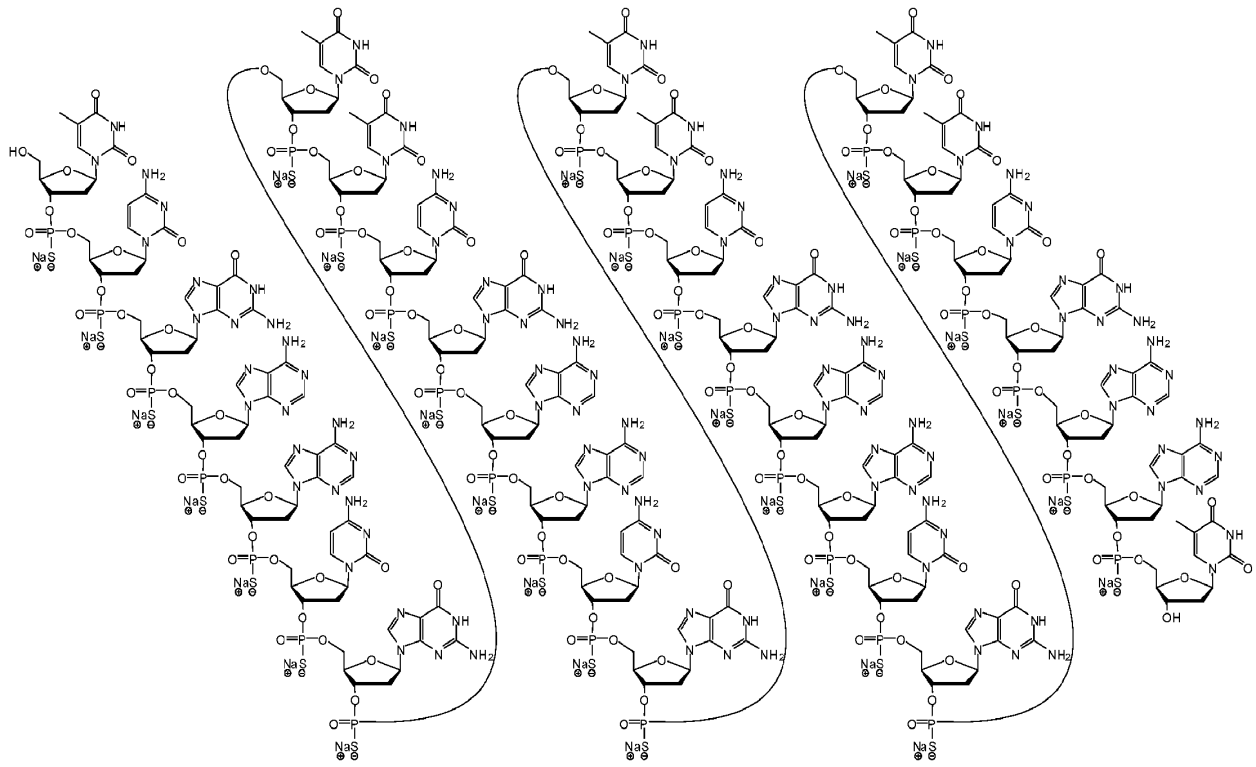


FIGURE 1

FIGURE 2A

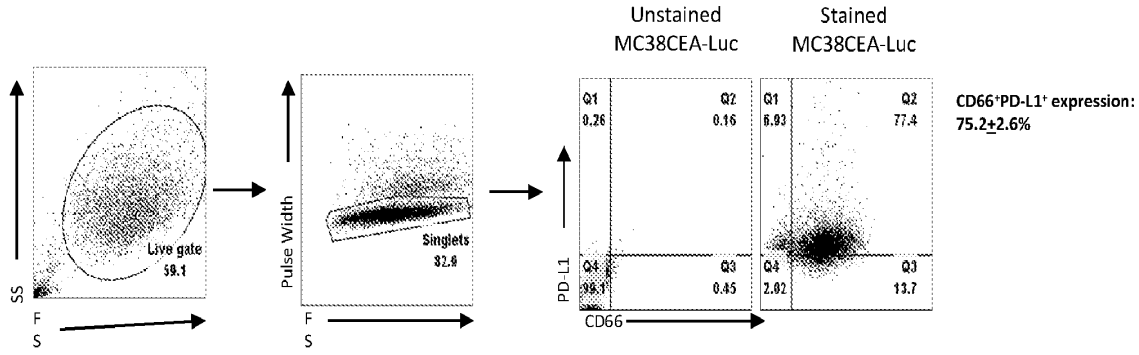


FIGURE 2B

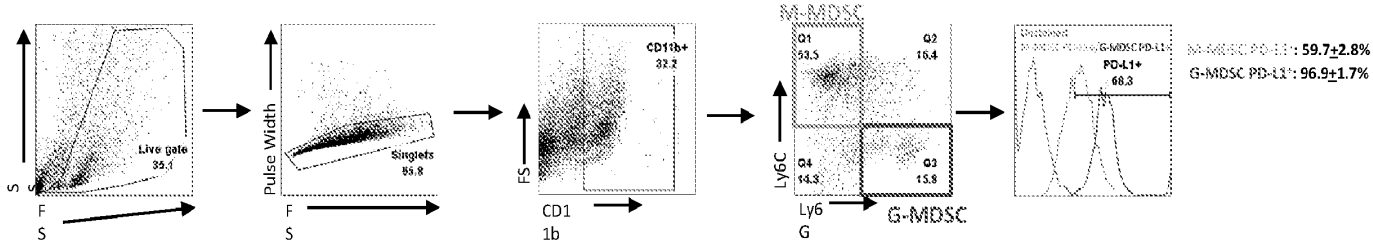


FIGURE 3A(I)

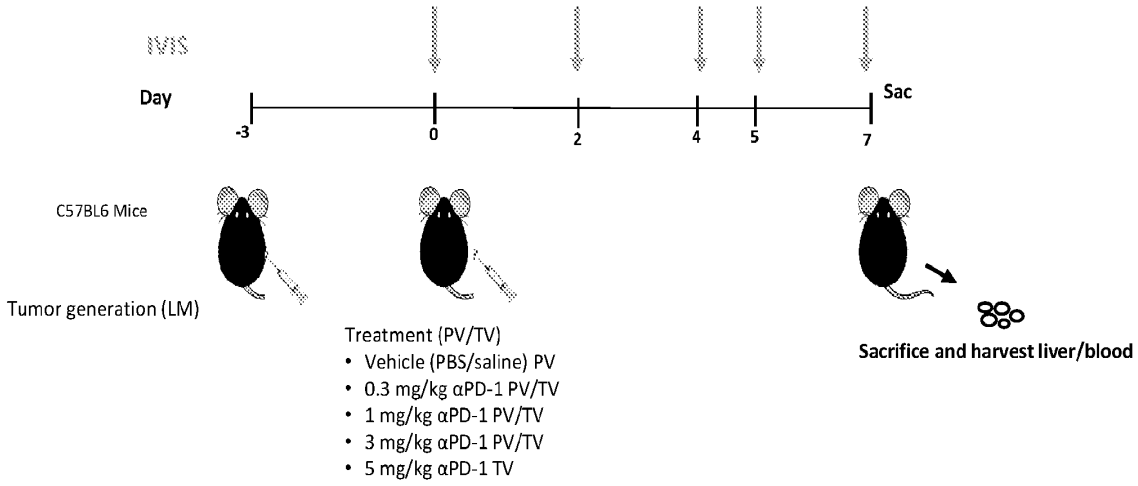
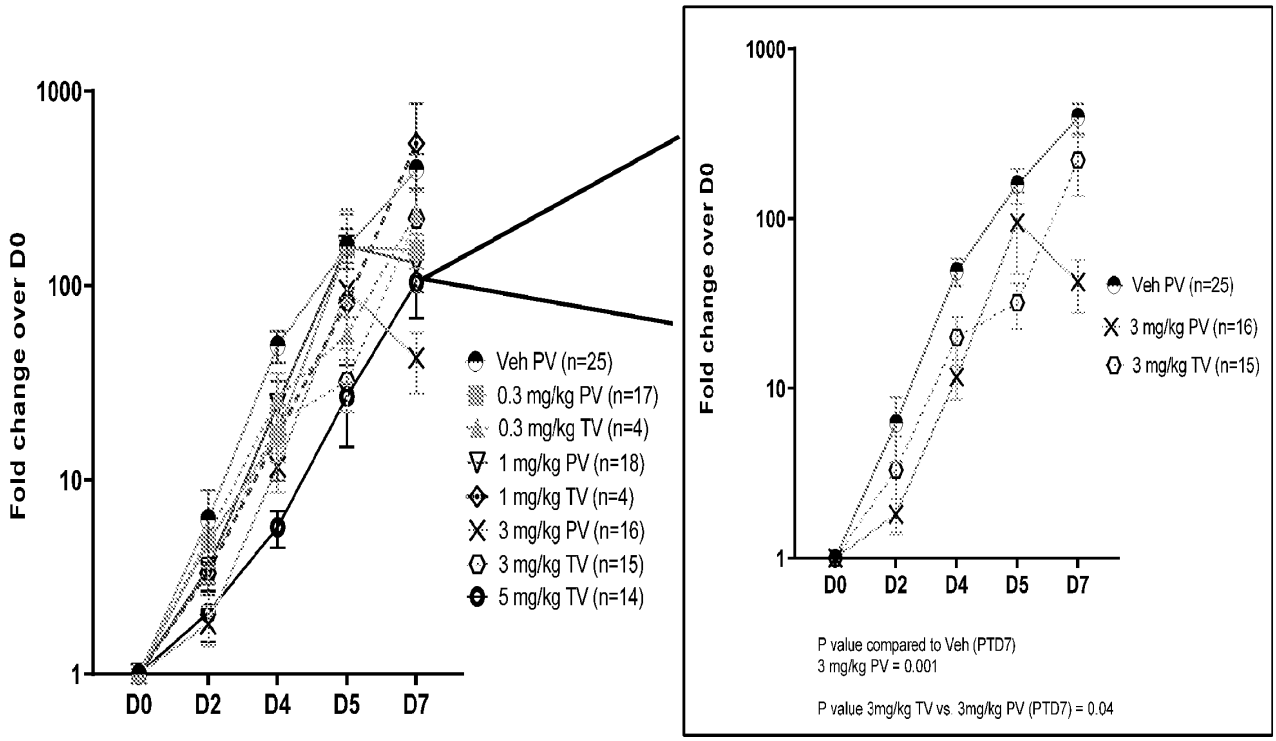

