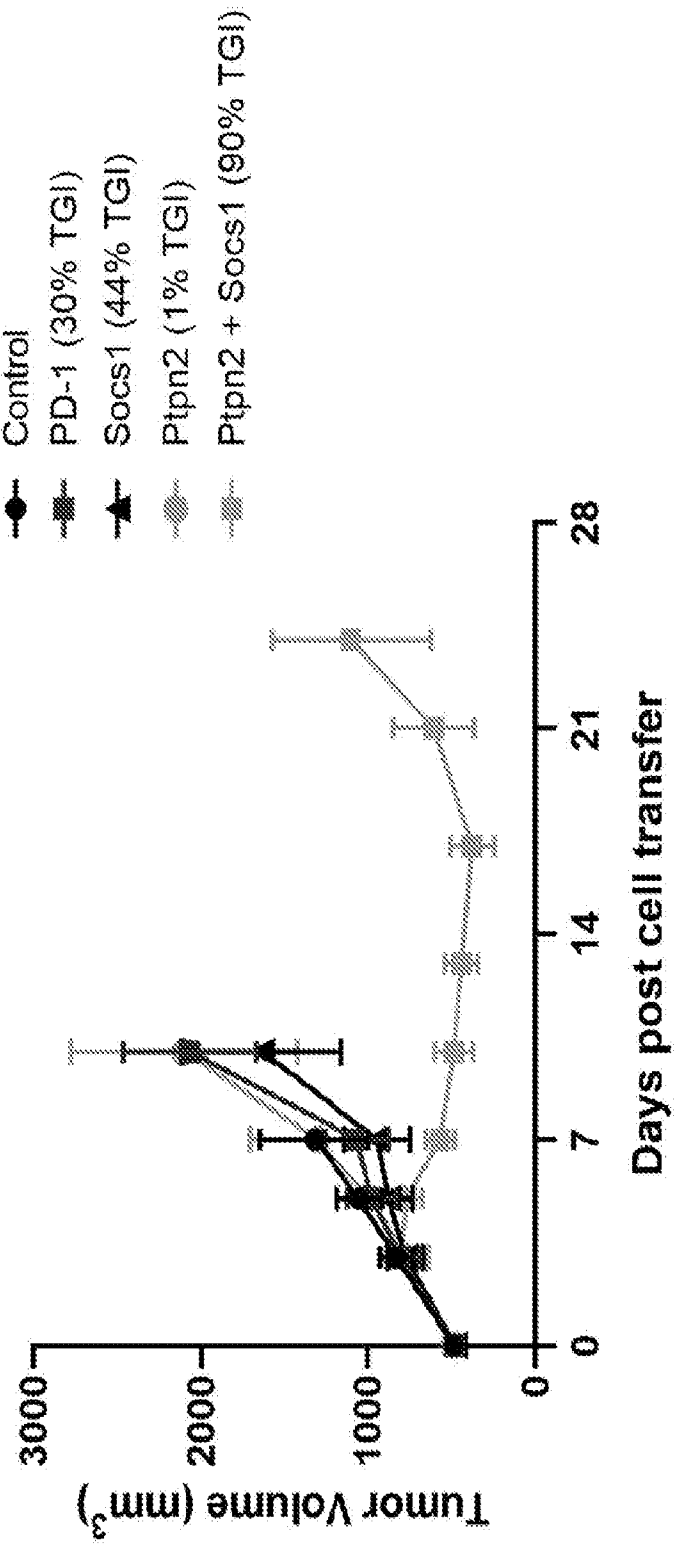

Control
PD-1 (30% TGI)
Socs1 (44% TGI)
Ptpn2 (1% TGI)
Ptpn2 + Socs1 (90% TGI)
Tumor Volume (mm3)
3000
2000
1000
0
0
7
14
21
28
Days post cell transfer

