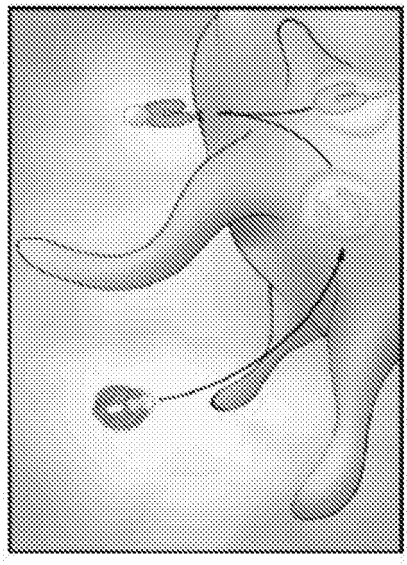


FIG. 4B

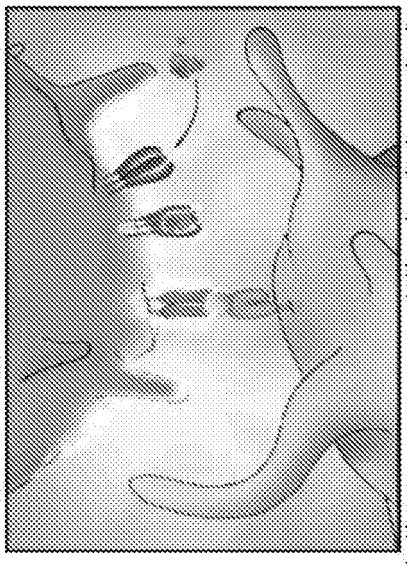


FIG. 4C

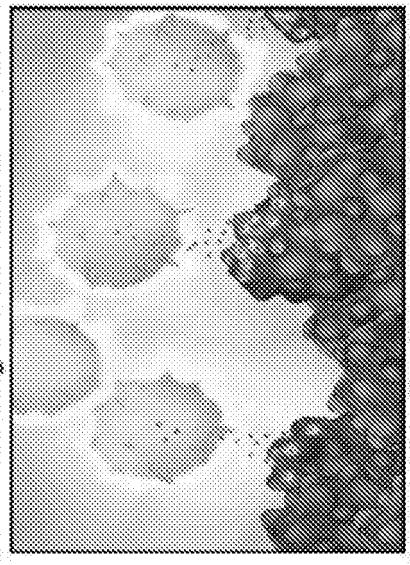


FIG. 4D

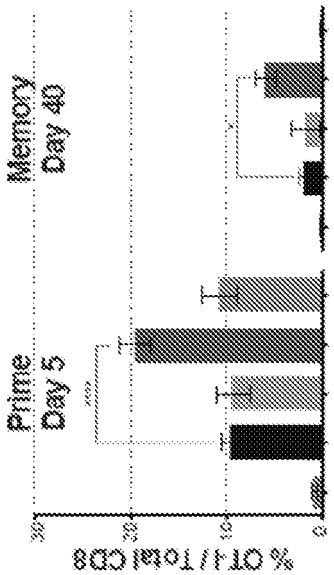

Prime
Day 5
Memory
Day 40
% OT1 / Total CD8
30
20
10
0

FIG. 4E

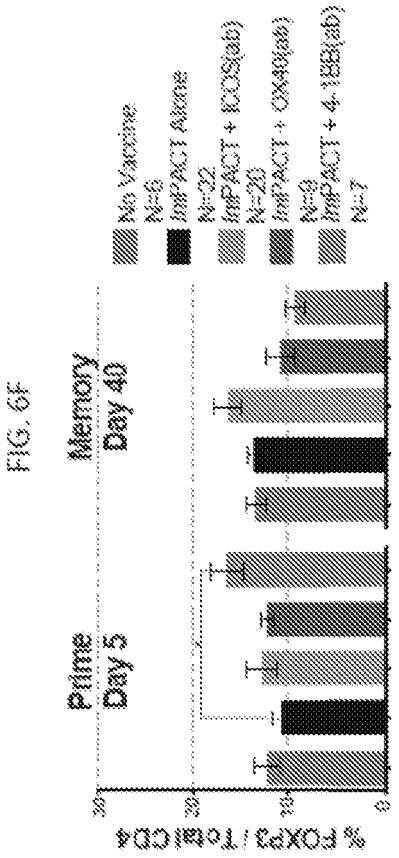

FIG. 6F
Prime
Day 5
Memory
Day 40
% FOXP3 / Total CD4
30
20
10
0
No Vaccine
N=6
ImPACT Alone
N=22
ImPACT + ICOS(ab)
N=20
ImPACT + OX40(ab)
N=9
ImPACT + 4-1BB(ab)
N=7

FIG. 4F

FIG. 4G

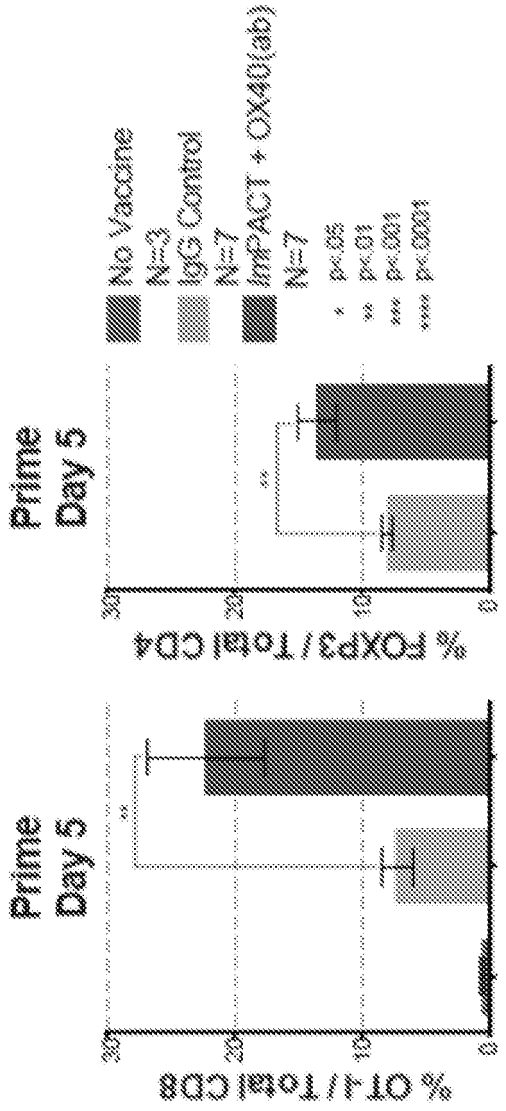

No Vaccine
N=3
IgG Control
N=7
ImPACT + OX40(ab)
N=7
* p<.05
** p<.01
*** p<.001
**** p<.0001
Prime
Day 5
% FOXP3 / Total CD4
30
20
10
0
**
Prime
Day 5
% OT-I / Total CD8
30
20
10
0
**