IVIS
Day
-3
0
2
4
5
7
Sac
C57BL6 Mice
Tumor generation (LM)
Treatment (PV/TV)
• Vehicle (PBS/saline) PV
• 0.3 mg/kg αPD-1 PV/TV
• 1 mg/kg αPD-1 PV/TV
• 3 mg/kg αPD-1 PV/TV
• 5 mg/kg αPD-1 TV
Sacrifice and harvest liver/blood

FIGURE 3A(II)



P value compared to Veh (PTD7)
0.3 mg/kg PV =0.003
1 mg/kg PV = 0.024
3 mg/kg PV = 0.001
5 mg/kg TV = 0.01

P value 3mg/kg TV vs. 3mg/kg PV (PTD7) = 0.04

FIGURE 3A(III)

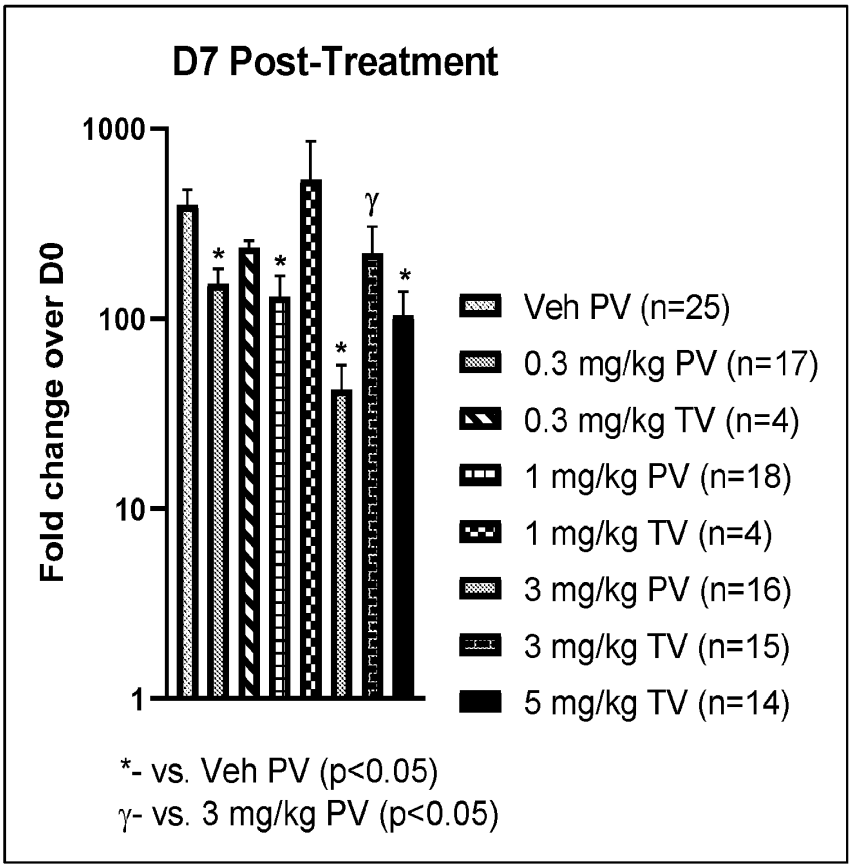


FIGURE 3B

Ciculating levels of anti- PD-1 antibody in serum

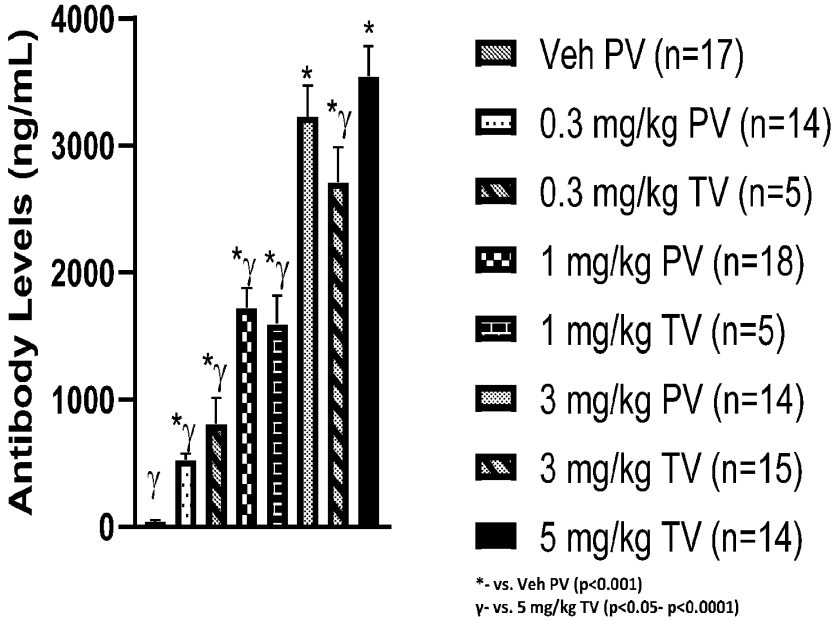


FIGURE 4

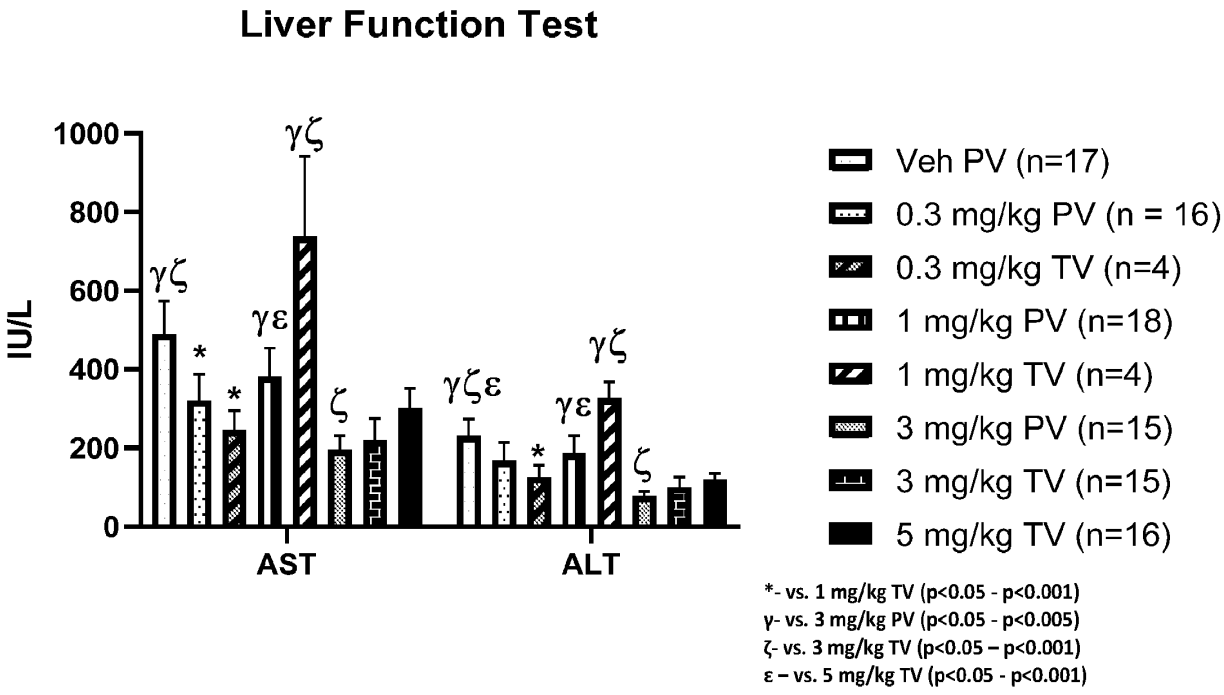

Liver Function Test
IU/L
1000
800
600
400
200
0
AST
ALT
γζ
*
*
γε
γζ
ζ
γζε
*
γε
γζ
ζ
Veh PV (n=17)
0.3 mg/kg PV (n = 16)
0.3 mg/kg TV (n=4)
1 mg/kg PV (n=18)
1 mg/kg TV (n=4)
3 mg/kg PV (n=15)
3 mg/kg TV (n=15)
5 mg/kg TV (n=16)
*- vs. 1 mg/kg TV (p<0.05 - p<0.001)
γ- vs. 3 mg/kg PV (p<0.05 - p<0.005)
ζ- vs. 3 mg/kg TV (p<0.05 – p<0.001)
ε – vs. 5 mg/kg TV (p<0.05 - p<0.001)