Fig. 1

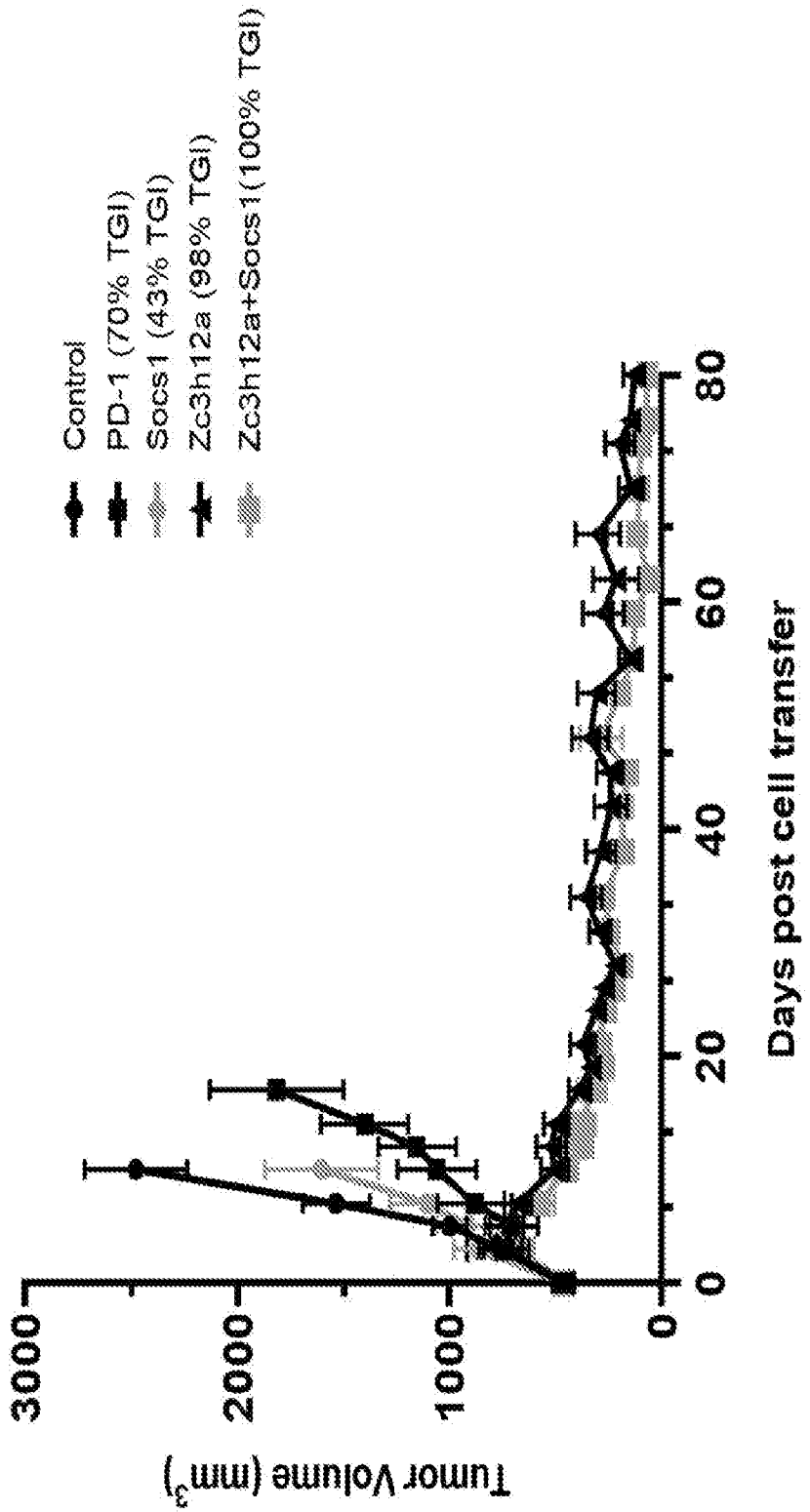

Control
PD-1 (70% TGI)
Socs1 (43% TGI)
Zc3h12a (98% TGI)
Zc3h12a+Socs1(100% TGI)
Tumor Volume (mm3)
3000
2000
1000
0
0
20
40
60
80
Days post cell transfer

Fig. 2

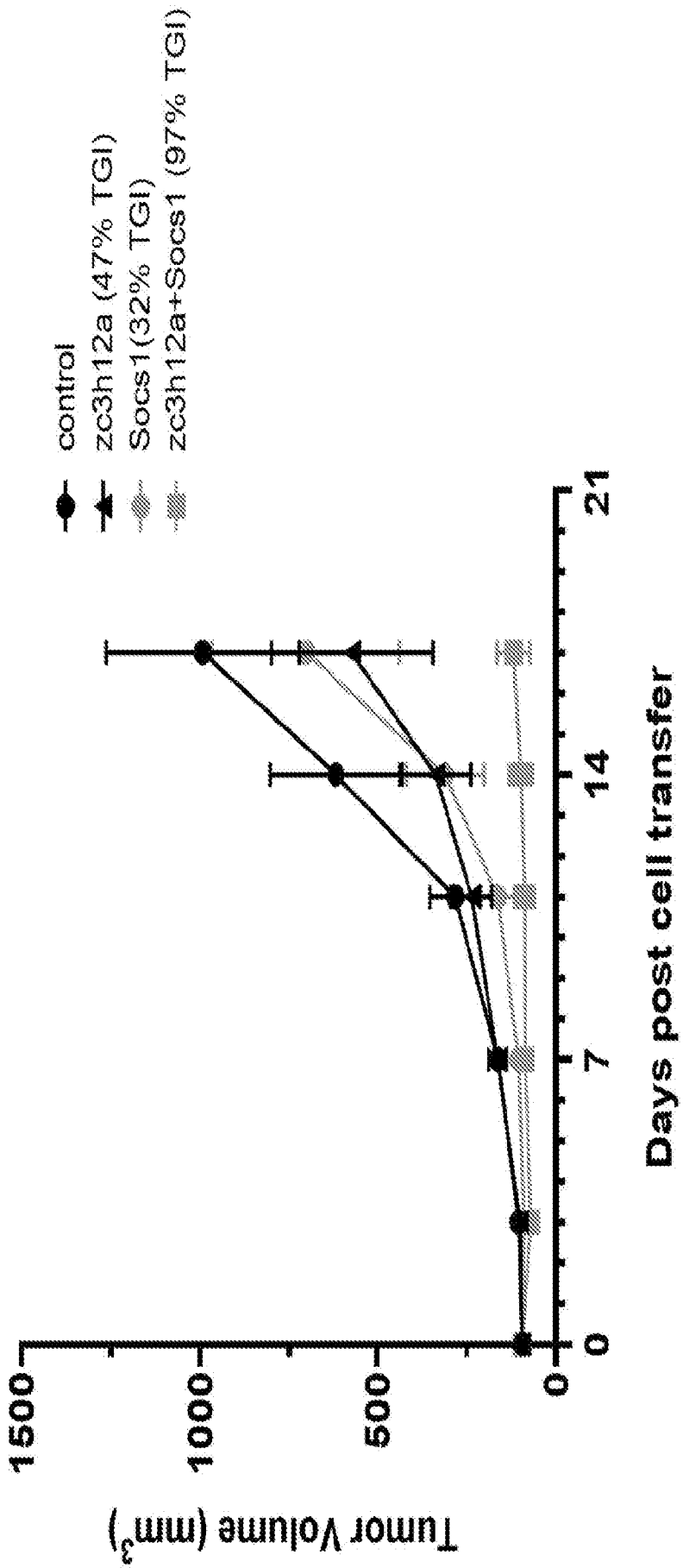

control
zc3h12a (47% TGI)
Socs1(32% TGI)
zc3h12a+Socs1 (97% TGI)
Tumor Volume (mm³)
1500
1000
500
0
0
7
14
21
Days post cell transfer