FIG. 5A

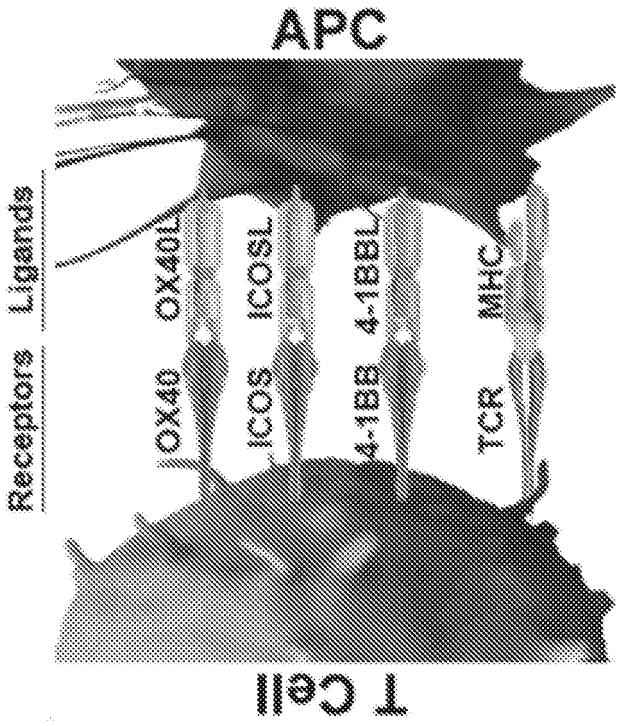

APC
Ligands
Receptors
OX40L
ICOSL
4-1BBL
MHC
OX40
ICOS
4-1BB
TCR
T Cell

FIG. 5B

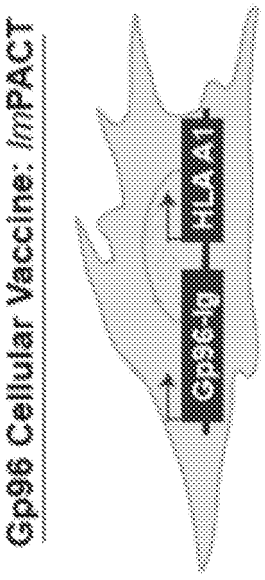


FIG. 5C

Co-Stimulator	Agonist Antibody(ab)
OX40	OX86
ICOS	C398.4A
4-1BB	3H3

FIG. 5D

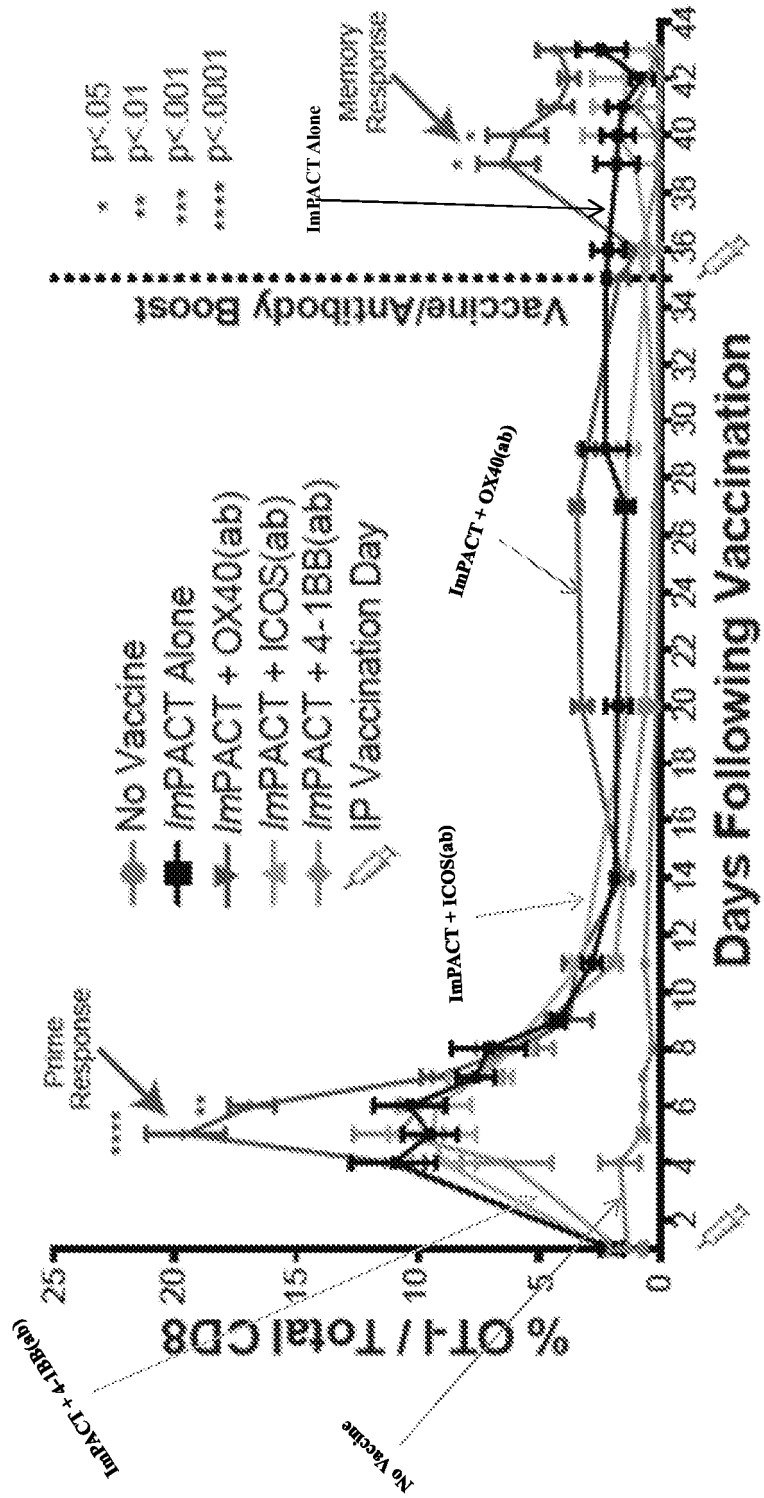

% OT-I / Total CD8
Days Following Vaccination
Vaccine/Antibody Boost
Prime Response
Memory Response
ImPACT Alone
ImPACT + OX40(ab)
ImPACT + ICOS(ab)
ImPACT + 4-1BB(ab)
No Vaccine
IP Vaccination Day
* p<.05
** p<.01
*** p<.001
**** p<.0001

FIG. 6A

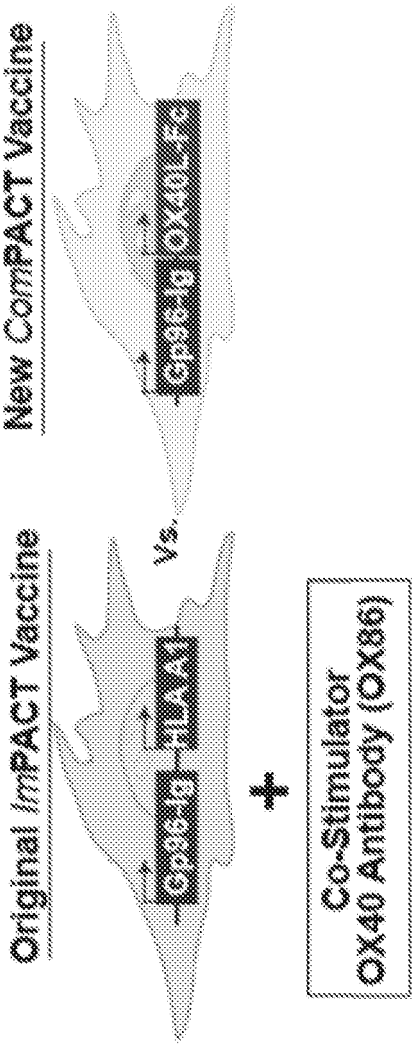

Original ImPACT Vaccine
New ComPACT Vaccine
Vs.
+
Co-Stimulator
OX40 Antibody (OX86)

FIG. 6B

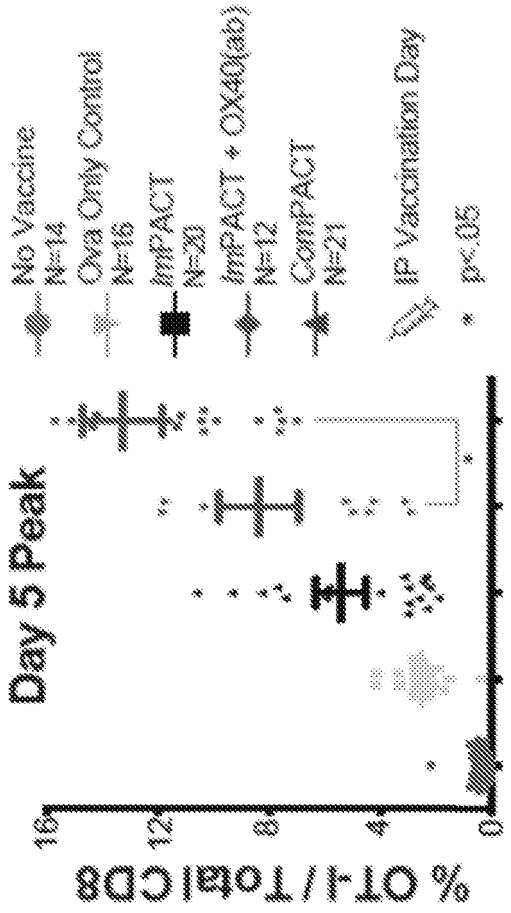

Day 5 Peak
% OT-I / Total CD8
16
12
8
4
0
No Vaccine N=14
Ova Only Control N=16
ImPACT N=20
ImPACT + OX40(ab) N=12
ComPACT N=21
IP Vaccination Day
p<.05

FIG. 6C

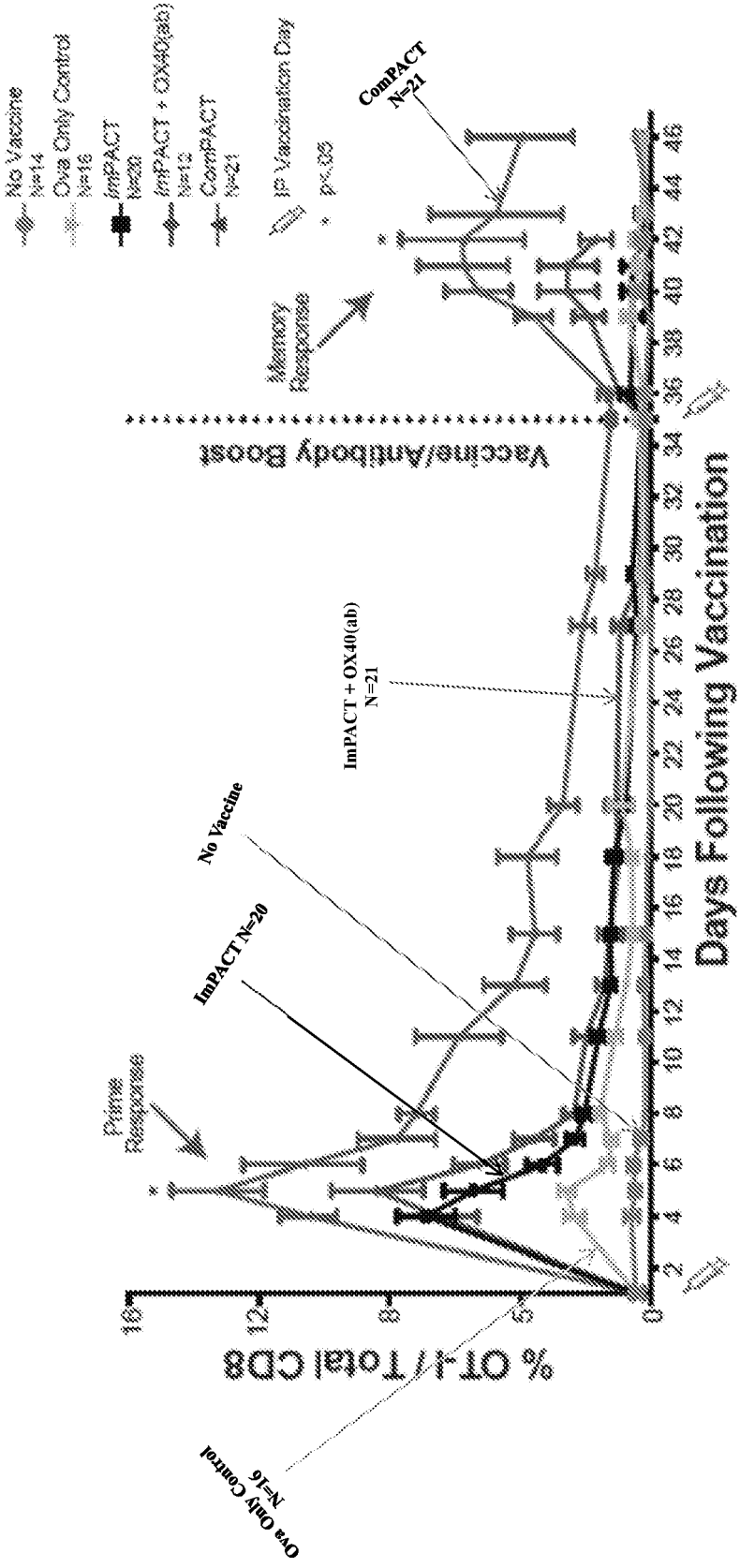

No Vaccine N=14
Ova Only Control N=16
ImPACT N=20
ImPACT + OX40(ab) N=12
ComPACT N=21
IP Vaccination Day
* p<.05
ComPACT N=21
Memory Response
Vaccine/Antibody Boost
ImPACT + OX40(ab) N=21
No Vaccine
ImPACT N=20
Prime Response
Ova Only Control N=16
% OT-I / Total CD8
Days Following Vaccination