FIGURE 5

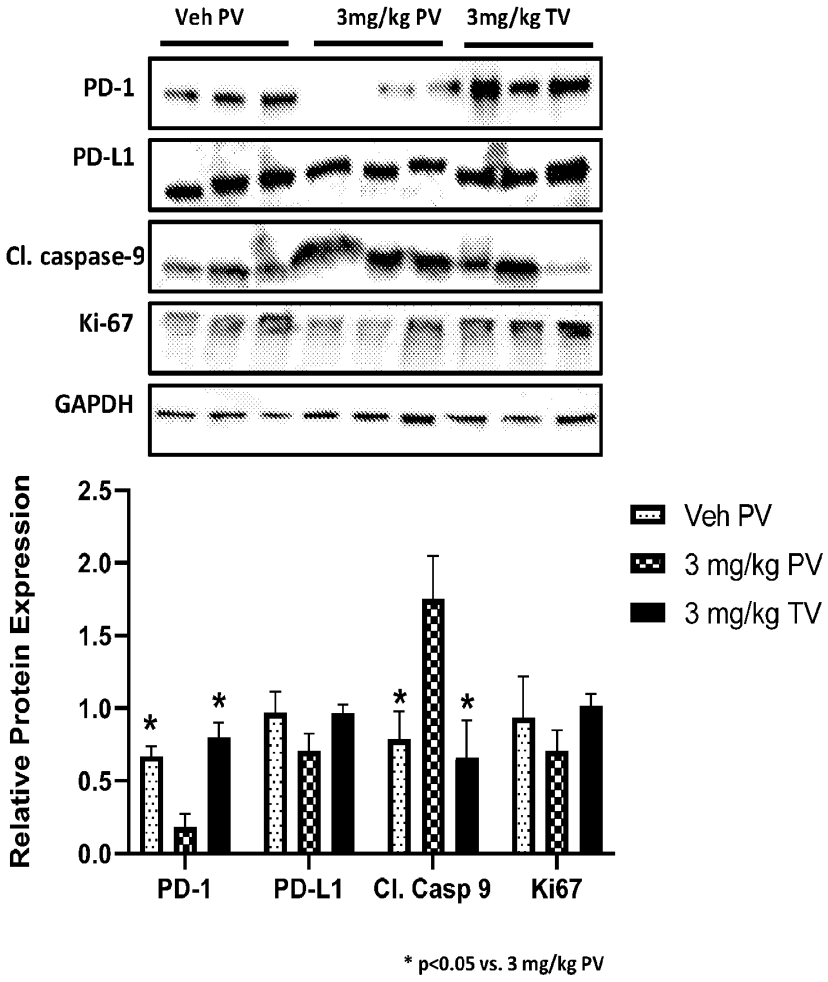

Veh PV
3mg/kg PV
3mg/kg TV
PD-1
PD-L1
Cl. caspase-9
Ki-67
GAPDH
Relative Protein Expression
2.5
2.0
1.5
1.0
0.5
0.0
PD-1
PD-L1
Cl. Casp 9
Ki67
Veh PV
3 mg/kg PV
3 mg/kg TV
* p<0.05 vs. 3 mg/kg PV

FIGURE 6A

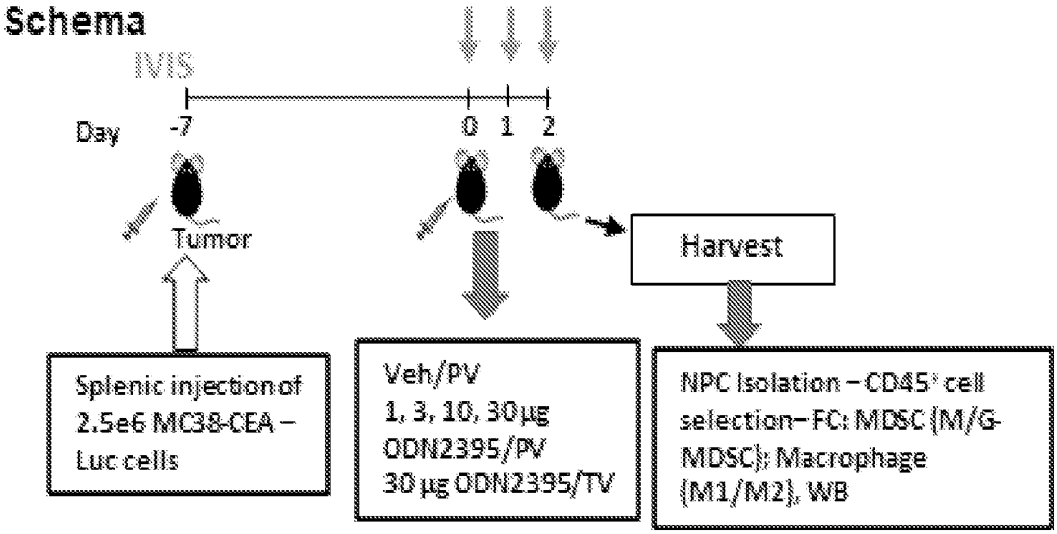
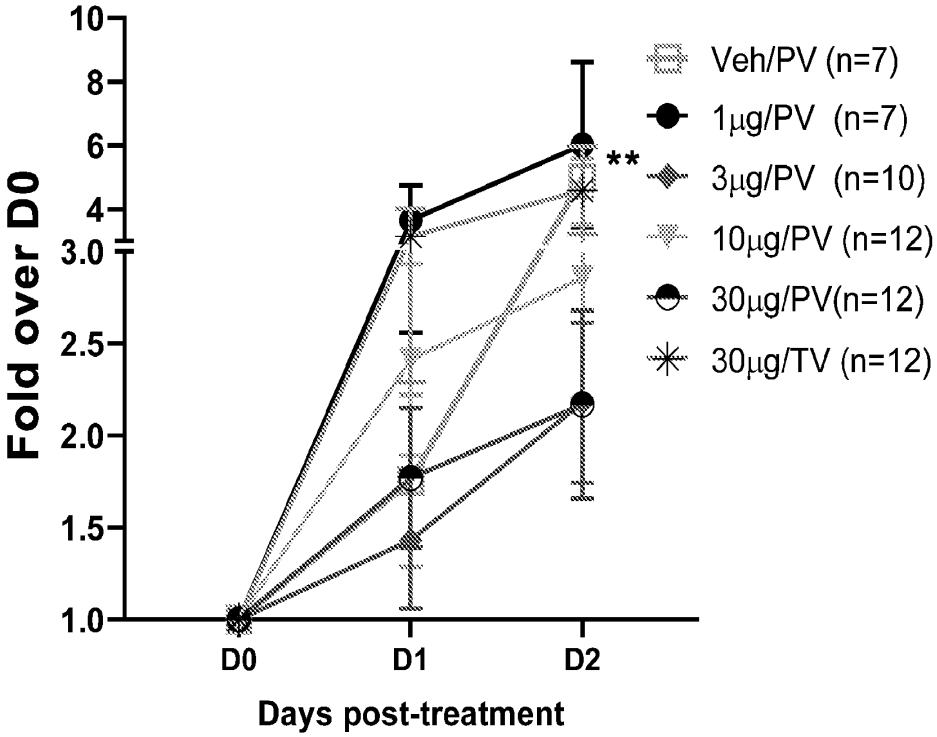

Schema
IVIS
Day
-7
0
1
2
Tumor
Harvest
Splenic injection of 2.5e6 MC38-CEA – Luc cells
Veh/PV
1, 3, 10, 30µg ODN2395/PV
30 µg ODN2395/TV
NPC Isolation – CD45+ cell selection– FC: MDSC (M/G-MDSC); Macrophage (M1/M2), WB

