FIGURE 1

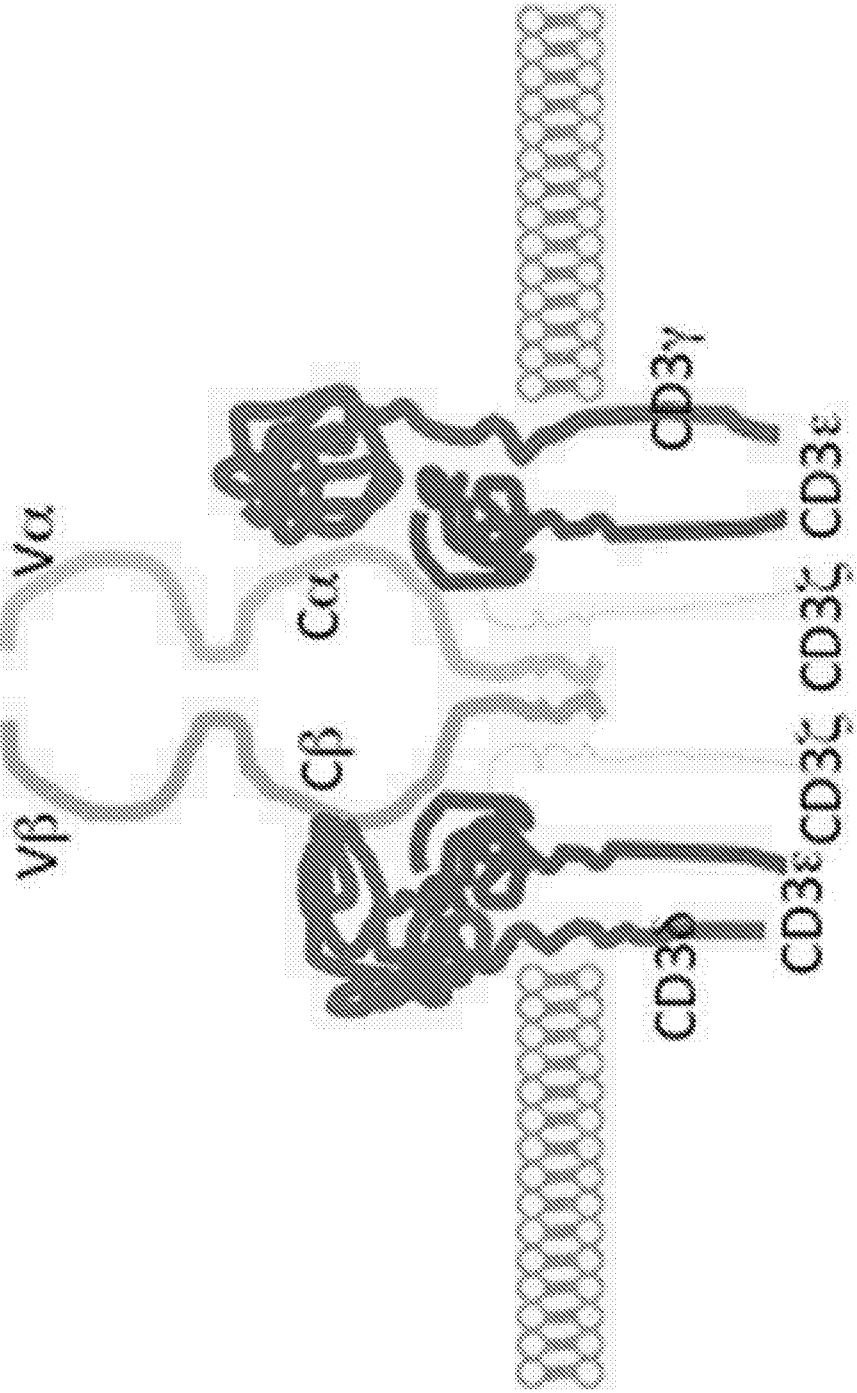


FIGURE 2

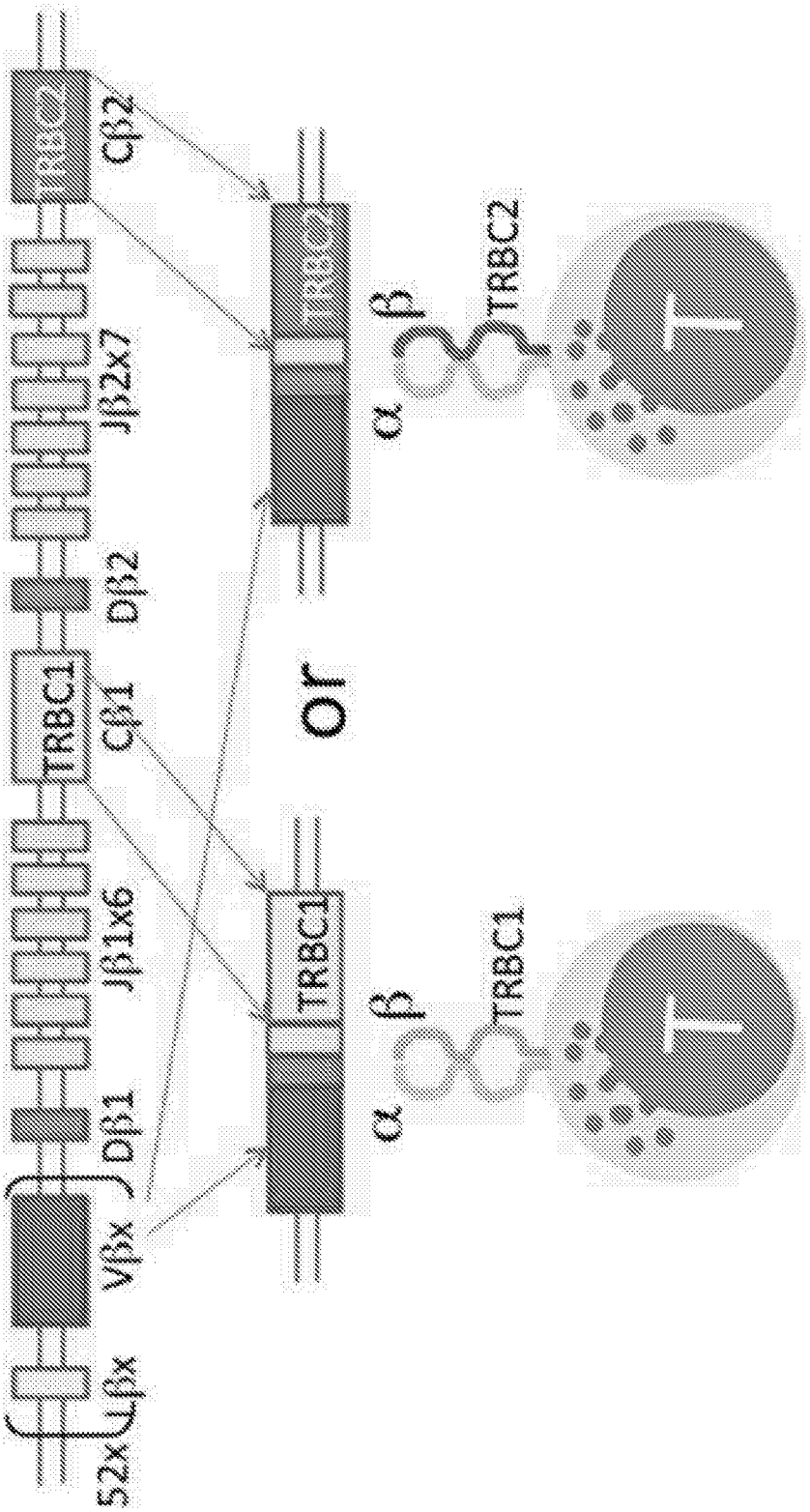

TRBC2
Cβ2
Jβ2x7
Dβ2
TRBC1
Cβ1
Jβ1x6
Dβ1
Vβx
52xVβx
or
TRBC2
α
β
TRBC1
α
β

FIGURE 3

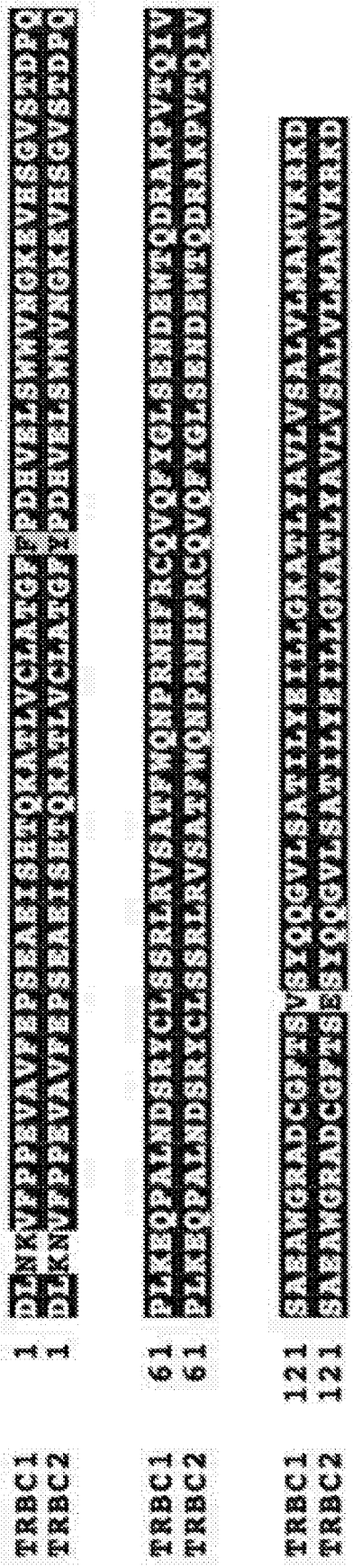

TRBC1 1 DLNKVFPPEVAVFEPSEAEISHTQKATLVCLATGFYPDHVELSWWVNGKEVHSGVSTDPQ
TRBC2 1 DLKNVFPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWWVNGKEVHSGVSTDPQ
TRBC1 61 PLKEQPALNDSRYCLSSRLRVSATFWQNPRNHFRCQVQFYGLSENDEWTQDRAKPVTQIV
TRBC2 61 PLKEQPALNDSRYCLSSRLRVSATFWQNPRNHFRCQVQFYGLSENDEWTQDRAKPVTQIV
TRBC1 121 SAEAWGRADCGFTSVSYQQGVLSATILYEILLGKATLYAVLVSALVLMAMVKRKD
TRBC2 121 SAEAWGRADCGFTSESYQQGVLSATILYEILLGKATLYAVLVSALVLMAMVKRKD