FIG. 7A

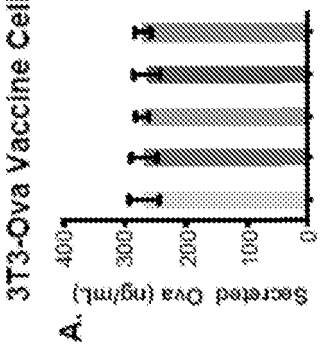


FIG. 7B

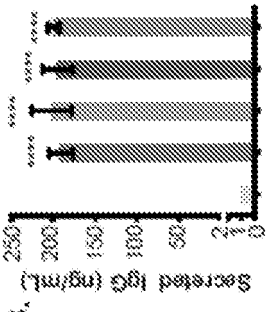
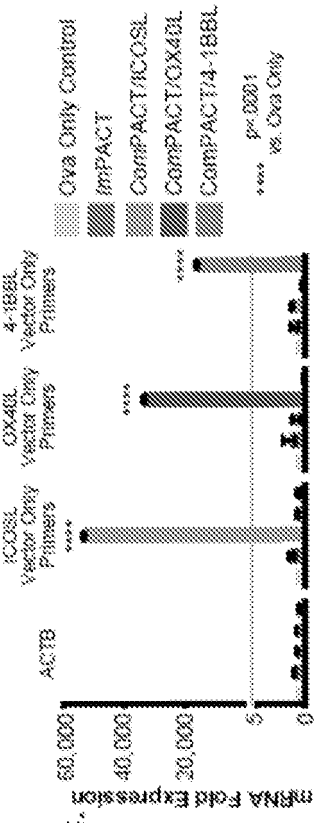


FIG. 7C



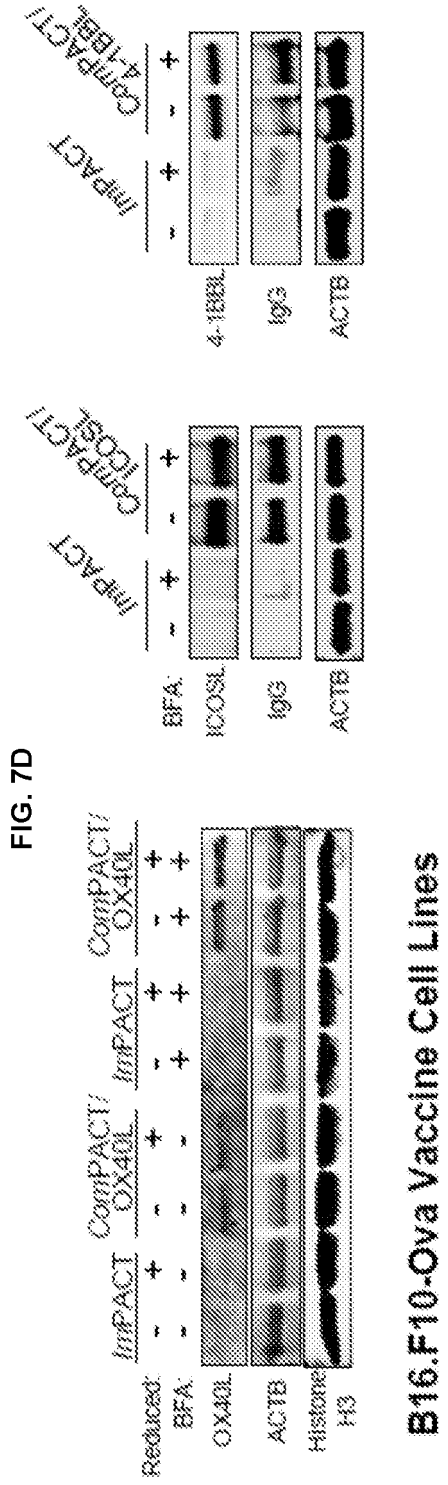

ImPACT
ComPACT/ OX40L
ImPACT
ComPACT/ OX40L
Reduced
BFA
OX40L
ACTB
Histone H3
B16.F10-Ova Vaccine Cell Lines
ImPACT
ComPACT/ ICOSL
BFA
ICOSL
IgG
ACTB
ImPACT
ComPACT/ 4-1BBL
4-1BBL
IgG
ACTB

FIG. 7D

FIG. 7E

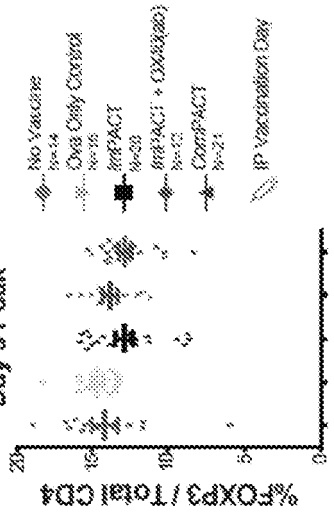

Day 5 Peak
%FOXP3 / Total CD4
20
15
10
5
0
No Vaccine
n=14
Ova Only Control
n=15
ImPACT
n=20
ImPACT + OX40(gal)
n=13
ComPACT
n=21
IP Vaccination Day

FIG. 7F

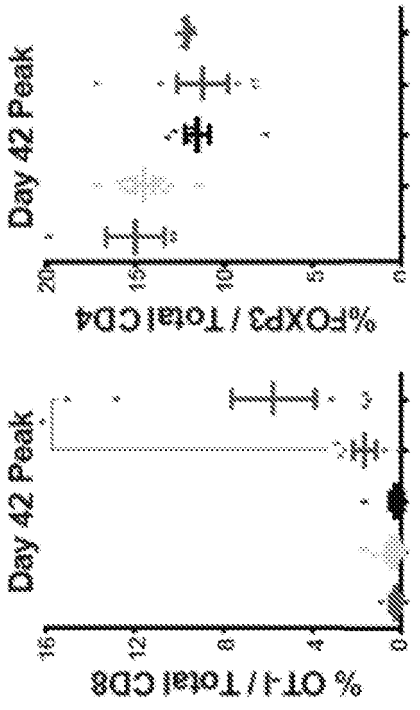

Day 42 Peak
% OT-I / Total CD8
16
12
8
4
0
Day 42 Peak
%FOXP3 / Total CD4
20
15
10
5
0
No Vaccine
n=4
Ova Only Control
n=11
ImPACT
n=7
ImPACT + OX40(gal)
n=8
ComPACT
n=8
IP Vaccination Day
p<.05