FIGURE 6B



**p<0.01 (Veh/PV vs. 30 μg/PV)

FIGURE 6C

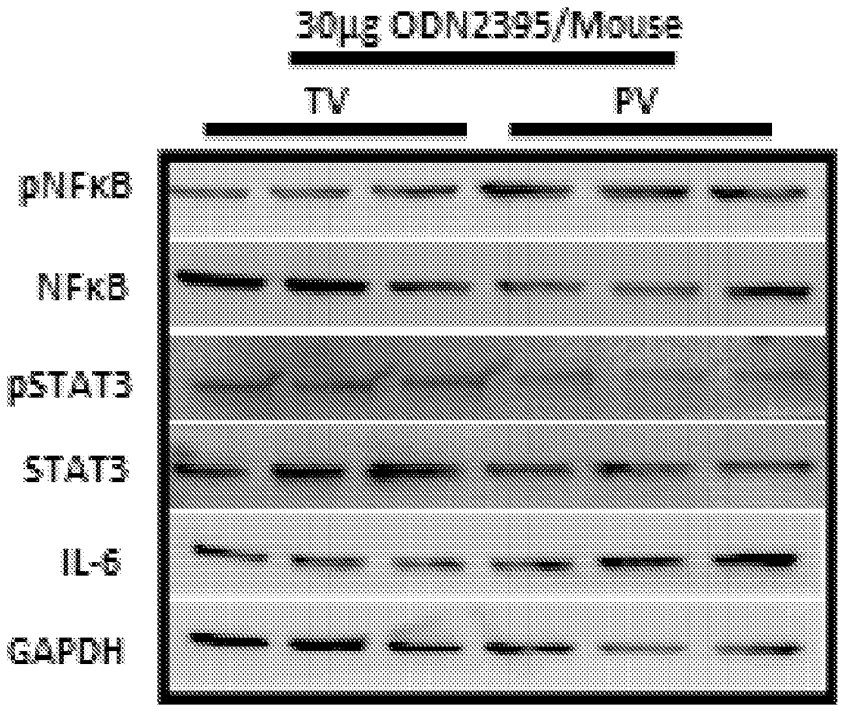


FIGURE 7A

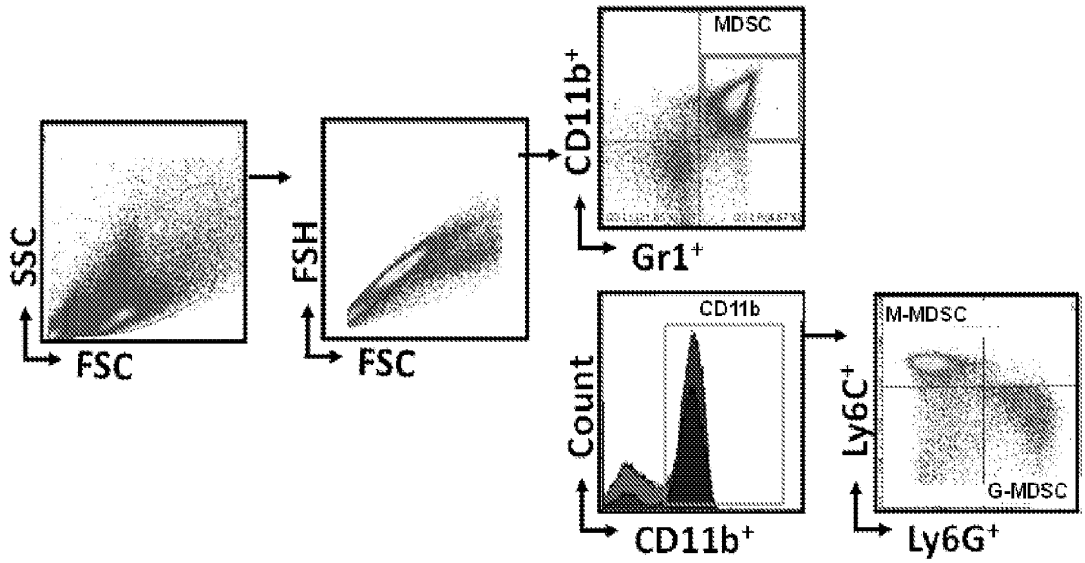
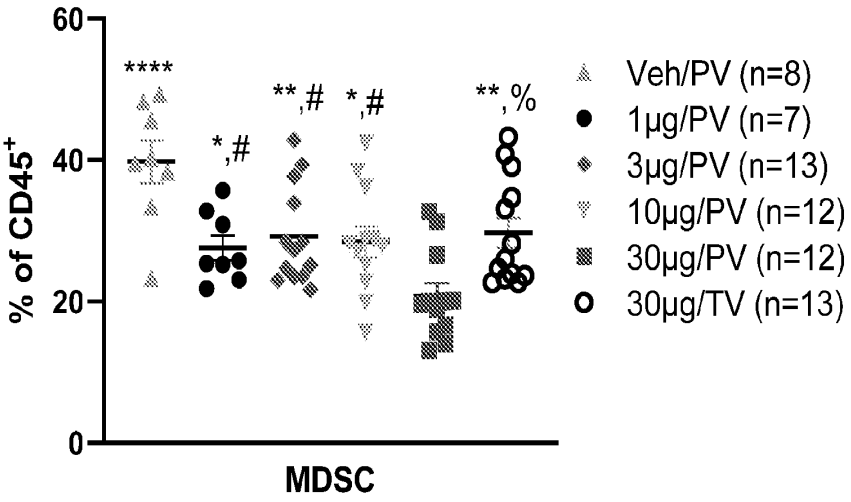
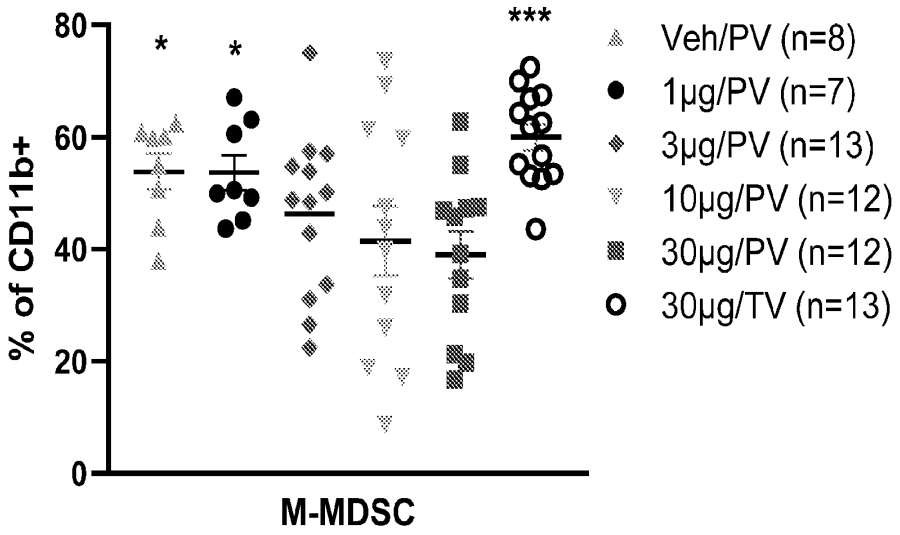

SSC
FSC
FSH
FSC
CD11b+
Gr1+
MDSC
Count
CD11b+
CD11b
Ly6C+
Ly6G+
M-MDSC
G-MDSC

FIGURE 7B



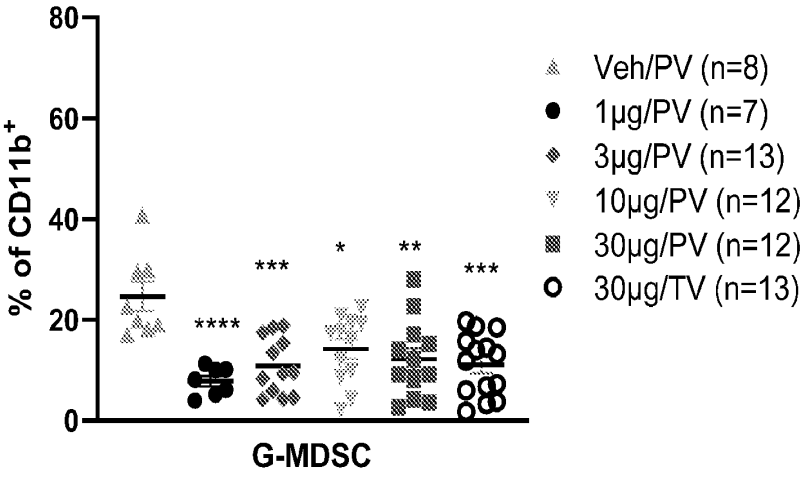
*p<0.05, **p<0.01,****p<0.0001 (compared to 30µg/PV)
%p<0.05, #p<0.01 (compared to Veh/PV)

FIGURE 7C



*p<0.05, ***p<0.001 (compared to 30 µg/PV)

FIGURE 7D



*p<0.05, **p<0.01, ***p<0.001,
**p<0.0001
(compared to Veh/PV)

FIGURE 7E

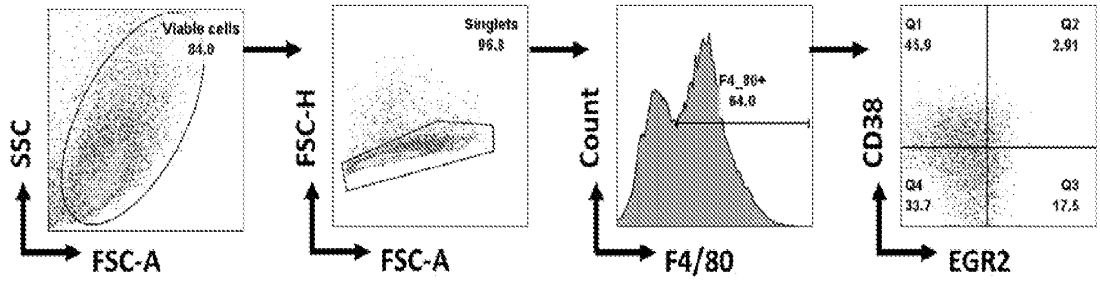
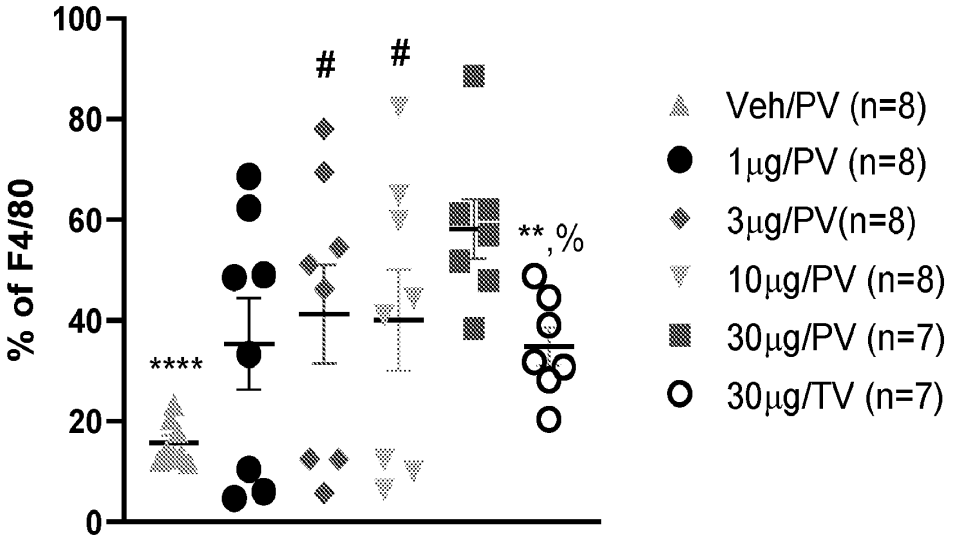
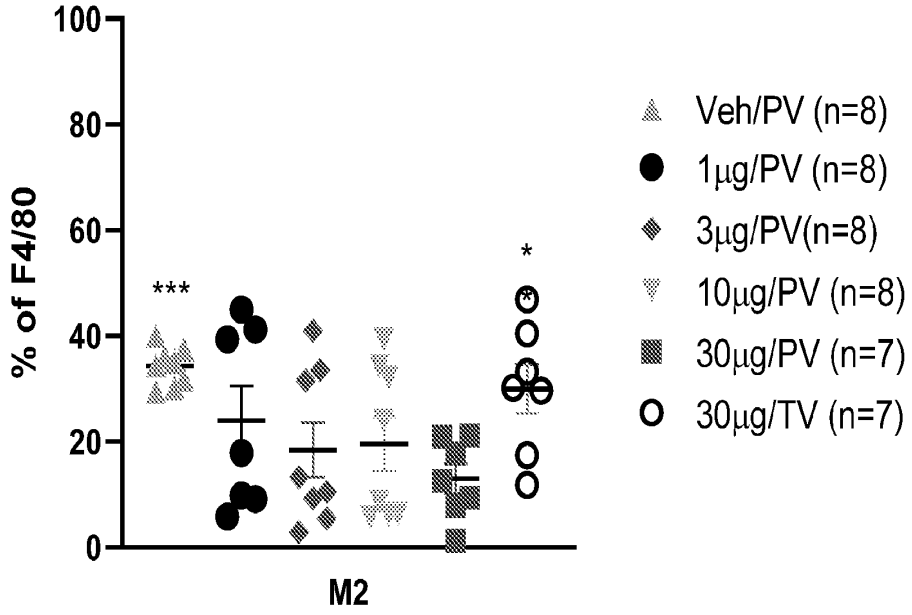