FIGURE 4

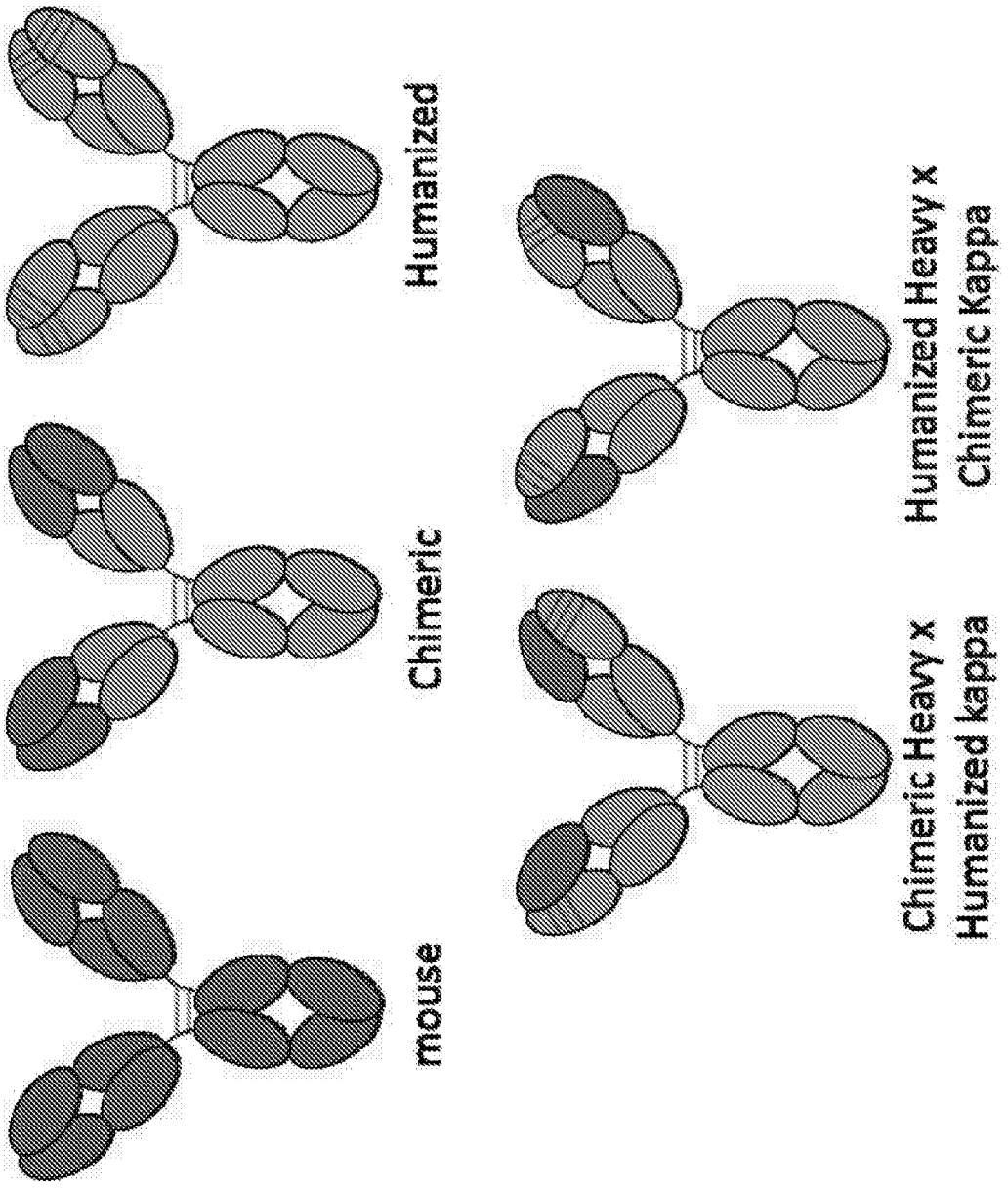

mouse
Chimeric
Humanized
Chimeric Heavy x
Humanized kappa
Humanized Heavy x
Chimeric Kappa