Fig. 3

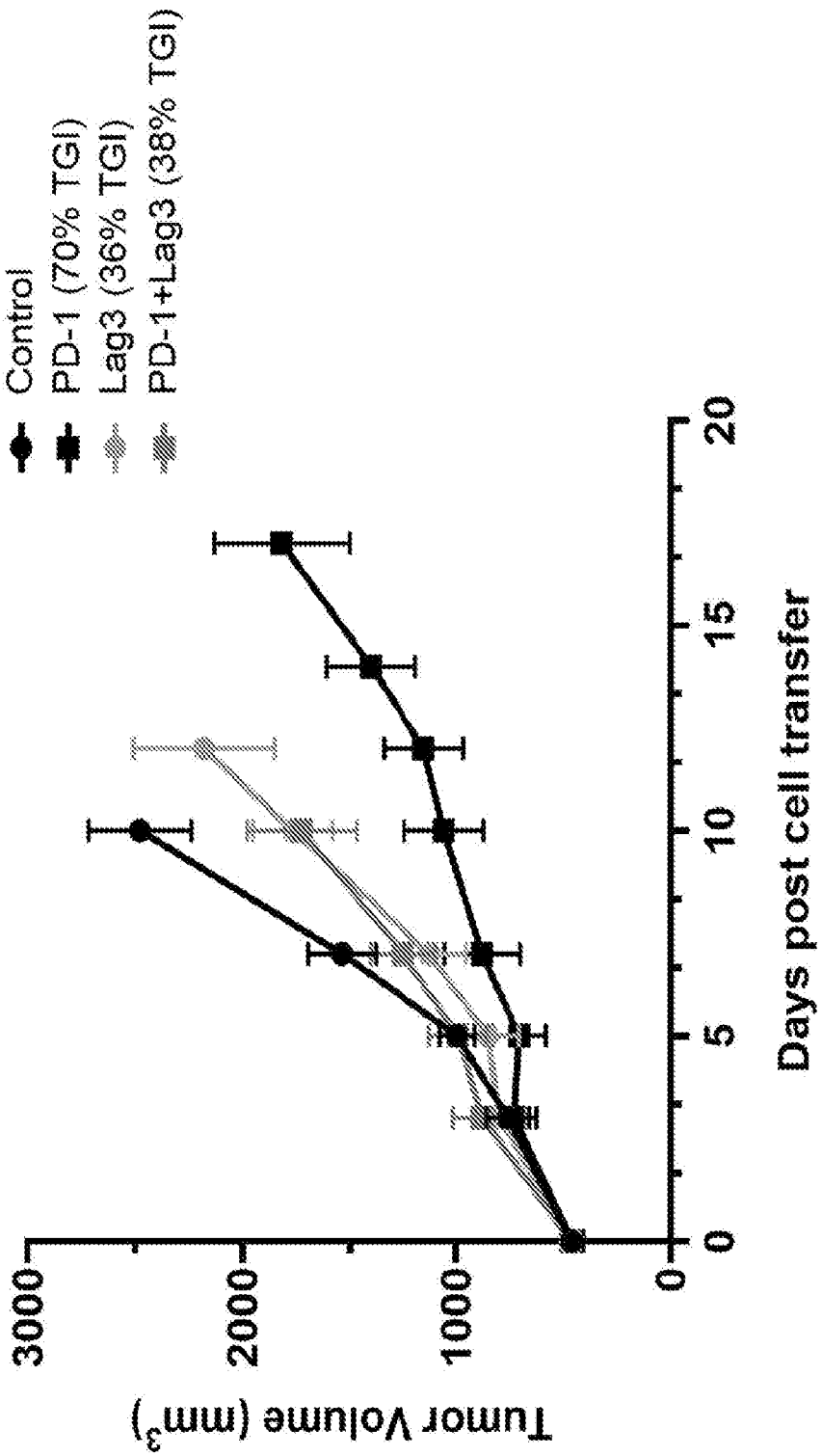

Control
PD-1 (70% TGI)
Lag3 (36% TGI)
PD-1+Lag3 (38% TGI)
Tumor Volume (mm³)
3000
2000
1000
0
0
5
10
15
20
Days post cell transfer

Fig. 4

Fig. 6

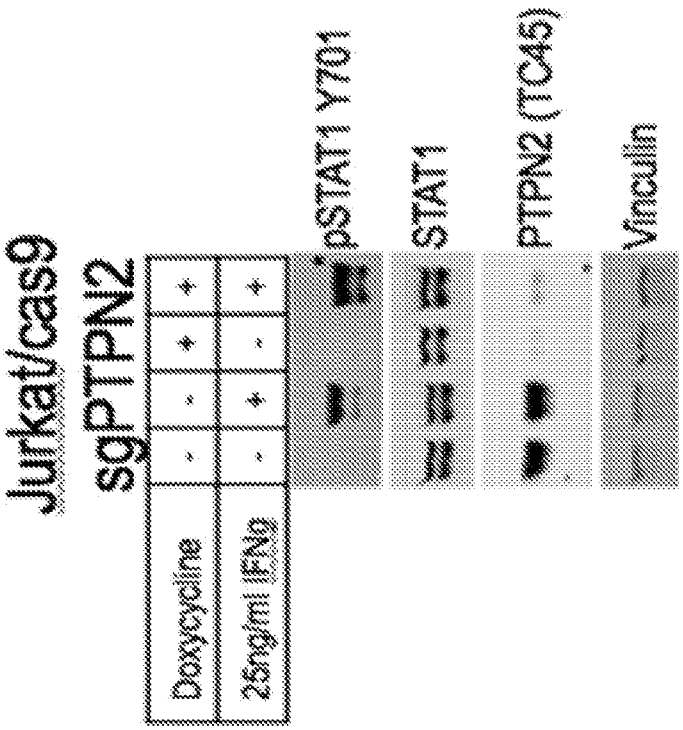

Jurkat/cas9
sgPTPN2
Doxycycline
25ng/ml IFNg
pSTAT1 Y701
STAT1
PTPN2 (TC45)
Vinculin