Viable cells
84.8
SSC
FSC-A
Singlets
96.8
FSC-H
FSC-A
F4_80+
64.8
Count
F4/80
Q1
45.9
Q2
2.91
Q4
33.7
Q3
17.5
CD38
EGR2

FIGURE 7F



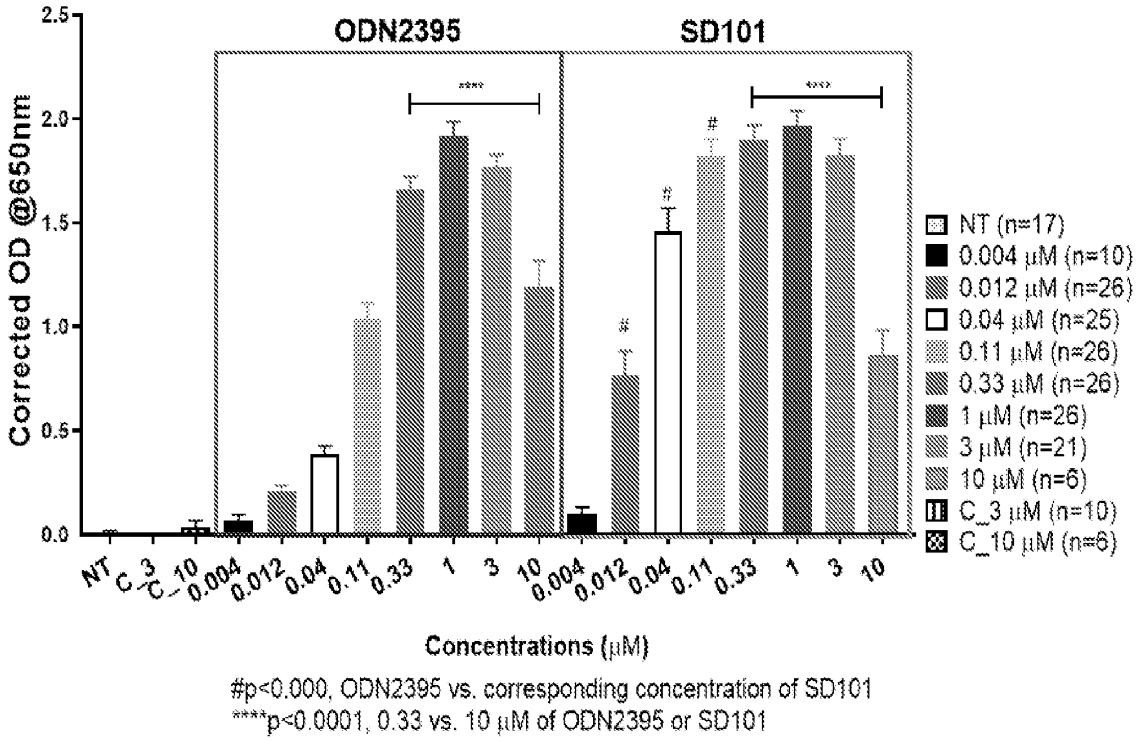
p<0.01,**p<0.0001 (compared to 30μg/PV)
#p<0.05,%p<0.01 (compared to Veh/PV)

FIGURE 7G



p<0.01,*p<0.001 (compared to 30μg/PV)

FIGURE 8A



#p<0.000, ODN2395 vs. corresponding concentration of SD101
****p<0.0001, 0.33 vs. 10 μM of ODN2395 or SD101

FIGURE 8B

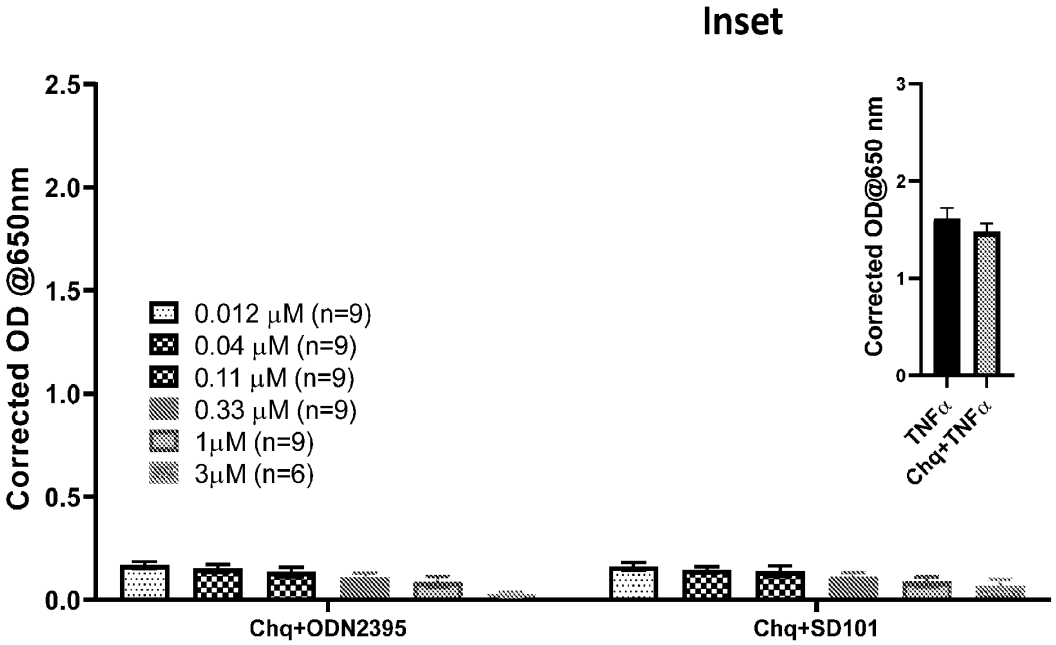

Inset
Corrected OD @650nm
2.5
2.0
1.5
1.0
0.5
0.0
0.012 μM (n=9)
0.04 μM (n=9)
0.11 μM (n=9)
0.33 μM (n=9)
1μM (n=9)
3μM (n=6)
Chq+ODN2395
Chq+SD101
Corrected OD@650 nm
3
2
1
0
TNFα
Chq+TNFα

FIGURE 9A

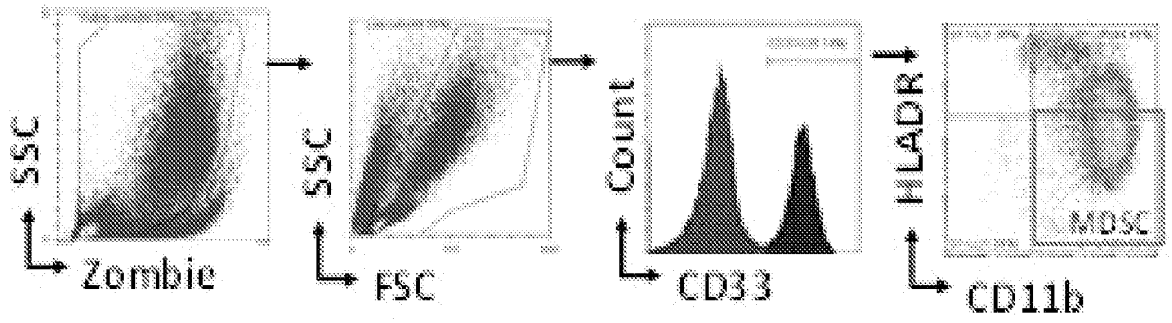
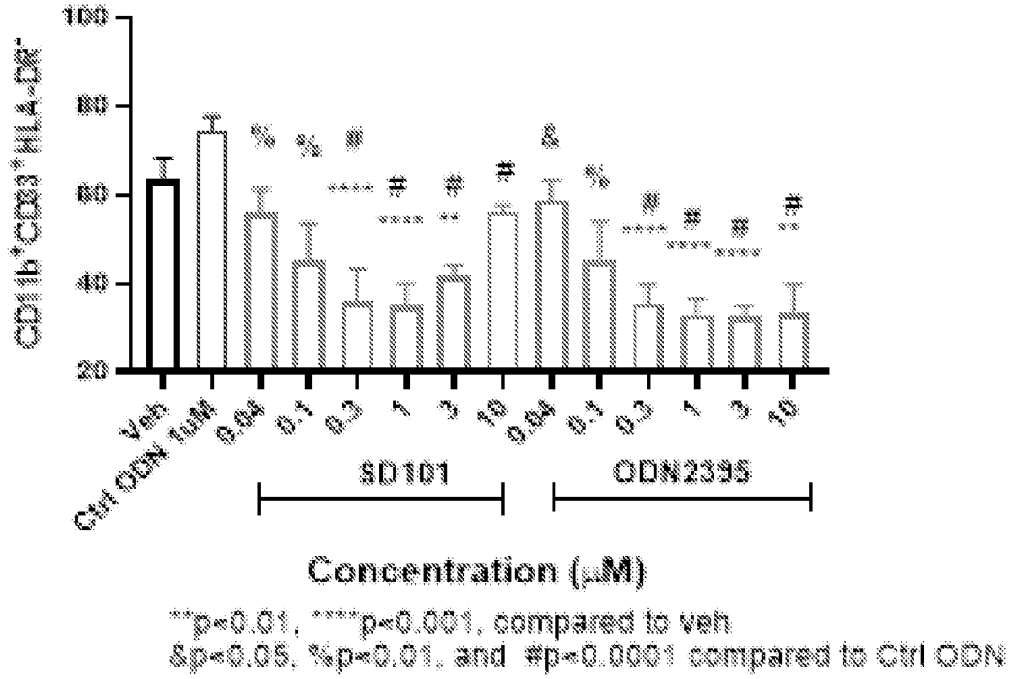