FIGURE 5

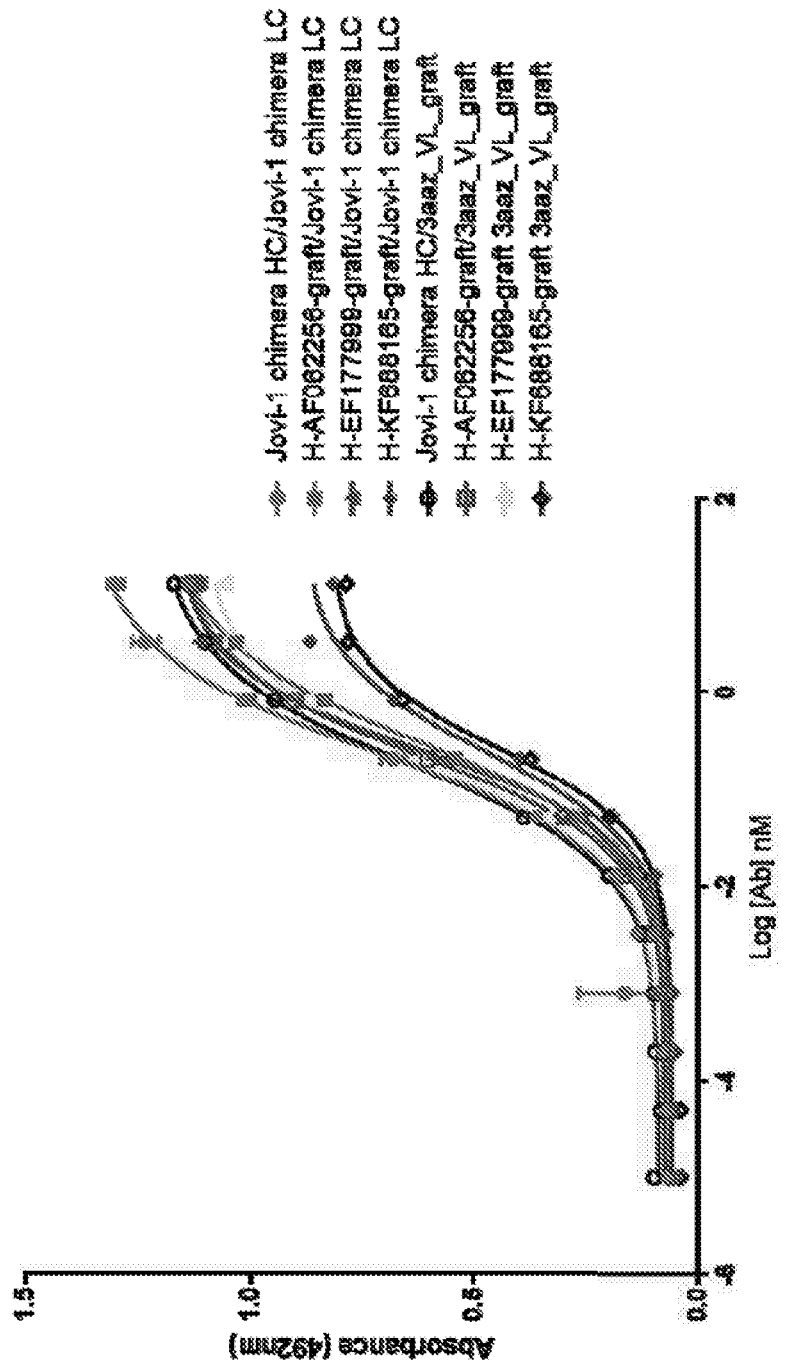

Humanized Antibody binding to TRBC1
Absorbance (492nm)
1.5
1.0
0.5
0.0
-6
-4
-2
0
2
Log [Ab] nM
Jovi-1 chimera HC/Jovi-1 chimera LC
H-AF062256-graft/Jovi-1 chimera LC
H-EF177999-graft/Jovi-1 chimera LC
H-KF888165-graft/Jovi-1 chimera LC
Jovi-1 chimera HC/3aaz_VL_graft
H-AF062256-graft/3aaz_VL_graft
H-EF177999-graft 3aaz_VL_graft
H-KF888165-graft 3aaz_VL_graft