Fig. 5

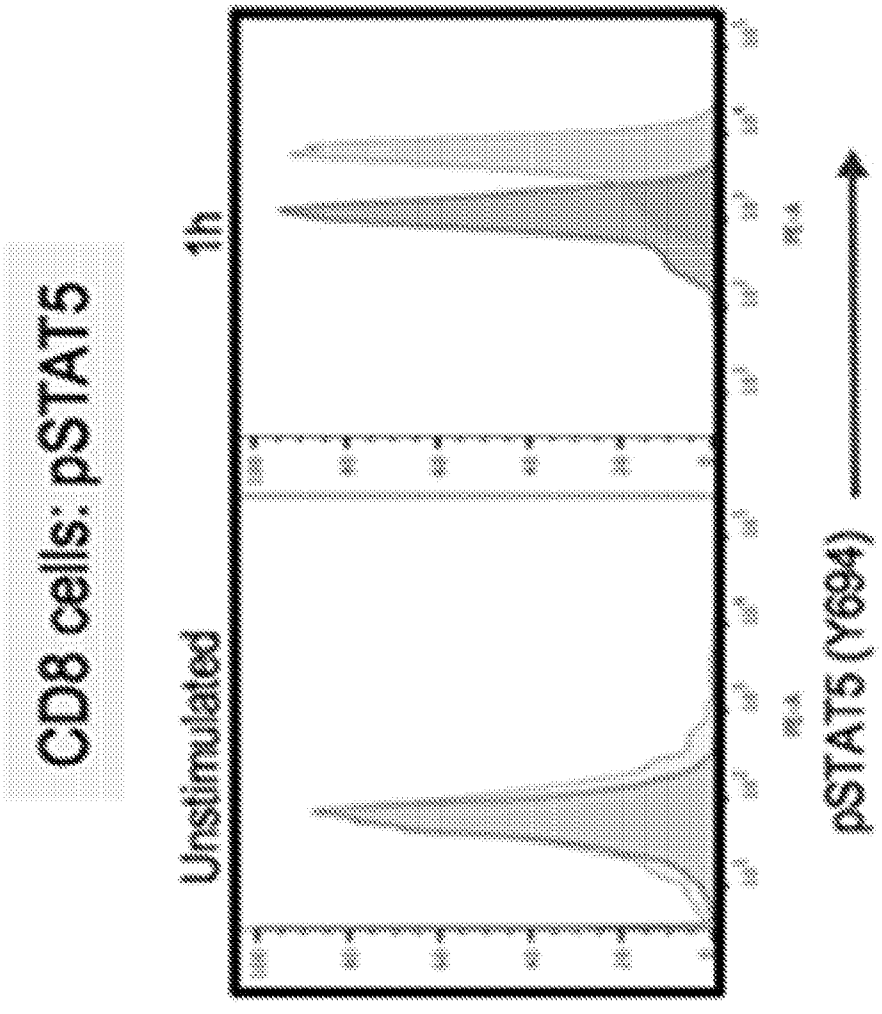
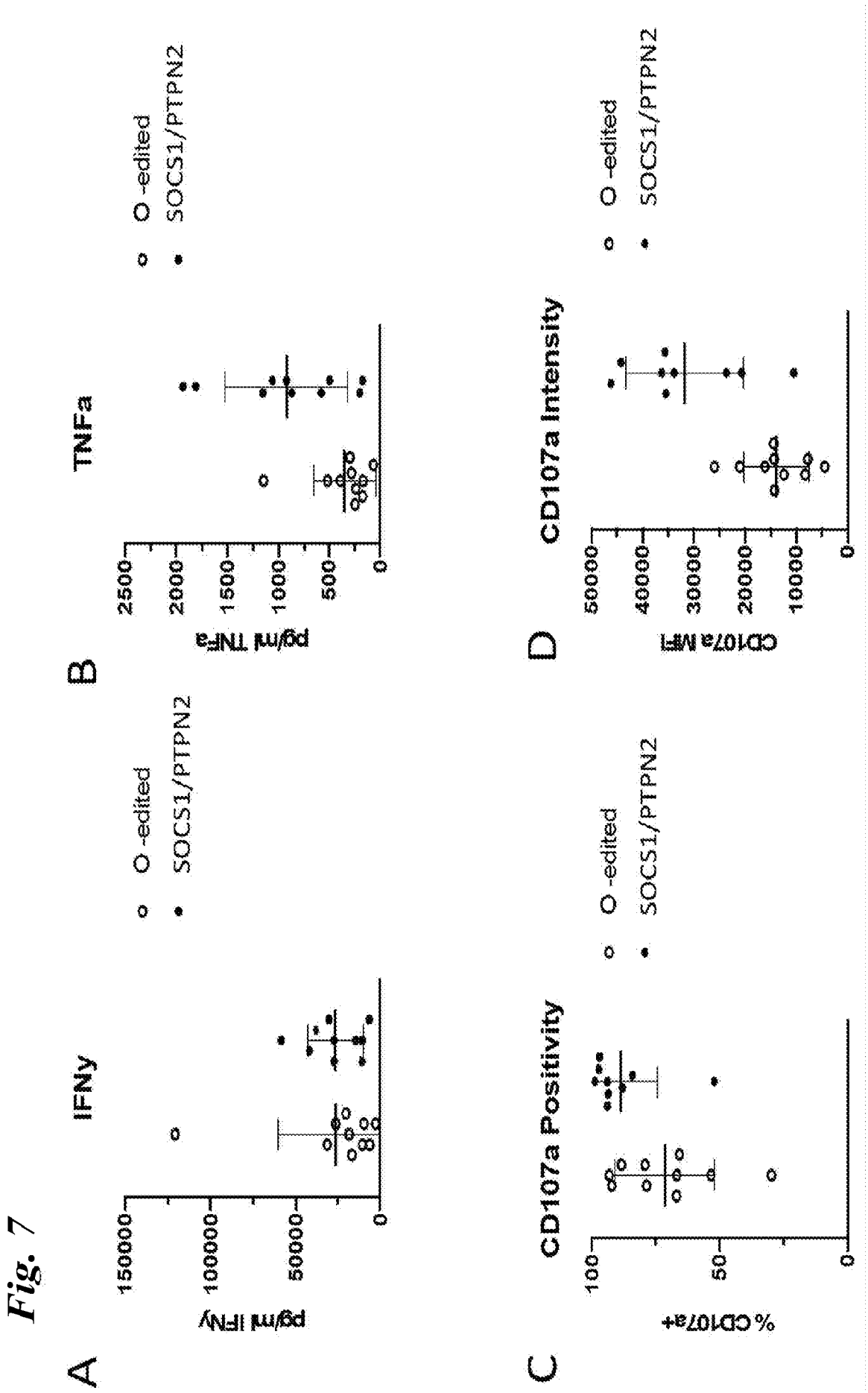

CD8 cells: pSTAT5
Unstimulated
1h
pSTAT5 (Y694)

Fig. 7


A
IFNγ
pg/ml IFNγ
150000
100000
50000
0
O -edited
SOCS1/PTPN2
B
TNFa
pg/ml TNFa
2500
2000
1500
1000
500
0
O -edited
SOCS1/PTPN2
C
CD107a Positivity
% CD107a+
100
50
0
O -edited
SOCS1/PTPN2
D
CD107a Intensity
CD107a MFI
50000
40000
30000
20000
10000
0
O -edited
SOCS1/PTPN2