FIG. 8A

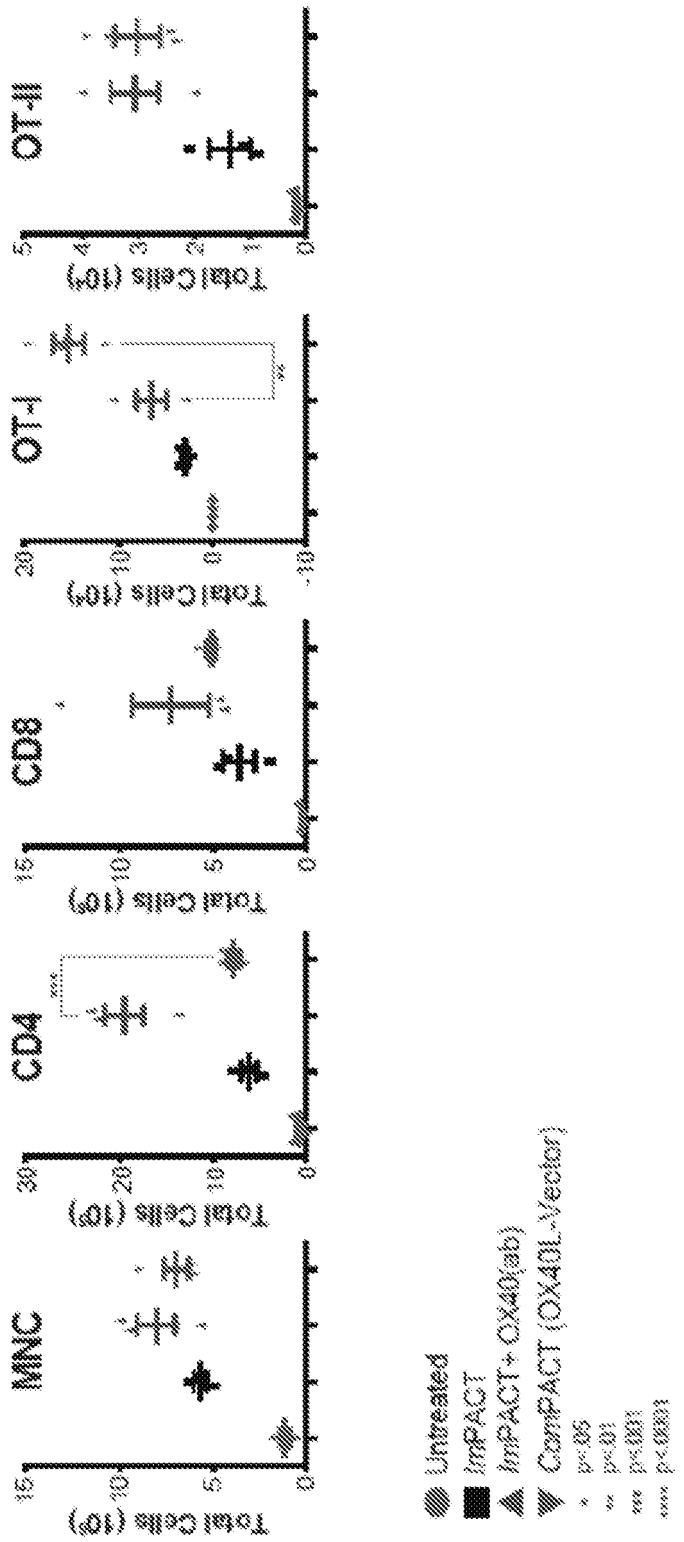

MNC
CD4
CD8
OT-I
OT-II
Total Cells (10^7)
Untreated
ImPACT
ImPACT+ OX40(ab)
ComPACT (OX40L-Vector)
* p<.05
** p<.01
*** p<.001
**** p<.0001

FIG. 8B

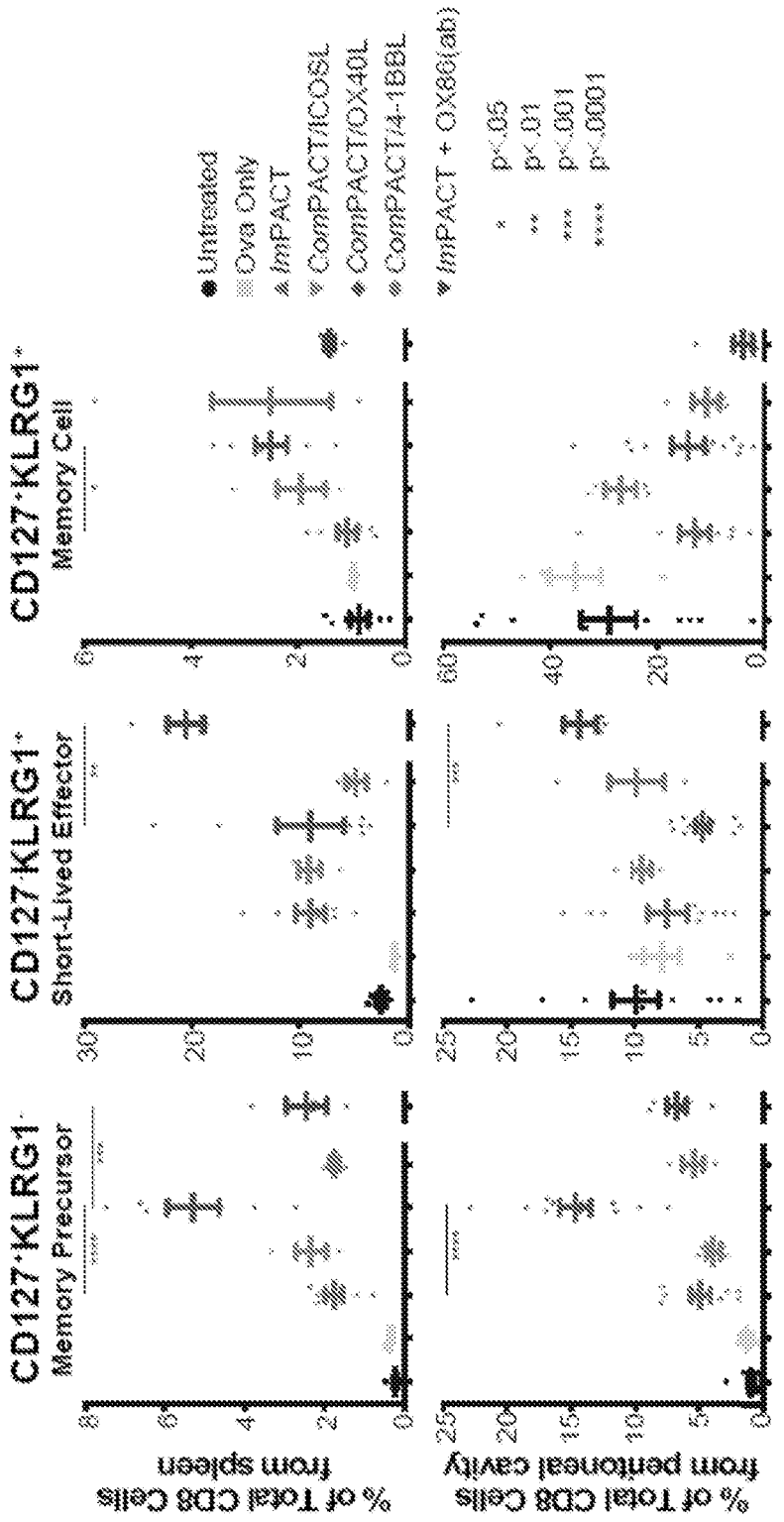

CD127+KLRG1+
Memory Precursor
CD127+KLRG1+
Short-Lived Effector
CD127+KLRG1+
Memory Cell
% of Total CD8 cells from spleen
% of Total CD8 cells from peritoneal cavity
Untreated
Ova Only
ImPACT
ComPACT/ICOSL
ComPACT/OX40L
ComPACT/4-1BBL
ImPACT + OX86(ab)
* p<.05
** p<.01
*** p<.001
**** p<.0001

FIG. 8C

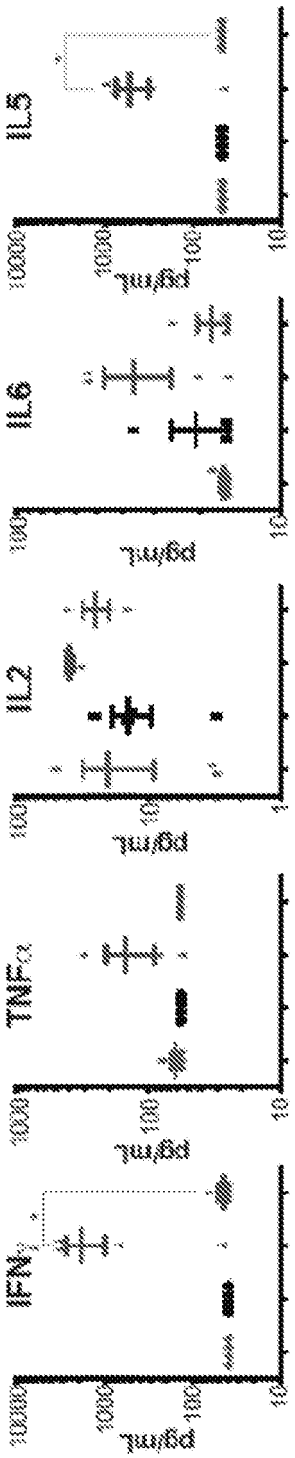

IFNγ
TNFα
IL2
IL6
IL5
pg/mL

FIG. 8D

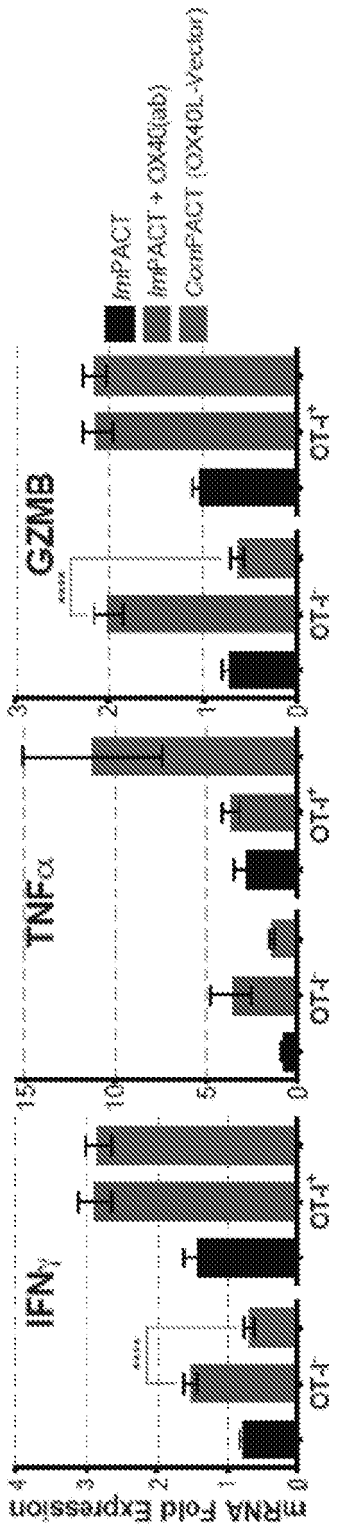

ImPACT
ImPACT + OX40(ab)
ComPACT (OX40L-Vector)
IFNγ
TNFα
GZMB
mRNA Fold Expression
OT-I-
OT-I+