FIGURE 6

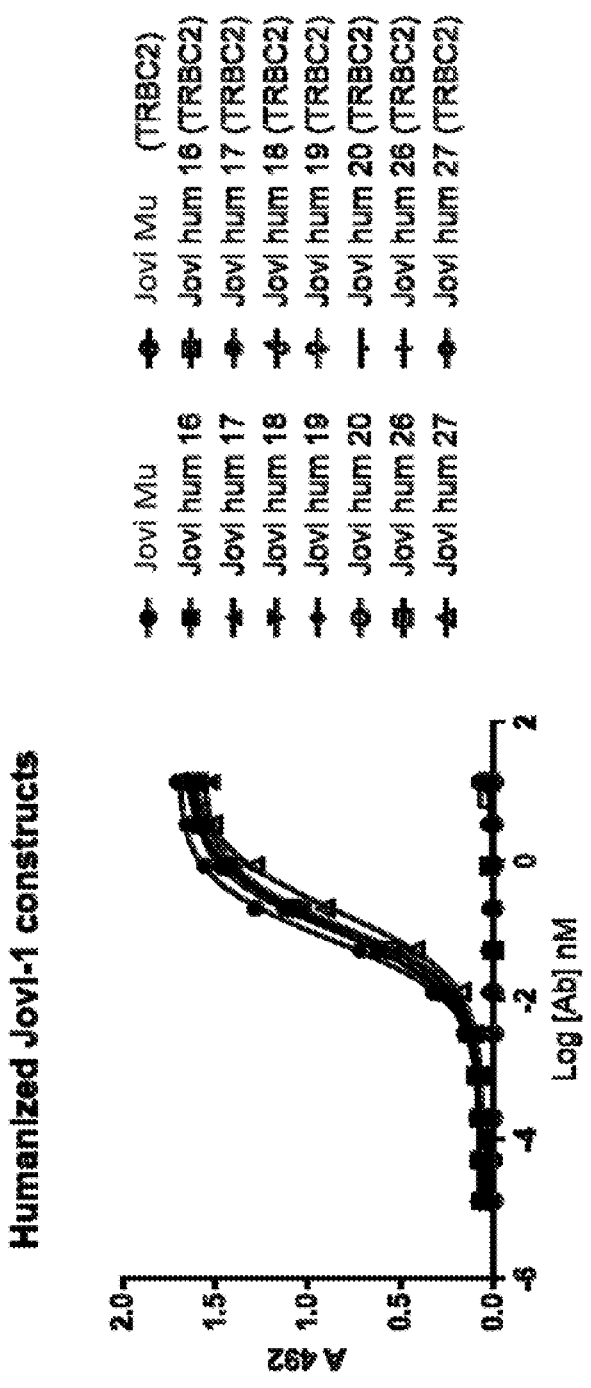

Humanized Jovi-1 constructs
A 492
2.0
1.5
1.0
0.5
0.0
-6
-4
-2
0
2
Log [Ab] nM
Jovi Mu
Jovi hum 16
Jovi hum 17
Jovi hum 18
Jovi hum 19
Jovi hum 20
Jovi hum 26
Jovi hum 27
Jovi Mu (TRBC2)
Jovi hum 16 (TRBC2)
Jovi hum 17 (TRBC2)
Jovi hum 18 (TRBC2)
Jovi hum 19 (TRBC2)
Jovi hum 20 (TRBC2)
Jovi hum 26 (TRBC2)
Jovi hum 27 (TRBC2)

FIGURE 7

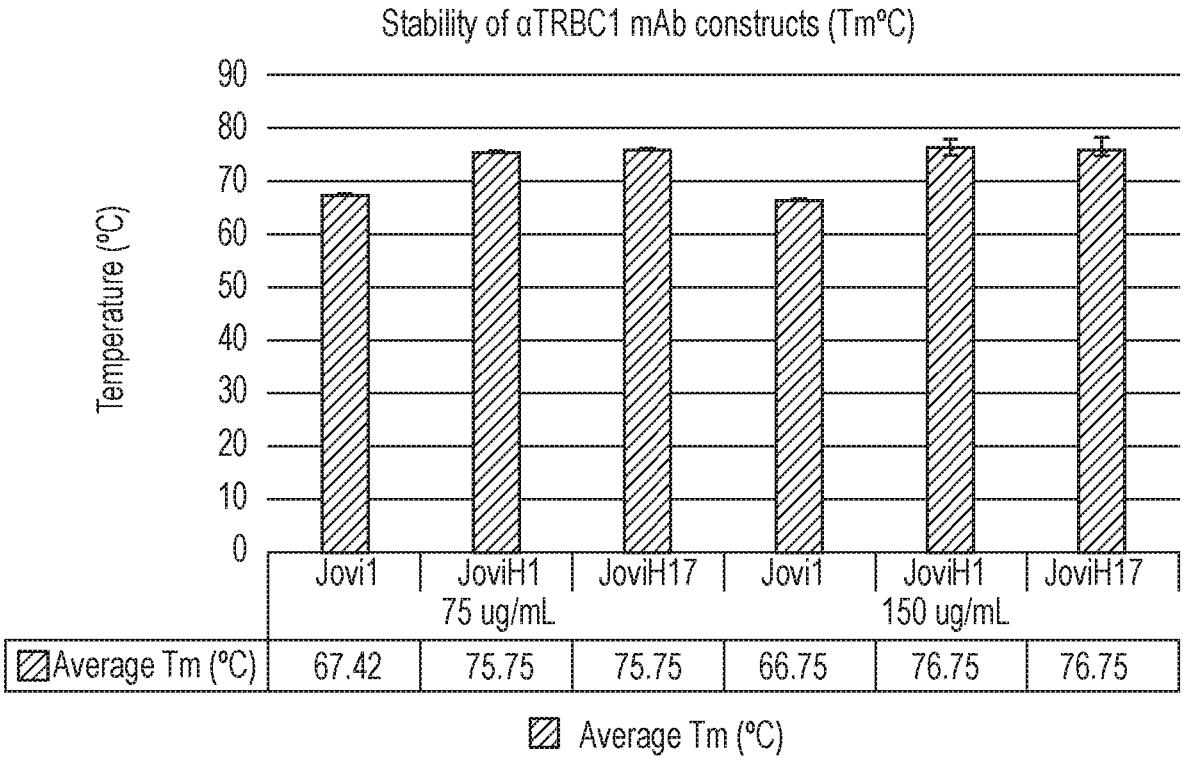

Stability of αTRBC1 mAb constructs (Tm°C)
Temperature (°C)
90
80
70
60
50
40
30
20
10
0
Jovi1
JoviH1
75 ug/mL
JoviH17
Jovi1
JoviH1
150 ug/mL
JoviH17
Average Tm (°C)
67.42
75.75
75.75
66.75
76.75
76.75
Average Tm (°C)