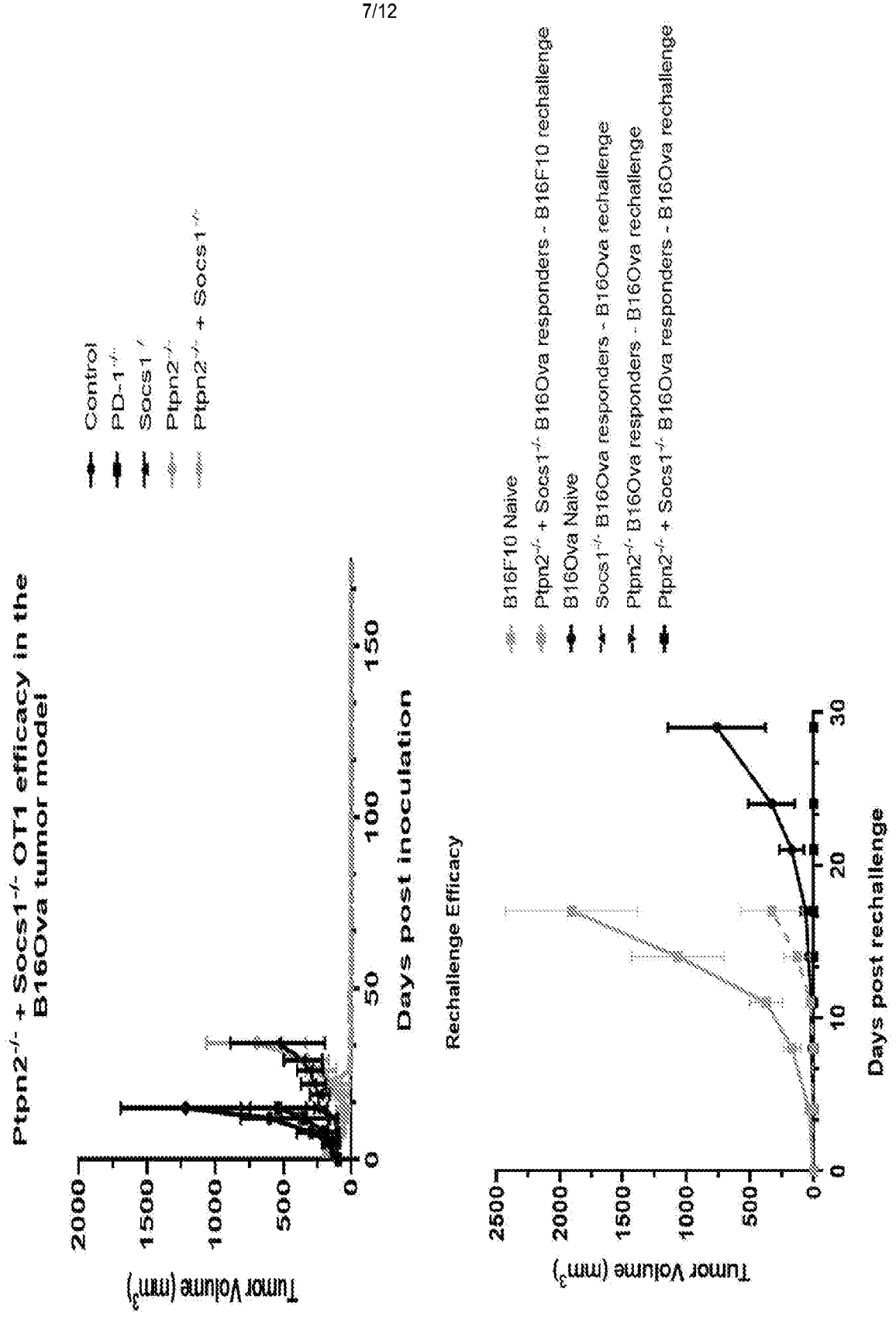

A
Ptpn2-/- + Socs1-/- OT1 efficacy in the B16Ova tumor model
Control
PD-1-/-
Socs1-/-
Ptpn2-/-
Ptpn2-/- + Socs1-/-
Tumor Volume (mm3)
2000
1500
1000
500
0
0
50
100
150
Days post inoculation
B
Rechallenge Efficacy
B16F10 Naive
Ptpn2-/- + Socs1-/- B16Ova responders - B16F10 rechallenge
B16Ova Naive
Socs1-/- B16Ova responders - B16Ova rechallenge
Ptpn2-/- B16Ova responders - B16Ova rechallenge
Ptpn2-/- + Socs1-/- B16Ova responders - B16Ova rechallenge
Tumor Volume (mm3)
2500
2000
1500
1000
500
0
0
10
20
30
Days post rechallenge