FIGURE 9B



**p<0.01, ****p<0.001, compared to veh
&p<0.05, %p<0.01, and #p<0.0001 compared to Ctrl ODN

FIGURE 9C

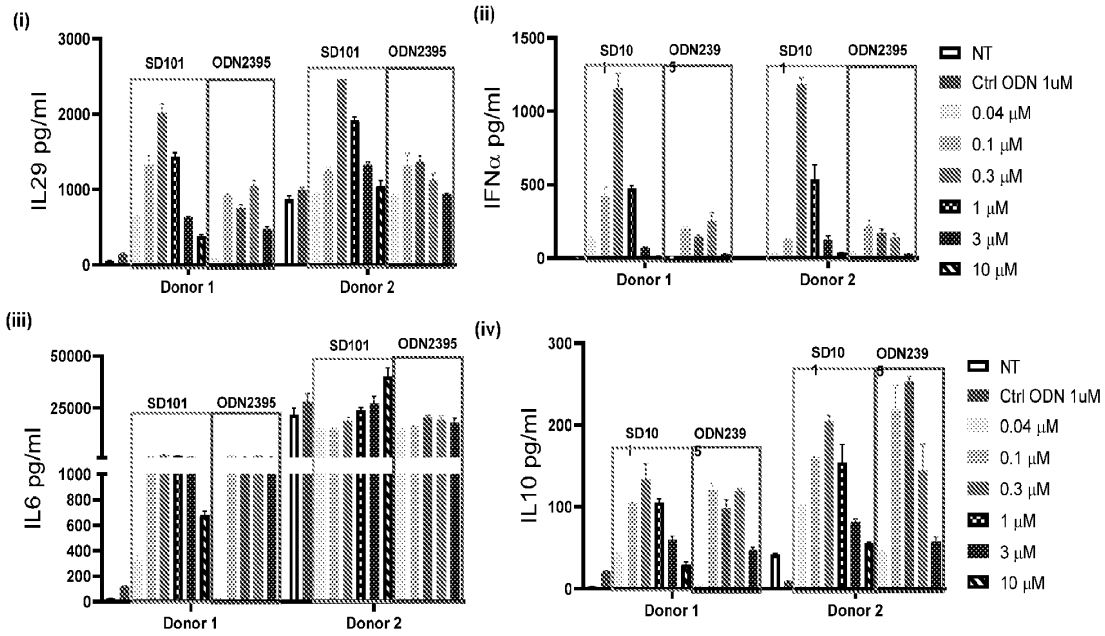

(i)
IL29 pg/ml
3000
2000
1000
0
SD101
ODN2395
SD101
ODN2395
Donor 1
Donor 2
(ii)
IFNα pg/ml
1500
1000
500
0
SD10
1
ODN239
5
SD10
1
ODN2395
Donor 1
Donor 2
NT
Ctrl ODN 1uM
0.04 μM
0.1 μM
0.3 μM
1 μM
3 μM
10 μM
(iii)
IL6 pg/ml
50000
25000
1000
800
600
400
200
0
SD101
ODN2395
SD101
ODN2395
Donor 1
Donor 2
(iv)
IL10 pg/ml
300
200
100
0
SD10
1
ODN239
5
SD10
1
ODN239
5
Donor 1
Donor 2
NT
Ctrl ODN 1uM
0.04 μM
0.1 μM
0.3 μM
1 μM
3 μM
10 μM

FIGURE 10A

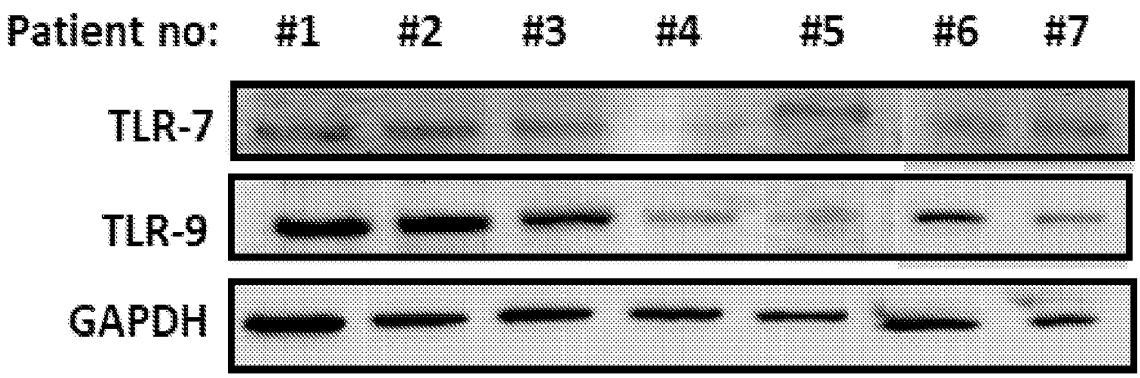


FIGURE 10B

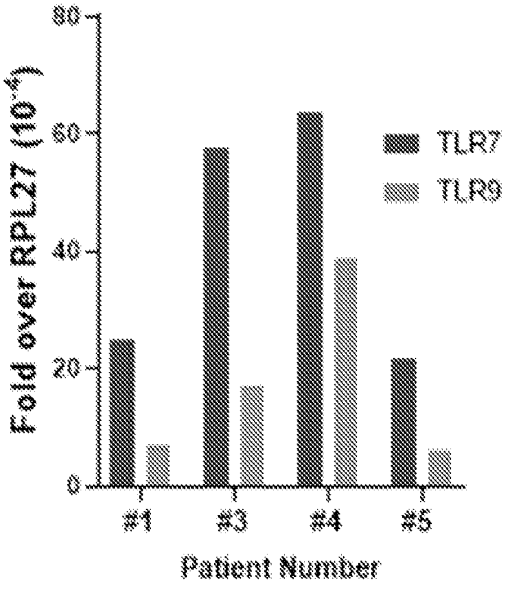

80
60
40
20
0
Fold over RPL27 (10^{-4})
TLR7
TLR9
#1
#3
#4
#5
Patient Number

FIGURE 10C

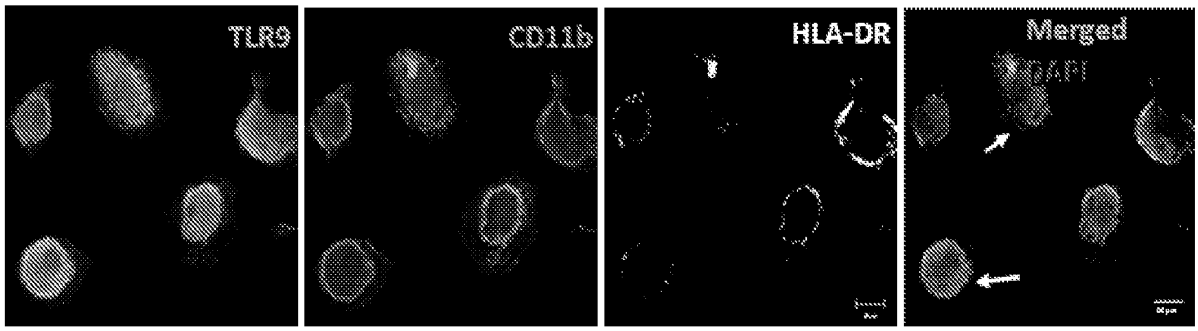


FIGURE 10D

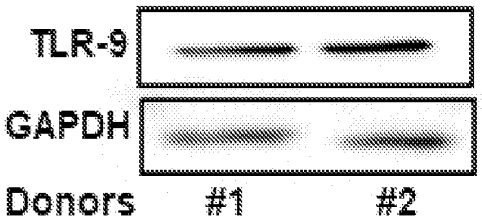


FIGURE 11A

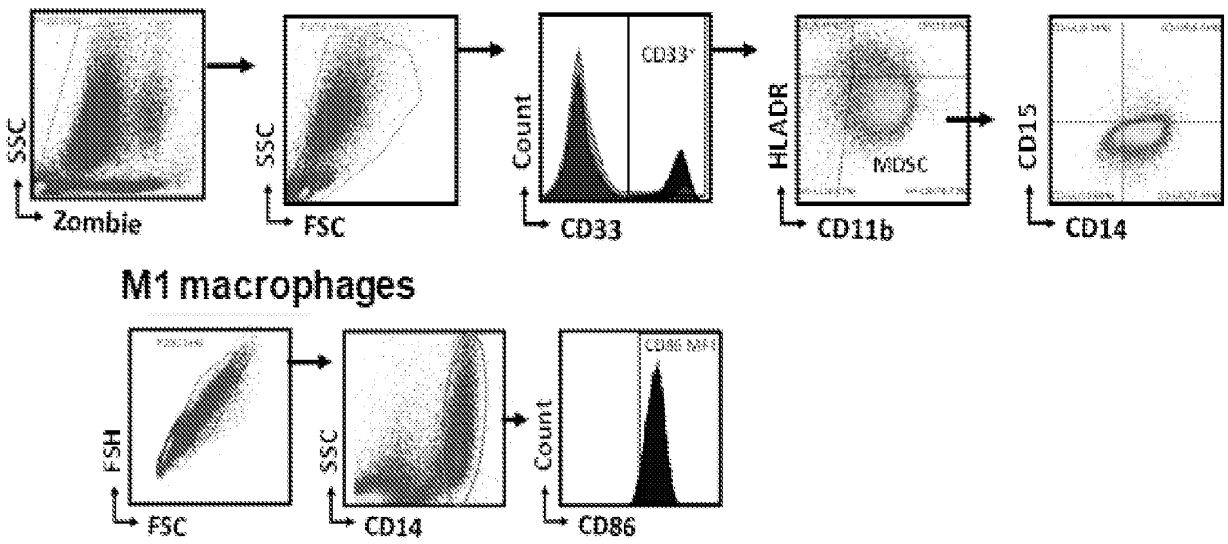

SSC
Zombie
SSC
FSC
Count
CD33
CD33+
HLADR
CD11b
MDSC
CD15
CD14
M1 macrophages
FSH
FSC
SSC
CD14
Count
CD86
CD86 MFI