FIGURE 8

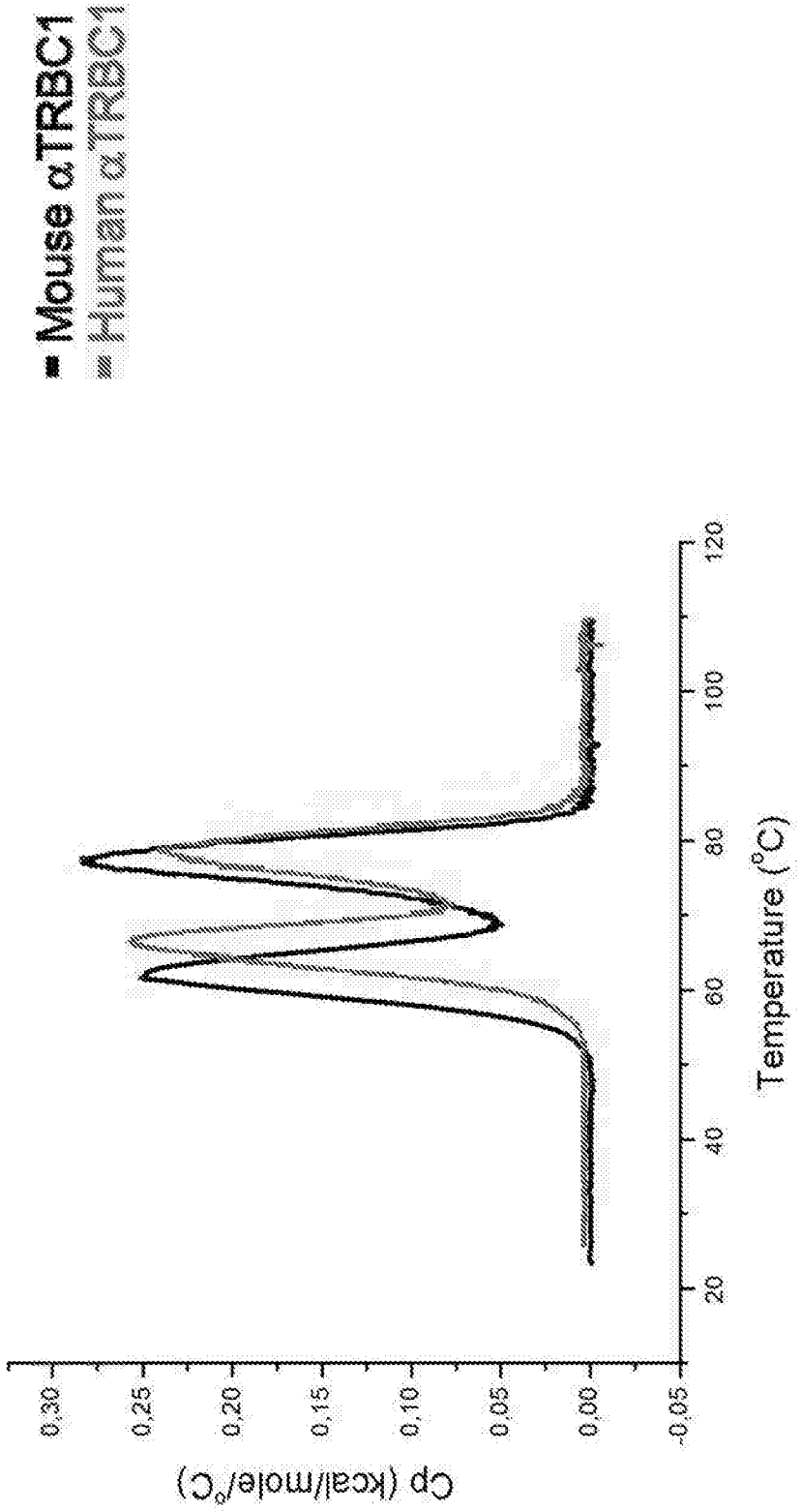

Mouse αTRBC1
Human αTRBC1
Cp (kcal/mole/°C)
0,30
0,25
0,20
0,15
0,10
0,05
0,00
-0,05
20
40
60
80
100
120
Temperature (°C)