Fig. 8

Fig. 8

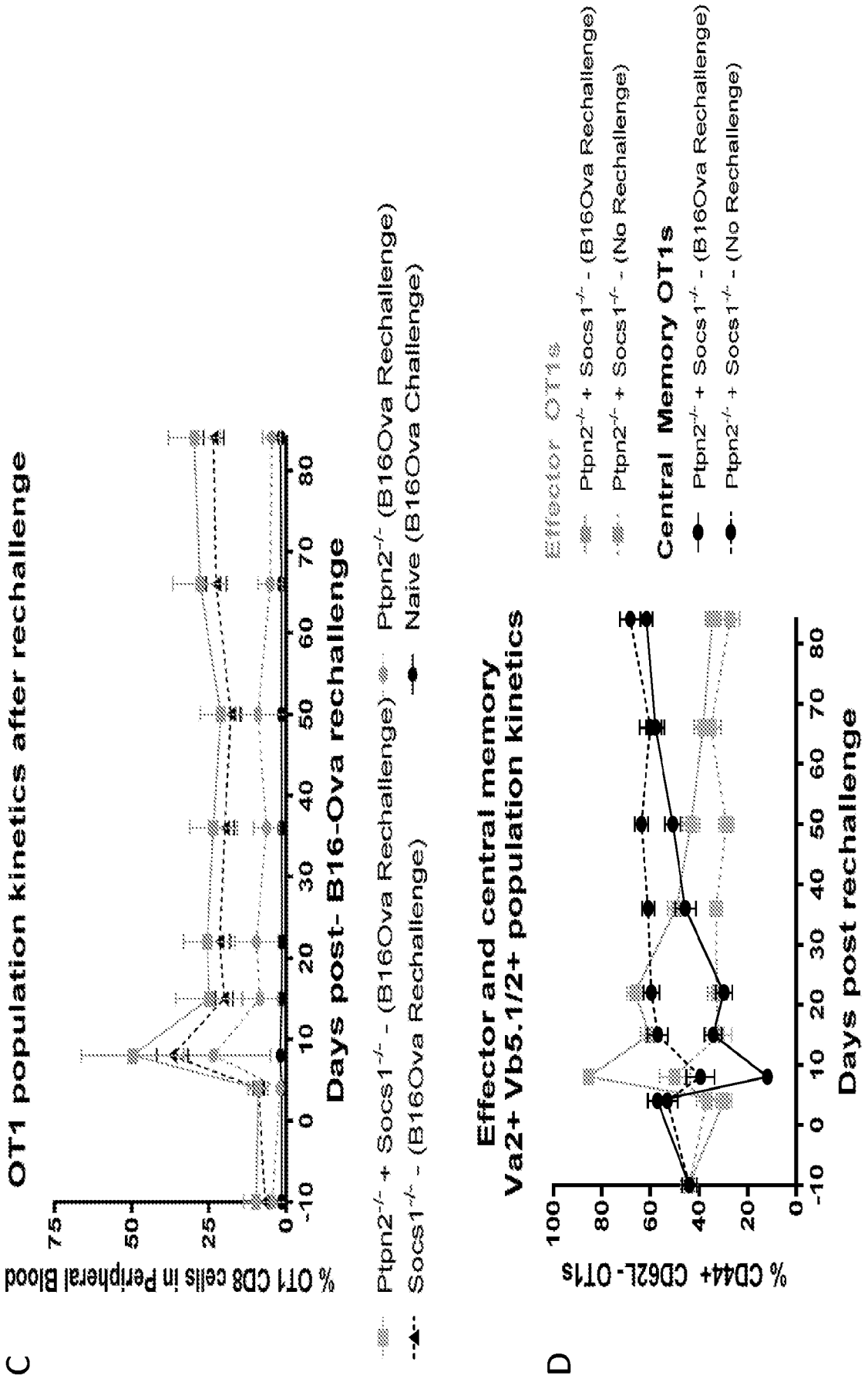

C
OT1 population kinetics after rechallenge
% OT1 CD8 cells in Peripheral Blood
75
50
25
0
-10
0
10
20
30
40
50
60
70
80
Days post- B16-Ova rechallenge
Ptpn2-/- + Socs1-/- - (B16Ova Rechallenge)
Ptpn2-/- (B16Ova Rechallenge)
Socs1-/- - (B16Ova Rechallenge)
Naive (B16Ova Challenge)
D
Effector and central memory
Va2+ Vb5.1/2+ population kinetics
% CD44+ CD62L- OT1s
100
80
60
40
20
0
-10
0
10
20
30
40
50
60
70
80
Days post rechallenge
Effector OT1s
Ptpn2-/- + Socs1-/- - (B16Ova Rechallenge)
Ptpn2-/- + Socs1-/- - (No Rechallenge)
Central Memory OT1s
Ptpn2-/- + Socs1-/- - (B16Ova Rechallenge)
Ptpn2-/- + Socs1-/- - (No Rechallenge)

Fig. 9

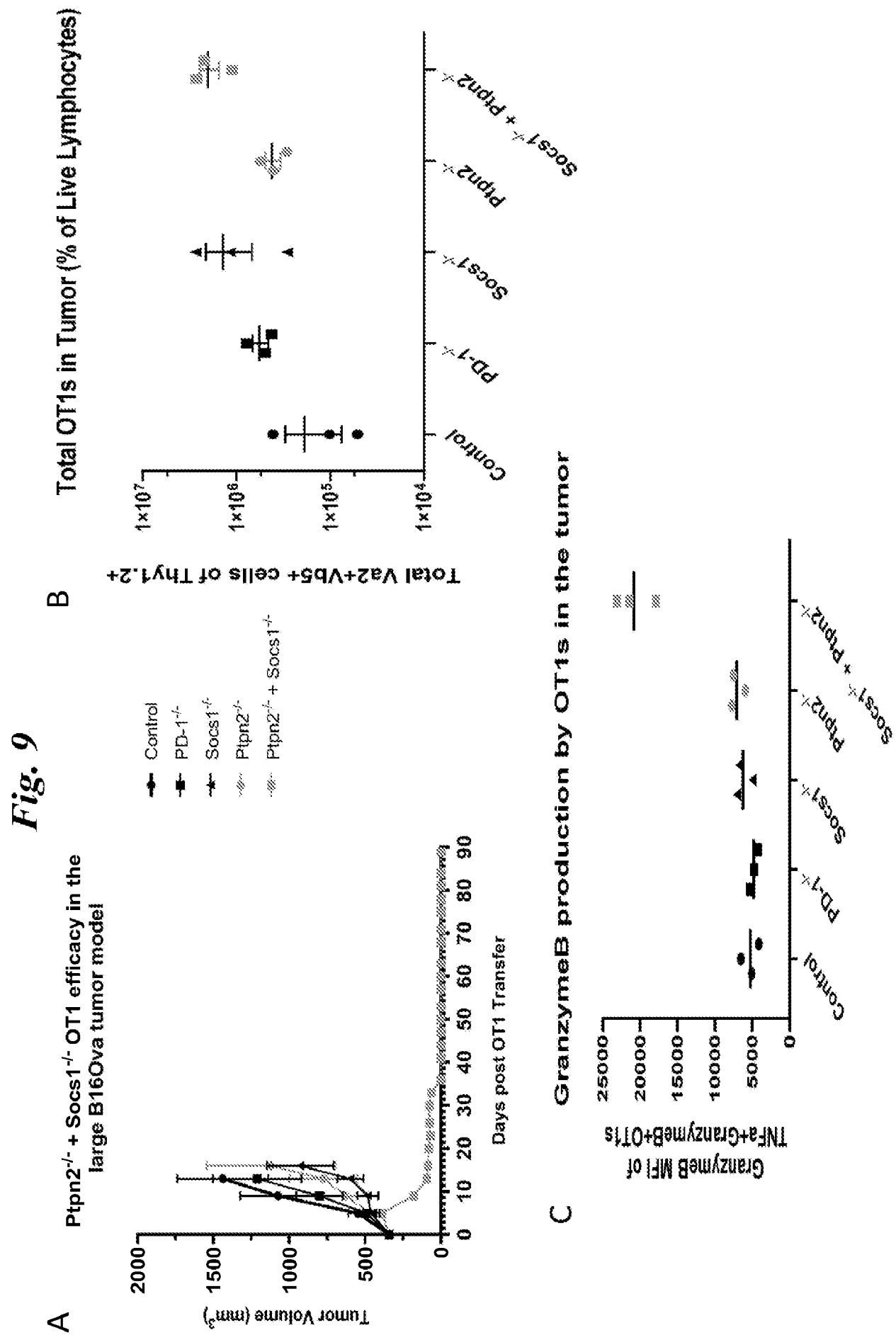
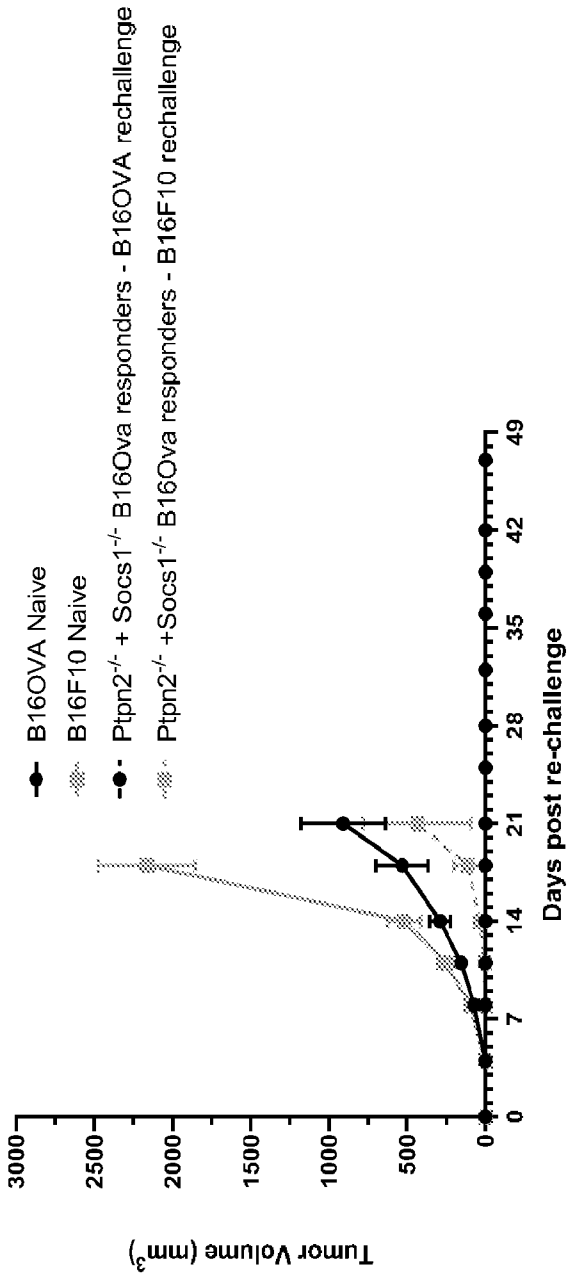
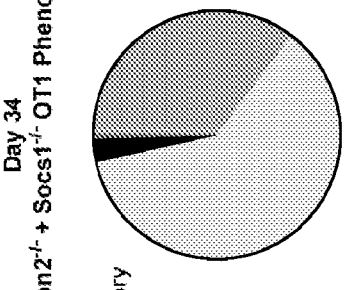