FIGURE 11B

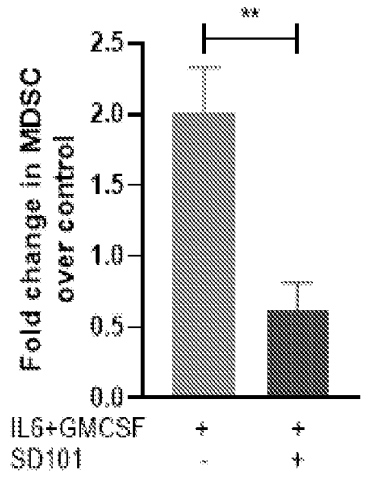


FIGURE 11C

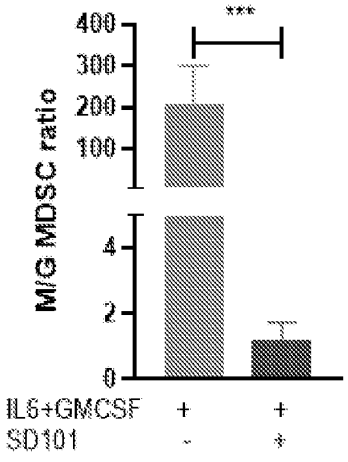


FIGURE 11D

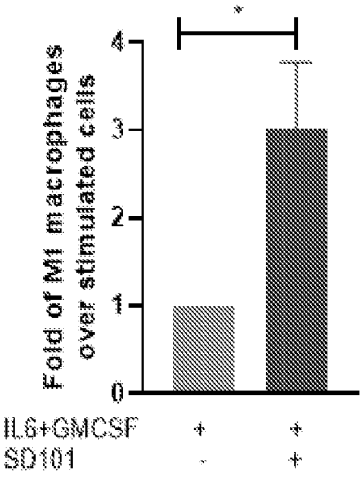


FIGURE 11E

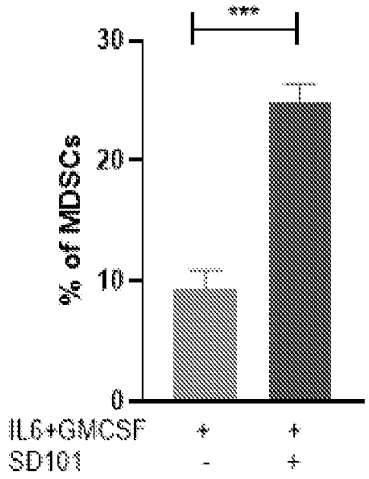


FIGURE 11F

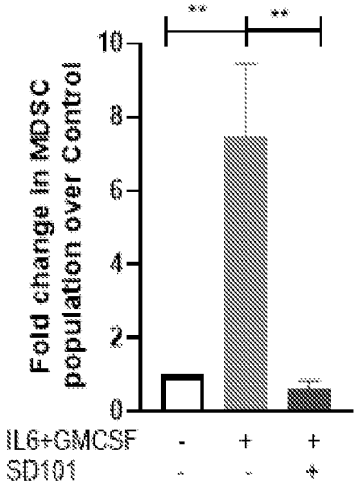


FIGURE 11G

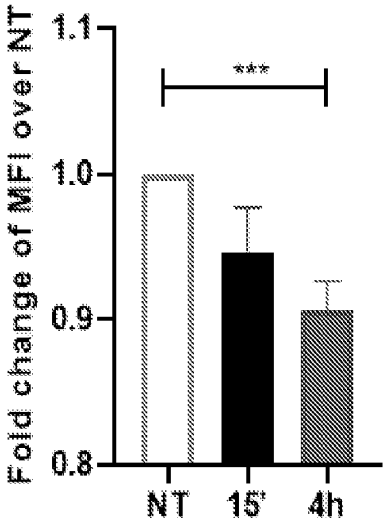


FIGURE 12A

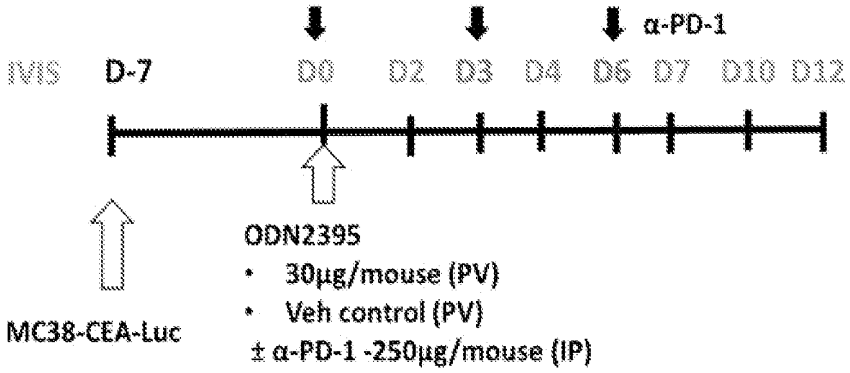
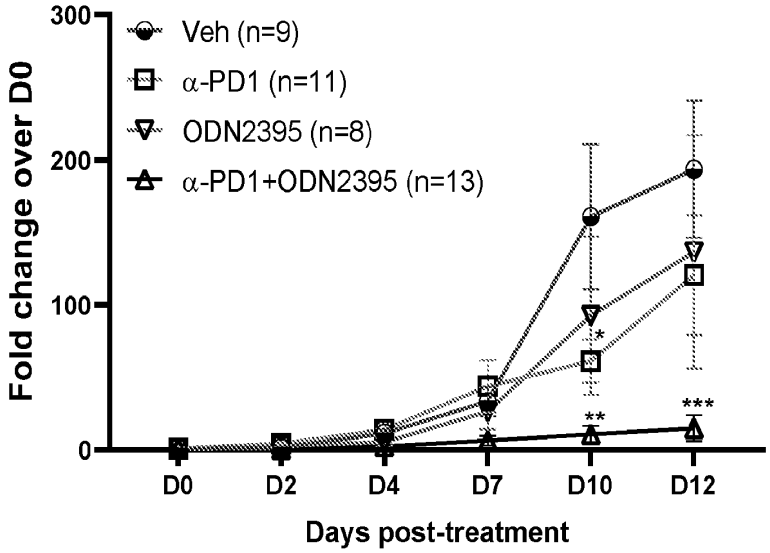

α-PD-1
IVIS
D-7
D0
D2
D3
D4
D6
D7
D10
D12
ODN2395
• 30µg/mouse (PV)
• Veh control (PV)
± α-PD-1 -250µg/mouse (IP)
MC38-CEA-Luc

FIGURE 12B



*p<0.05, α-PD1 vs. Veh group @D10
**p<0.01, α-PD1+ODN2395 vs. Veh group @D10.
* p<0.05, α-PD1+ODN2395 vs. α-PD1 @D10
***p<0.0001, α-PD1+ODN2395 vs. Veh group @D12
* p<0.05, α-PD1+ODN2395 vs. α-PD1 @D12

FIGURE 13

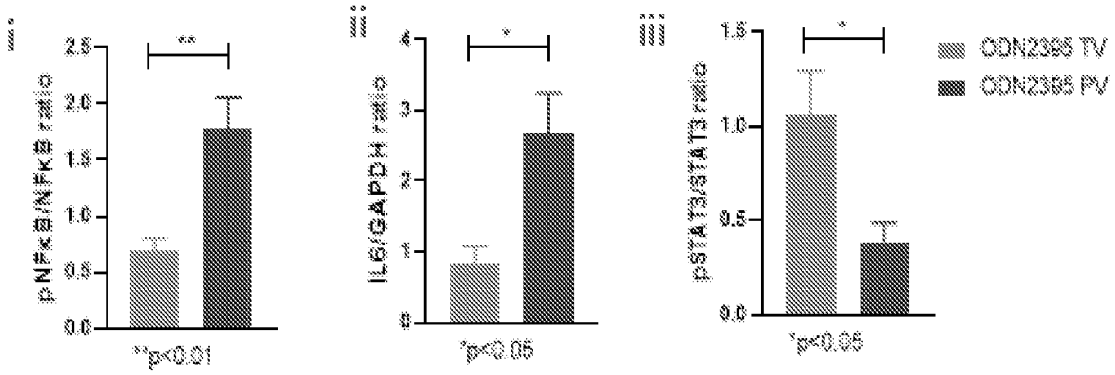

i
pNFκB/NFκB ratio
2.5
2.0
1.5
1.0
0.5
0.0
**
**p<0.01
ii
IL6/GAPDH ratio
4
3
2
1
0
*
*p<0.05
iii
pSTAT3/STAT3 ratio
1.5
1.0
0.5
0.0
*
*p<0.05
ODN2395 TV
ODN2395 PV

FIGURE 14(I)