FIG. 8E

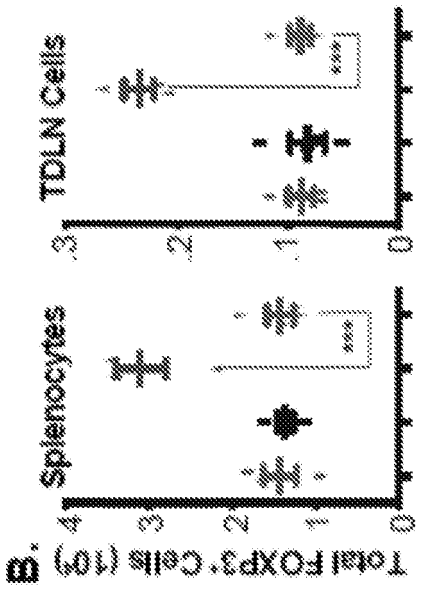


FIG. 9A

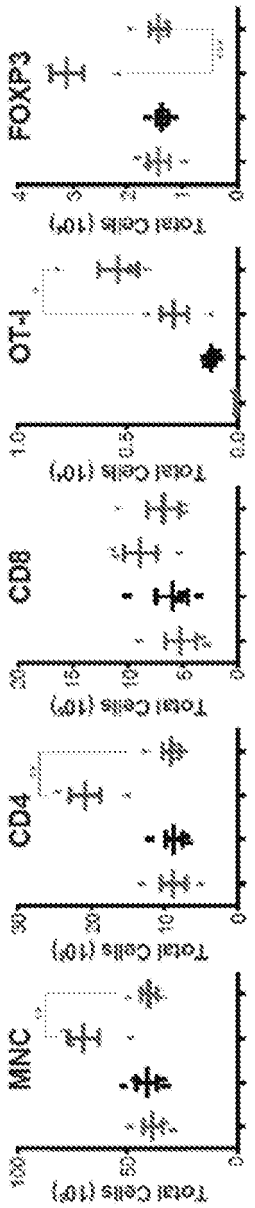

MNC
CD4
CD8
OT-I
FOXP3
Total Cells (10⁶)

FIG. 9B

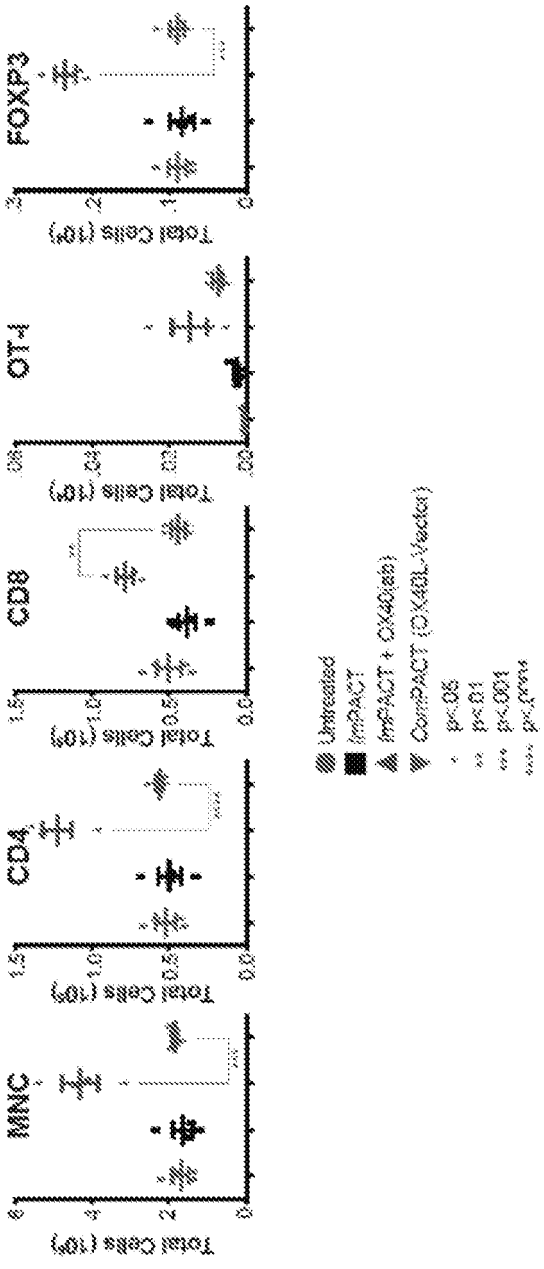

MNC
CD4
CD8
OT-I
FOXP3
Total Cells (10⁶)
Untreated
ImPACT
ImPACT + OX40(ab)
ComPACT (OX40L-Vector)
* p<.05
** p<.01
*** p<.001
**** p<.0001

FIG. 9C

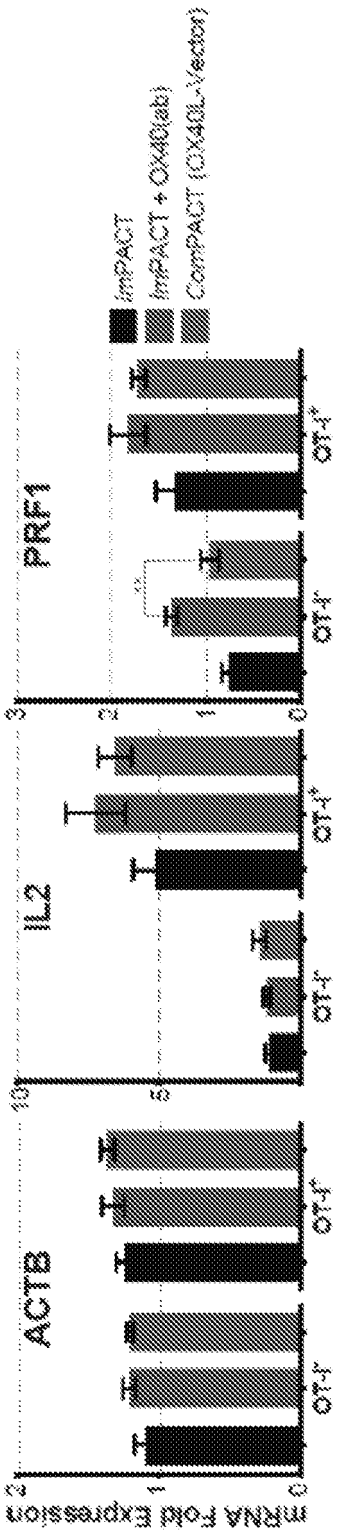

ImPACT
ImPACT + OX40(ab)
ComPACT (OX40L-Vector)
PRF1
IL2
ACTB
mRNA Fold Expression
OT-I-
OT-I+

FIG. 10A

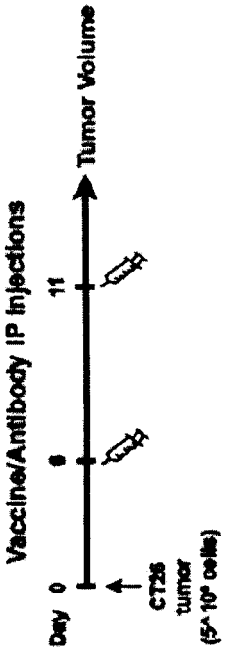


FIG. 10B

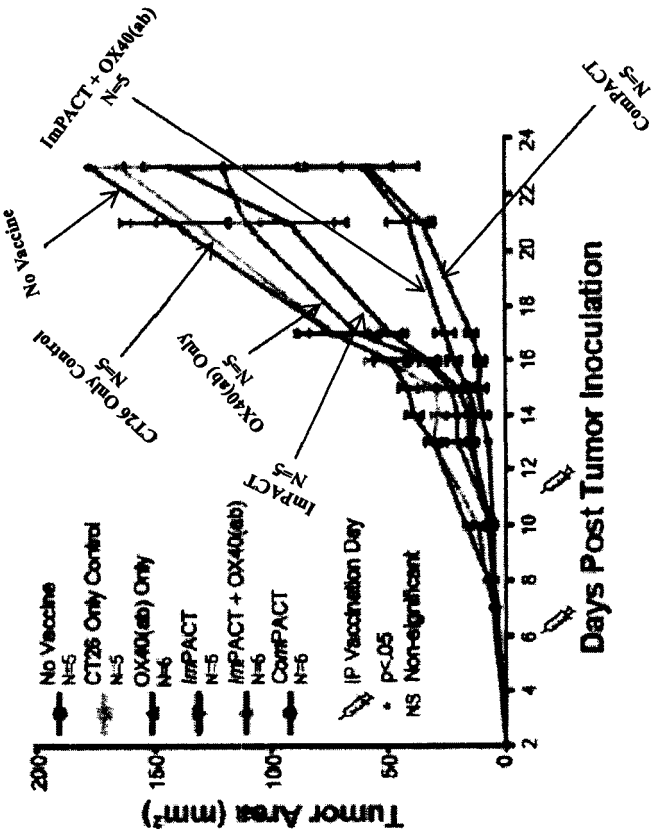
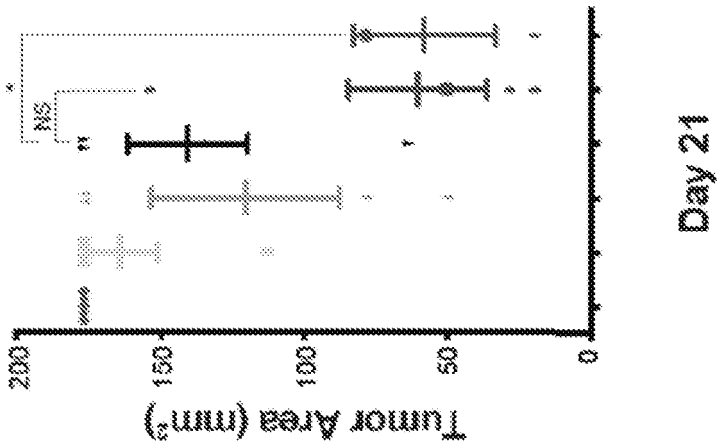