A
Ptpn2-/- + Socs1-/- OT1 efficacy in the large B16Ova tumor model
Tumor Volume (mm3)
Days post OT1 Transfer
Control
PD-1-/-
Socs1-/-
Ptpn2-/-
Ptpn2-/- + Socs1-/-
B
Total OT1s in Tumor (% of Live Lymphocytes)
Total Va2+Vb5+ cells of Thy1.2+
Control
PD-1-/-
Socs1-/-
Ptpn2-/-
Socs1-/- + Ptpn2-/-
C
GranzymeB production by OT1s in the tumor
GranzymeB MFI of TNFa+GranzymeB+OT1s

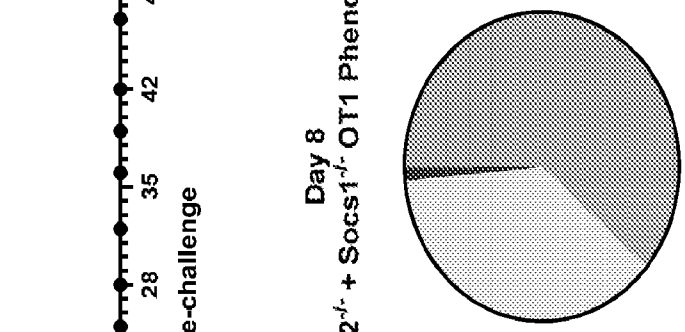
Fig. 9

D


Rechallenge Efficacy
B16OVA Naive
B16F10 Naive
Ptpn2-/- + Socs1-/- B16Ova responders - B16OVA rechallenge
Ptpn2-/- +Socs1-/- B16Ova responders - B16F10 rechallenge
Tumor Volume (mm3)
3000
2500
2000
1500
1000
500
0
0
7
14
21
28
35
42
49
Days post re-challenge

E


Day 34
Ptpn2-/- + Socs1-/- OT1 Phenotype
35.37% Effectors
61.12% Central Memory
3.06% Naive
0.46% Other


Day 8
Ptpn2-/- + Socs1-/- OT1 Phenotype
61.26% Effectors
37.34% Central Memory
1.27% Naive
0.13% Other

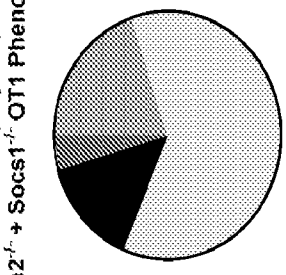

Baseline (Day -10)
Ptpn2-/- + Socs1-/- OT1 Phenotype
19.84% Effectors
61.50% Central Memory
14.21% Naive
4.45% Other