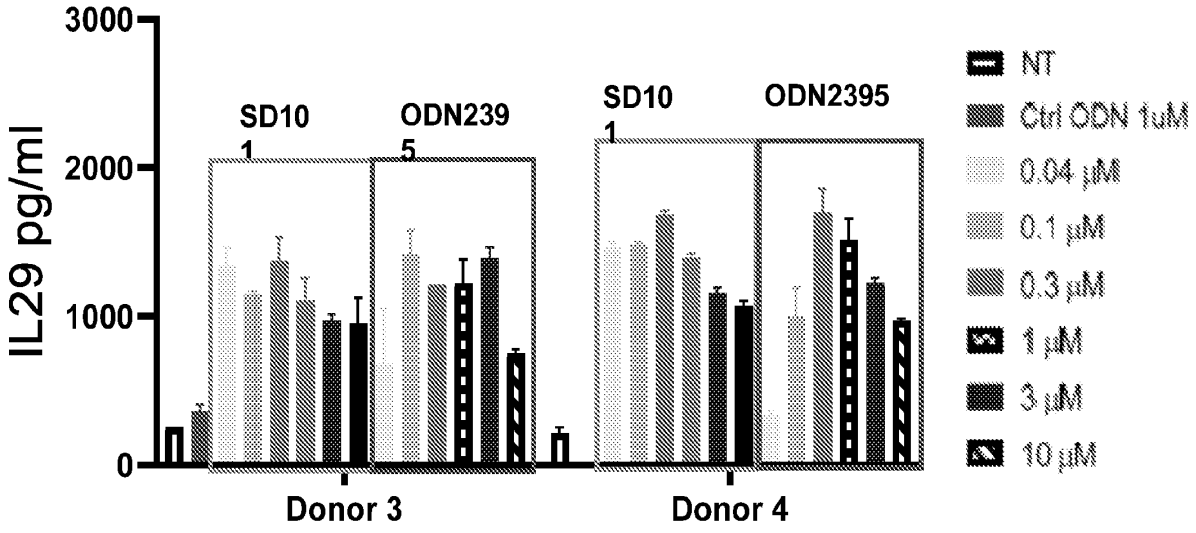

3000
2000
1000
0
IL29 pg/ml
SD10
1
ODN239
5
SD10
1
ODN2395
Donor 3
Donor 4
NT
Ctrl ODN 1uM
0.04 µM
0.1 µM
0.3 µM
1 µM
3 µM
10 µM

FIGURE 14(II)

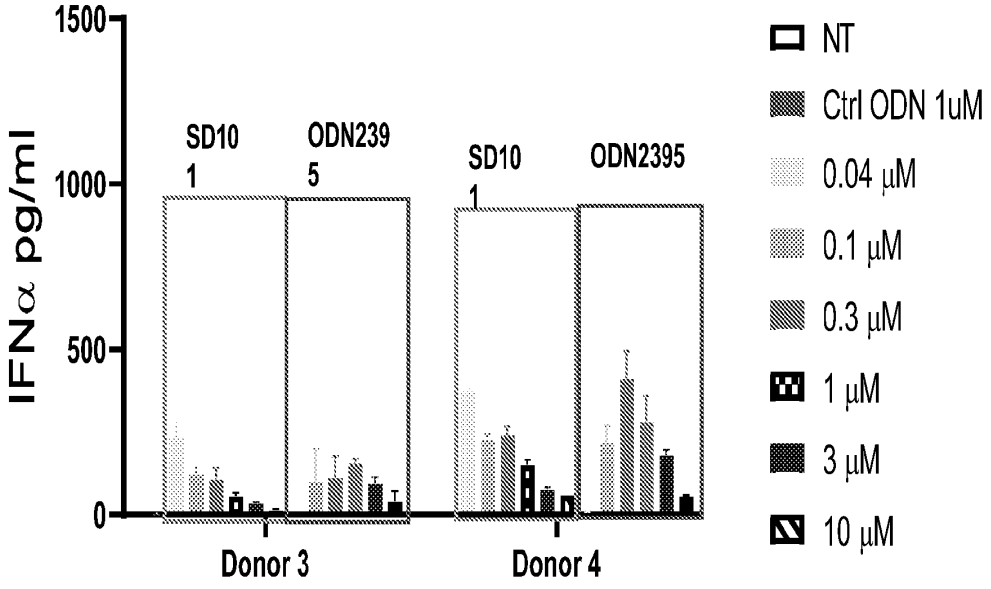

1500
1000
500
0
IFNα pg/ml
SD10
1
ODN239
5
SD10
1
ODN2395
Donor 3
Donor 4
NT
Ctrl ODN 1uM
0.04 μM
0.1 μM
0.3 μM
1 μM
3 μM
10 μM

FIGURE 14(III)

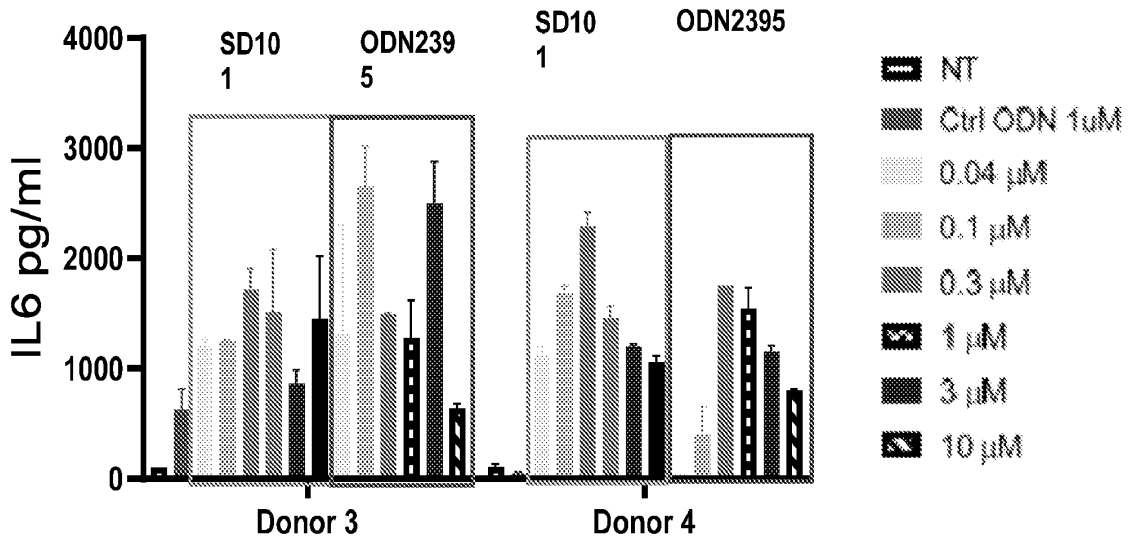


FIGURE 14(IV)

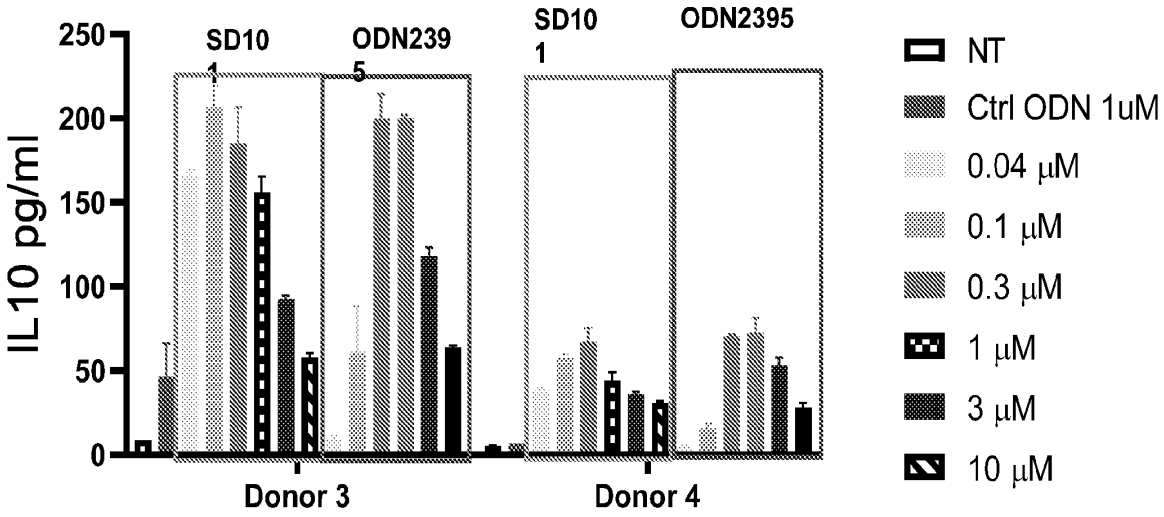
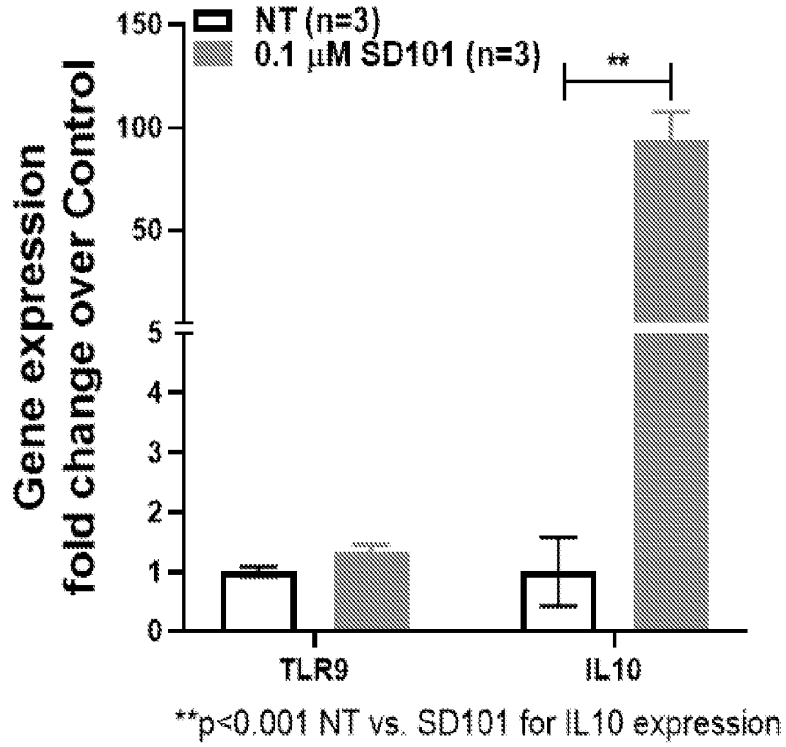

IL10 pg/ml
250
200
150
100
50
0
SD101
ODN2395
SD101
ODN2395
Donor 3
Donor 4
NT
Ctrl ODN 1uM
0.04 μM
0.1 μM
0.3 μM
1 μM
3 μM
10 μM

FIGURE 15


NT (n=3)
0.1 μM SD101 (n=3)
Gene expression
fold change over Control
150
100
50
5
4
3
2
1
0
**
TLR9
IL10
**p<0.001 NT vs. SD101 for IL10 expression