FIG. 10C



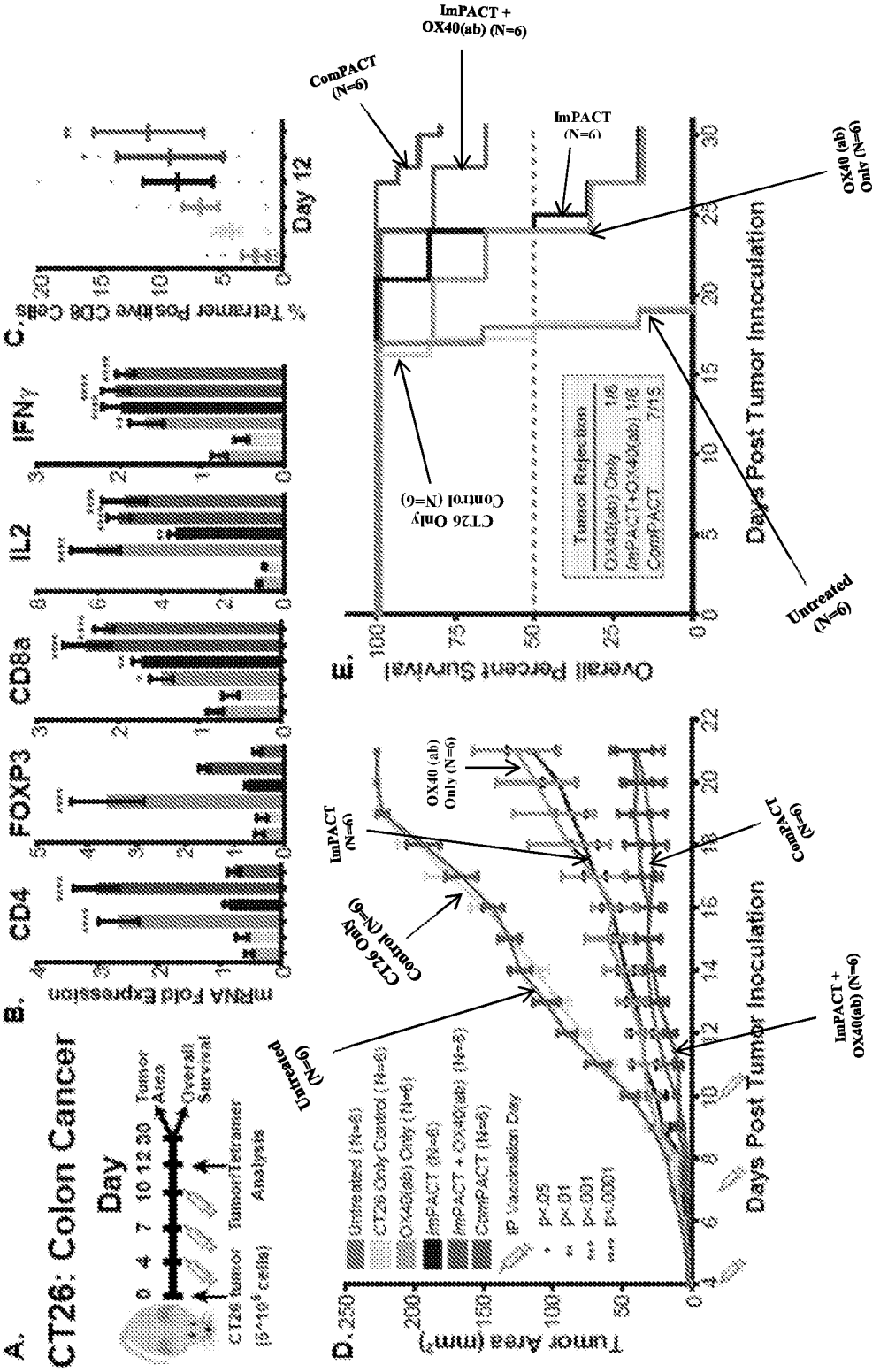

A.
CT26: Colon Cancer
Day
0 4 7 10 12 30
Tumor Area
Overall Survival
CT26 Tumor
Tumor Measurement
Analysis
B.
CD4
FOXP3
CD8a
IL2
IFNγ
mRNA Fold Expression
C.
% Tetramer Positive CD8 Cells
Day 12
D.
Tumor Area (mm²)
Days Post Tumor Inoculation
Untreated (N=6)
CT26 Only Control (N=6)
OX40(ab) Only (N=6)
ImPACT (N=6)
ImPACT + OX40(ab) (N=6)
ComPACT (N=6)
IP Vaccination Day
p<.05
p<.01
p<.001
p<.0001
E.
Overall Percent Survival
Days Post Tumor Inoculation
ComPACT (N=6)
ImPACT + OX40(ab) (N=6)
ImPACT (N=6)
OX40 (ab) Only (N=6)
CT26 Only Control (N=6)
Untreated (N=6)
Tumor Rejection
OX40(ab) Only 1/6
ImPACT+OX40(ab) 1/6
ComPACT 7/15