Fig. 10

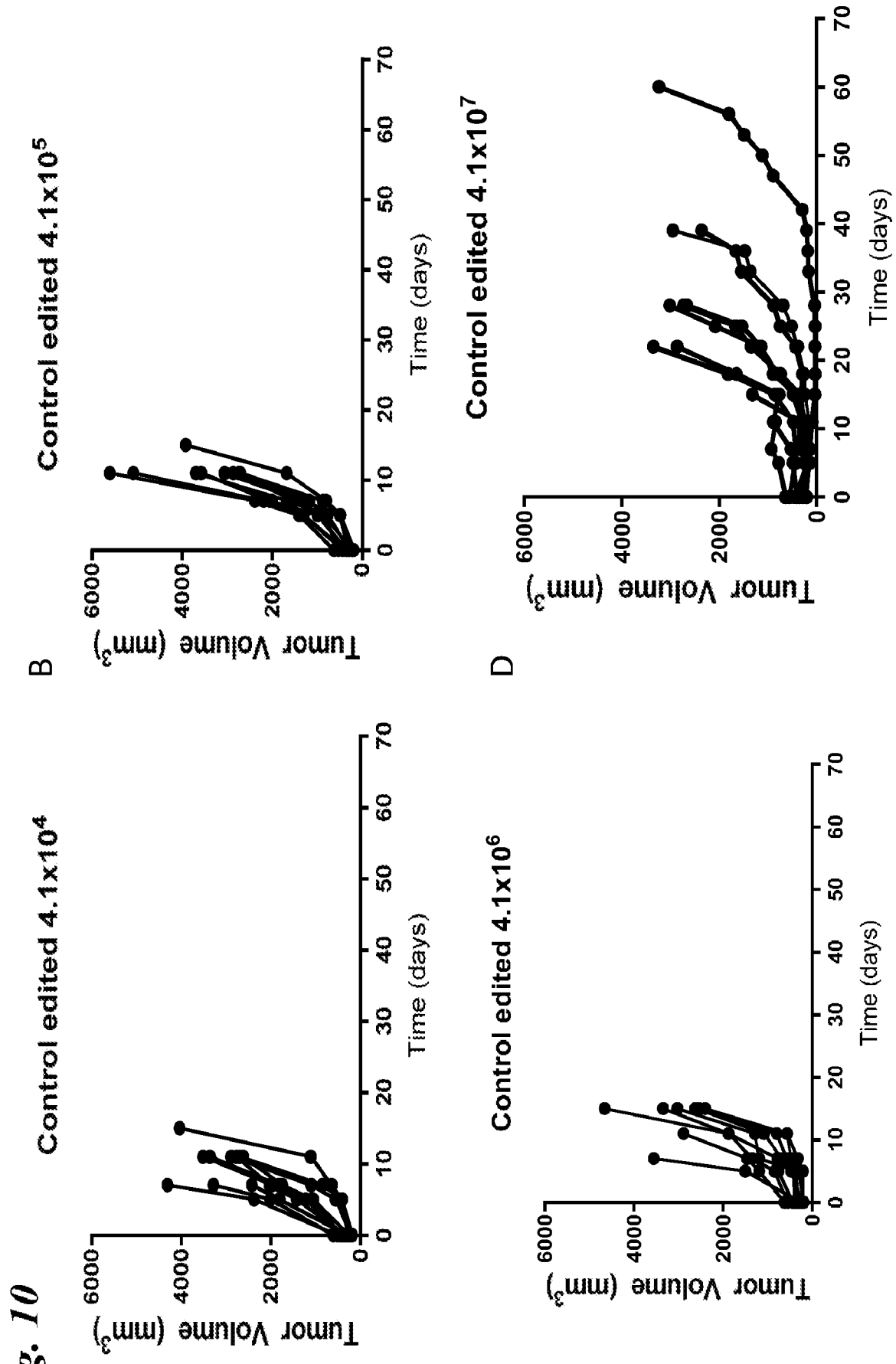
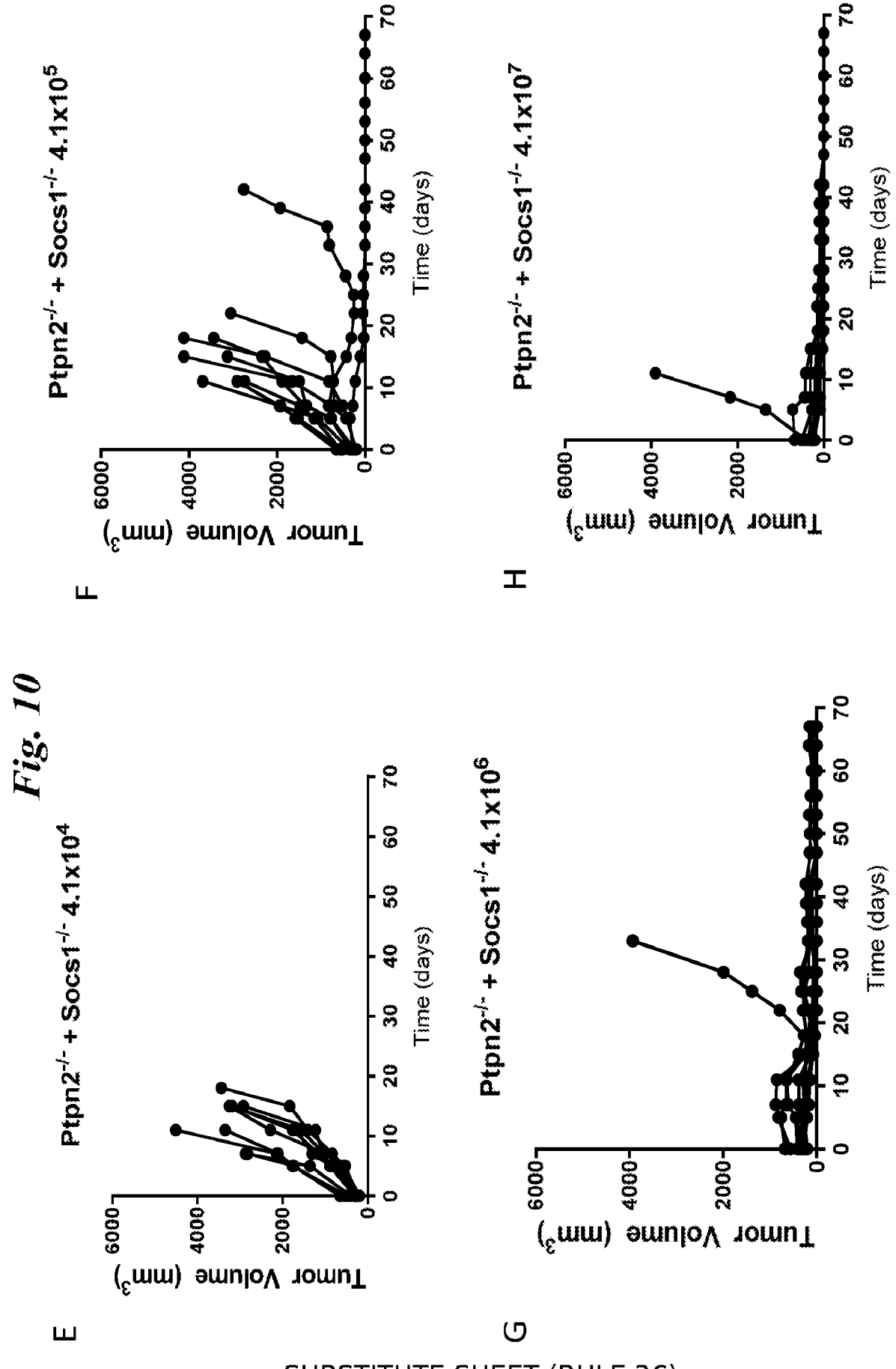

A
Control edited 4.1x10^4
B
Control edited 4.1x10^5
C
Control edited 4.1x10^6
D
Control edited 4.1x10^7
Tumor Volume (mm^3)
Time (days)
0
2000
4000
6000
0
10
20
30
40
50
60
70

Fig. 10


E
Ptpn2-/- + Socs1-/- 4.1x10^4
Tumor Volume (mm^3)
Time (days)
F
Ptpn2-/- + Socs1-/- 4.1x10^5
Tumor Volume (mm^3)
Time (days)
G
Ptpn2-/- + Socs1-/- 4.1x10^6
Tumor Volume (mm^3)
Time (days)
H
Ptpn2-/- + Socs1-/- 4.1x10^7
Tumor Volume (mm^3)
Time (days)