FIG. 11

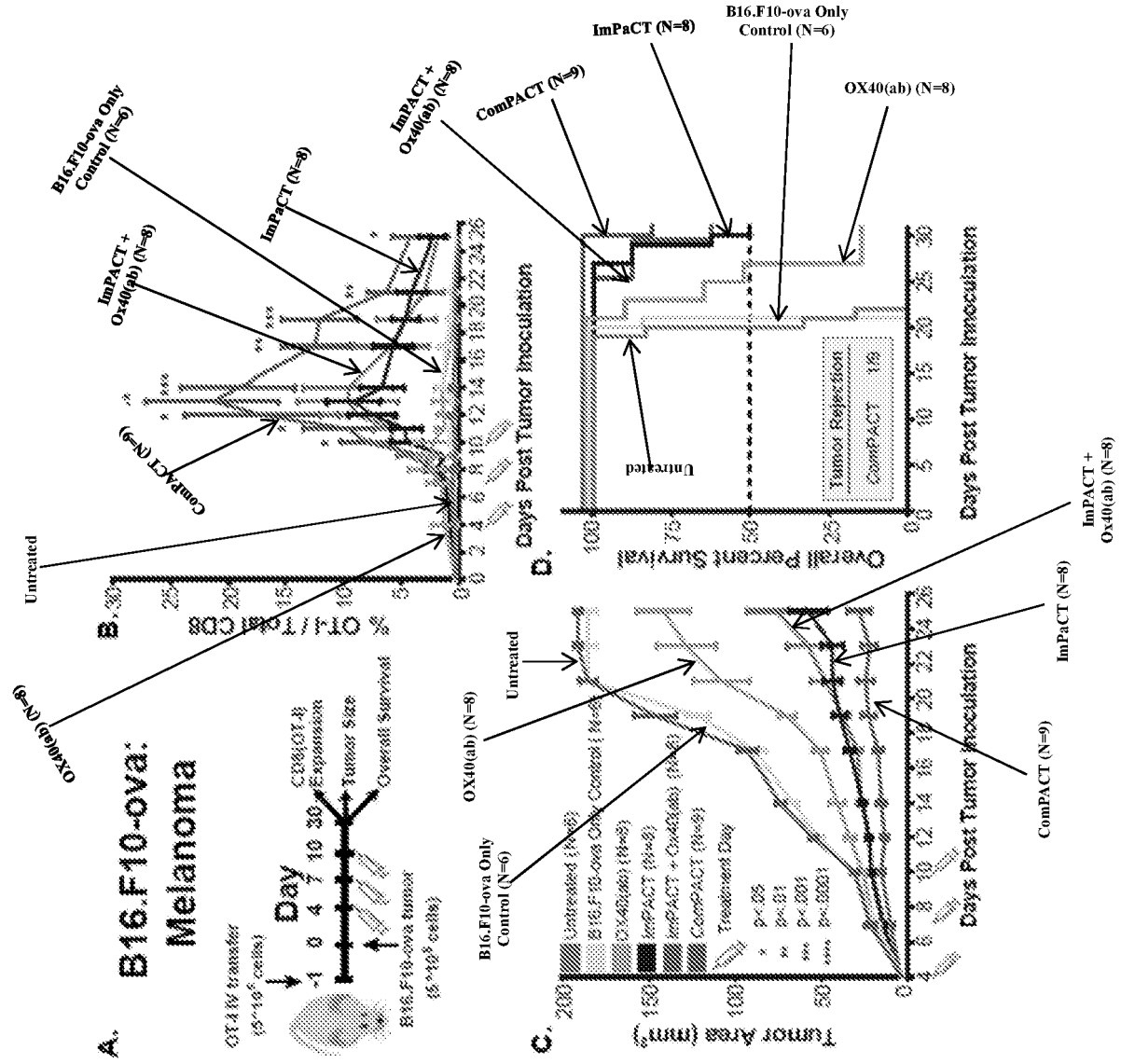
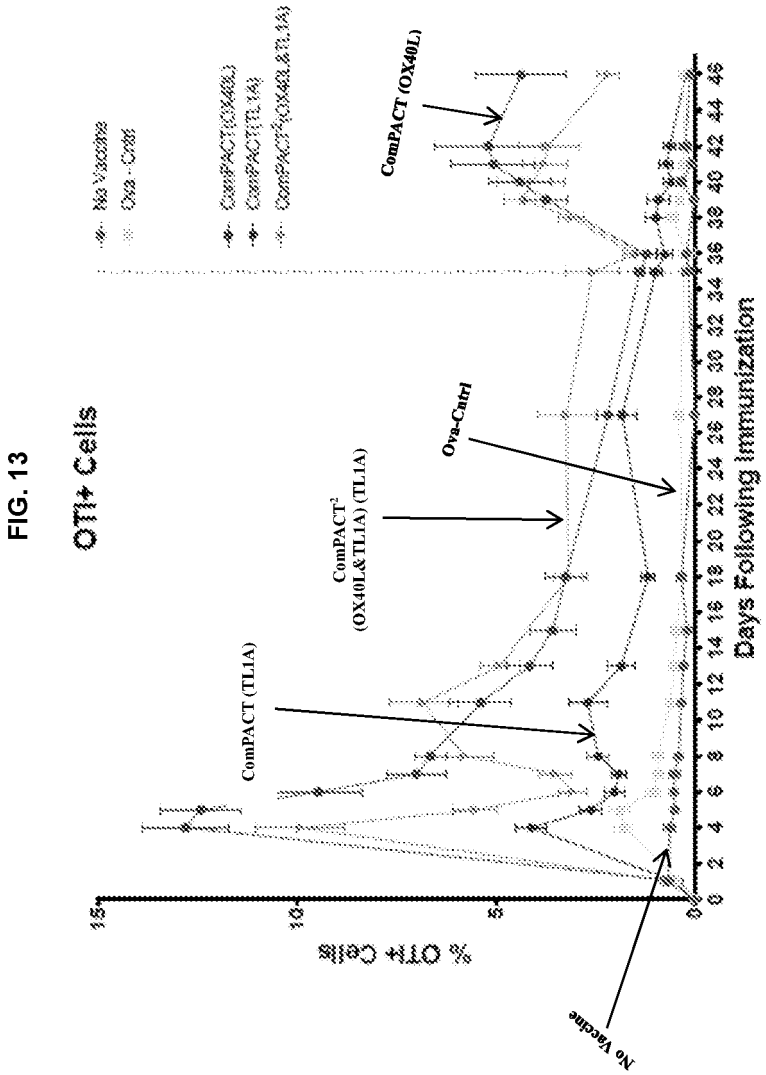
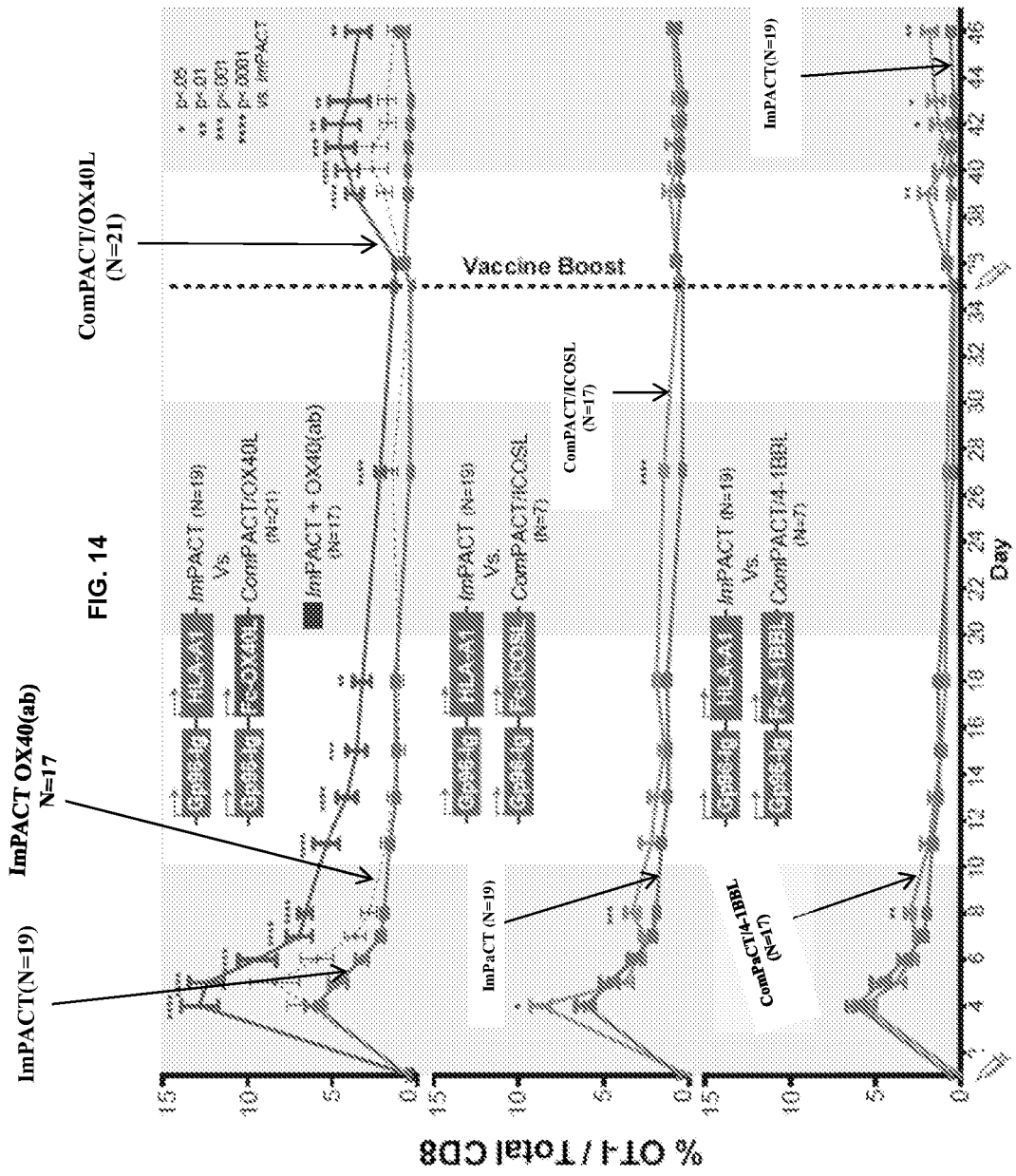

A.
B16.F10-ova: Melanoma
Day
-1 0 4 7 10 30
CD40/OX40 Expansion
Tumor Size
Overall Survival
B.
% OT1 / Total CD8
Days Post Tumor Inoculation
Untreated
OX40(ab) (N=8)
ImPACT + Ox40(ab) (N=8)
ImPACT (N=8)
B16.F10-ova Only Control (N=6)
ComPACT (N=9)
C.
Tumor Area (mm²)
Days Post Tumor Inoculation
D.
Overall Percent Survival
Days Post Tumor Inoculation
Tumor Rejection
ComPACT 1/9
Untreated
ImPaCT (N=8)
B16.F10-ova Only Control (N=6)
OX40(ab) (N=8)
ComPACT (N=9)

FIG. 12

FIG. 13


OTI+ Cells
No Vaccine
Ova + Cntrl
ComPACT (OX40L)
ComPACT (TL1A)
ComPACT²(OX40L&TL1A)
% OTI+ Cells
Days Following Immunization
ComPACT (TL1A)
ComPACT²
(OX40L&TL1A) (TL1A)
Ova-Cntrl
No Vaccine


FIG. 14
ImPACT(N=19)
ImPACT OX40(ab) N=17
ComPACT/OX40L (N=21)
ImPACT (N=19)
ComPACT/ICOSL (N=17)
ImPACT(N=19)
ComPACT/4-1BBL (N=17)
Vaccine Boost
% OT-1 / Total CD8
Day
ImPACT (N=19) Vs ComPACT/OX40L (N=21)
ImPACT + OX40(ab) (N=17)
ImPACT (N=19) Vs. ComPACT/ICOSL (N=17)
ImPACT (N=19) Vs. ComPACT/4-1BBL (N=17)
* p<.05
** p<.01
*** p<.001
**** p<.0001
vs. ImPACT

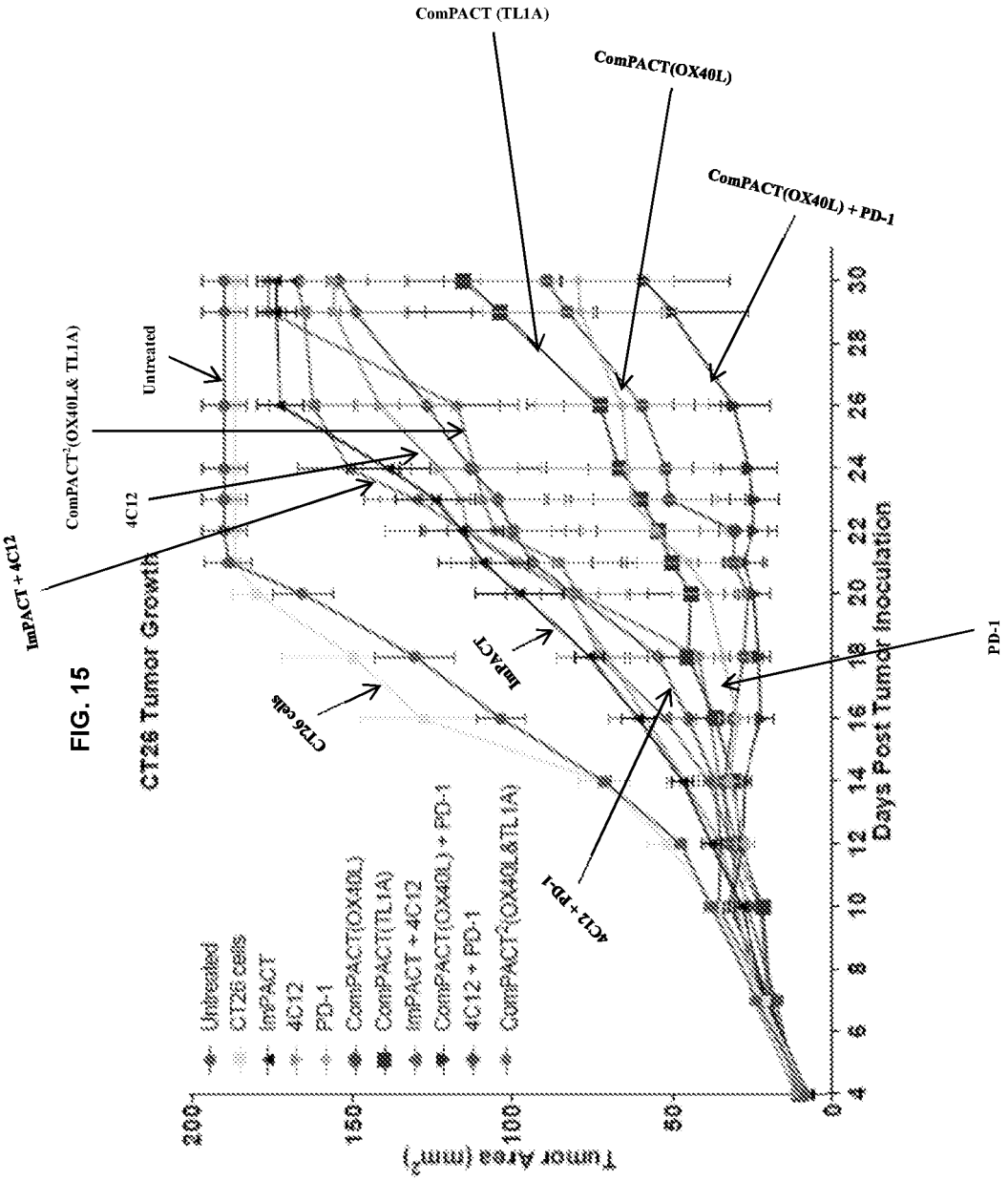

ComPACT (TL1A)
ComPACT(OX40L)
ComPACT(OX40L) + PD-1
Untreated
ComPACT²(OX40L& TL1A)
4C12
ImPACT + 4C12
CT26 Tumor Growth
CT26 cells
ImPACT
4C12 + PD-1
PD-1
Tumor Area (mm²)
Days Post Tumor Inoculation
0
50
100
150
200
4
6
8
10
12
14
16
18
20
22
24
26
28
30

FIG. 15

FIG. 16

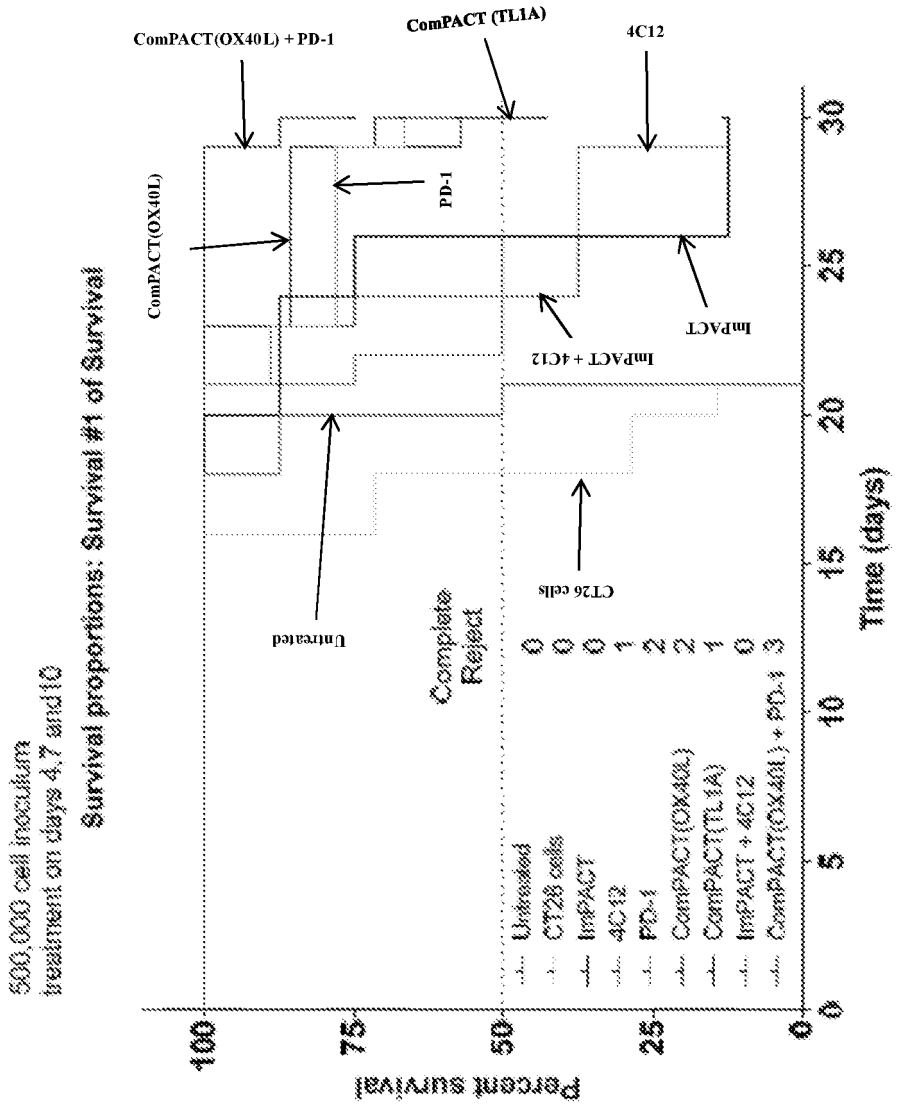

Survival proportions: Survival #1 of Survival
500,000 cell inoculum
treatment on days 4,7 and10
Percent survival
Time (days)
Complete Reject
Untreated
CT26 cells
ImPACT + 4C12
ImPACT
ComPACT(OX40L) + PD-1
ComPACT (TL1A)
4C12
ComPACT(OX40L)
PD-1
Untreated 0
CT26 cells 0
ImPACT 0
4C12 1
PD-1 2
ComPACT(OX40L) 2
ComPACT(TL1A) 1
ImPACT + 4C12 0
ComPACT(OX40L) + PD-1 3

FIG. 17

HS-1020

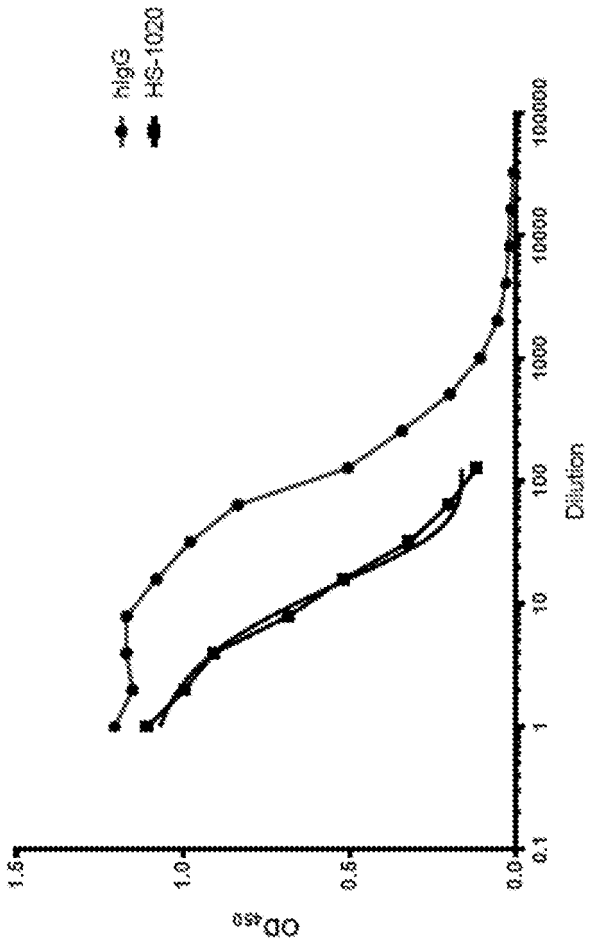
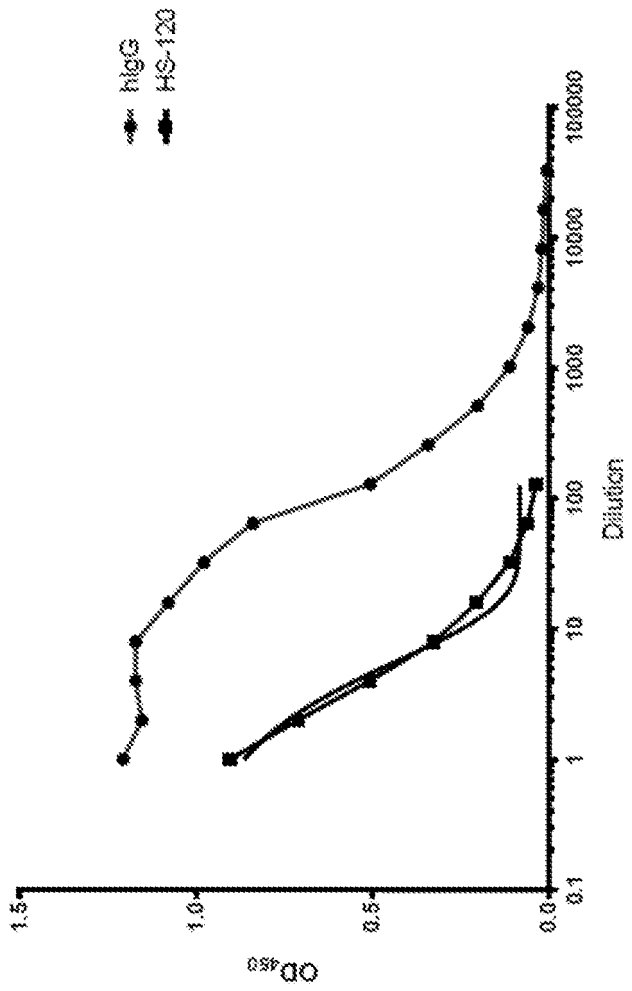


FIG. 18

HS-120


hIgG
HS-120
OD450
1.5
1.0
0.5
0.0
0.1
1
10
100
1000
10000
100000
Dilution