FIGURE 9

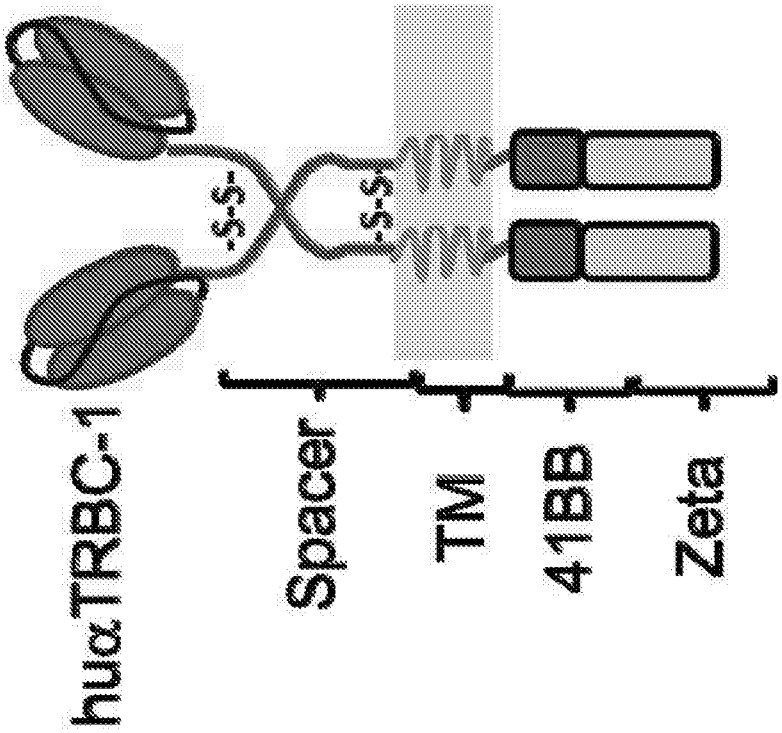


FIGURE 10A

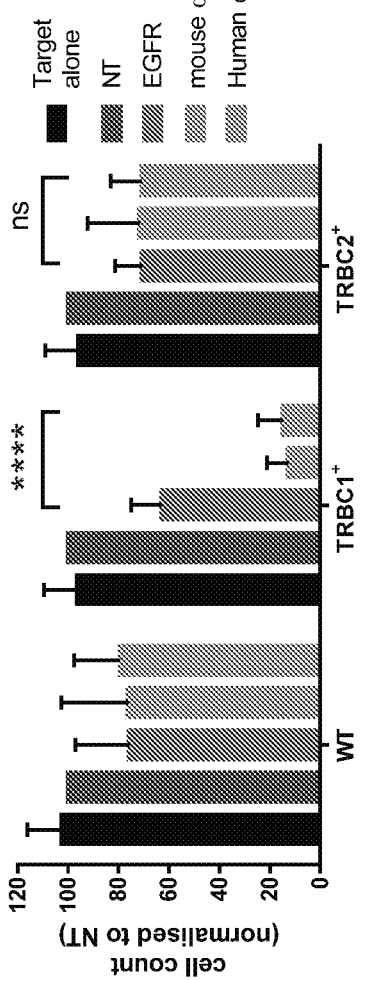


FIGURE 10B

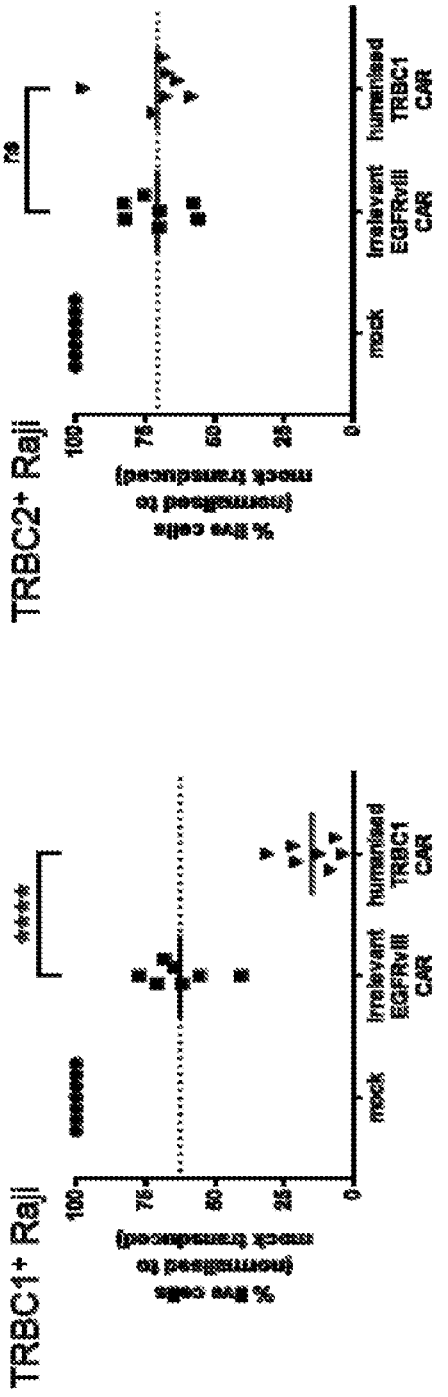


FIGURE 11

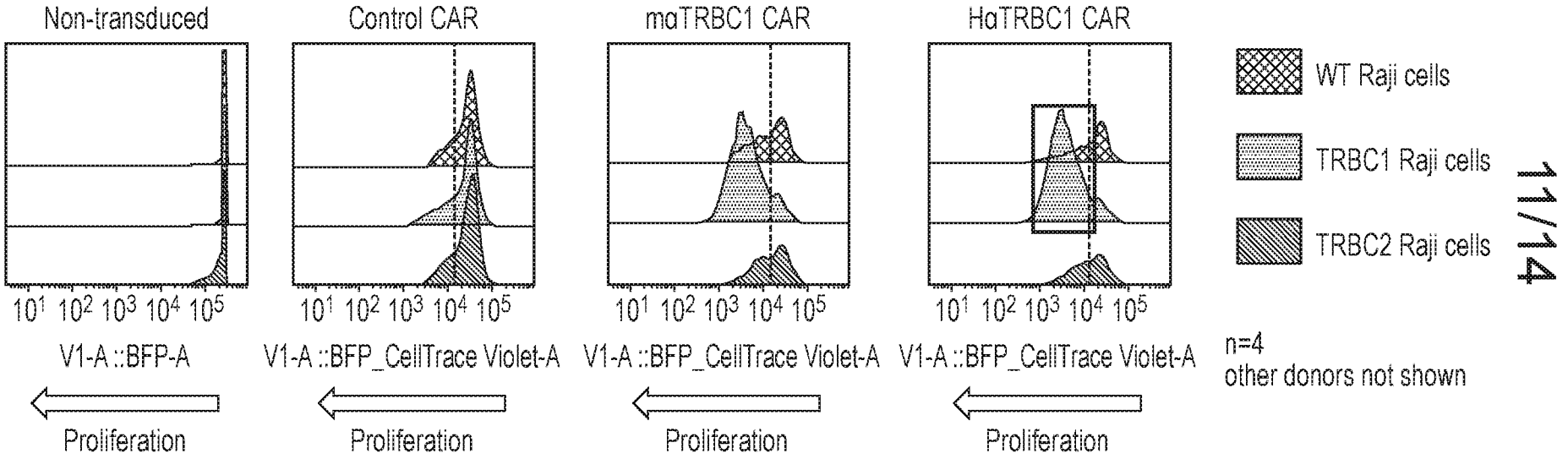
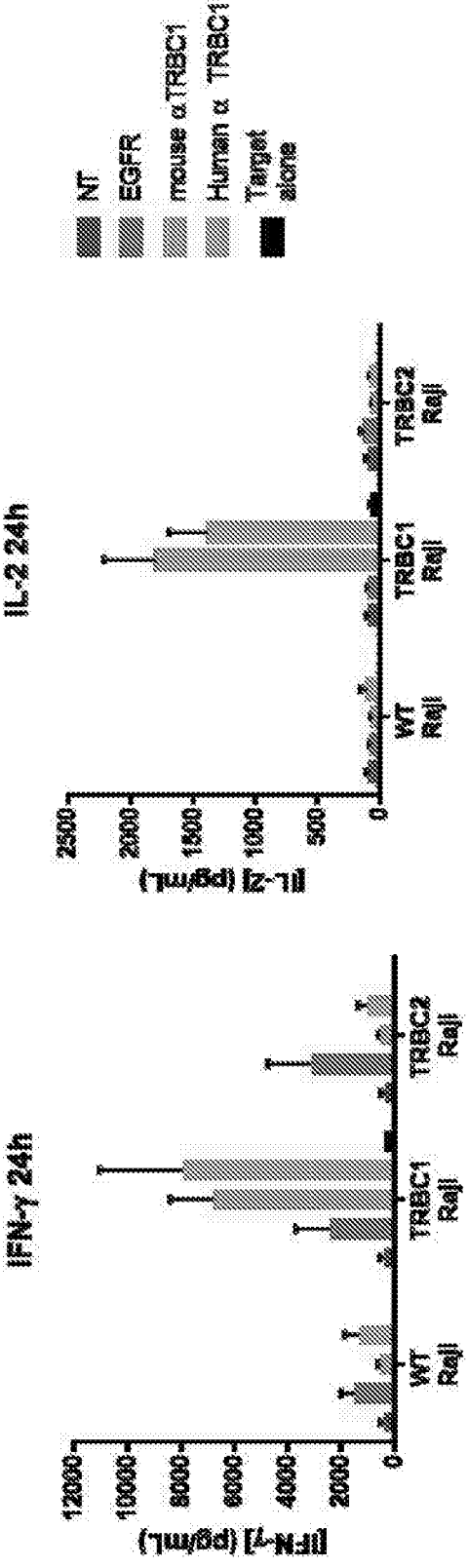

Non-transduced
Control CAR
mαTRBC1 CAR
HαTRBC1 CAR
WT Raji cells
TRBC1 Raji cells
TRBC2 Raji cells
10^1 10^2 10^3 10^4 10^5
V1-A ::BFP-A
V1-A ::BFP_CellTrace Violet-A
Proliferation
n=4
other donors not shown

FIGURE 12


NT
EGFR
mouse α TRBC1
Human α TRBC1
Target alone
IL-2 24h
[IL-2] (pg/mL)
2500
2000
1500
1000
500
0
WT Raji
TRBC1 Raji
TRBC2 Raji
IFN-γ 24h
[IFN-γ] (pg/mL)
12000
10000
8000
6000
4000
2000
0
WT Raji
TRBC1 Raji
TRBC2 Raji

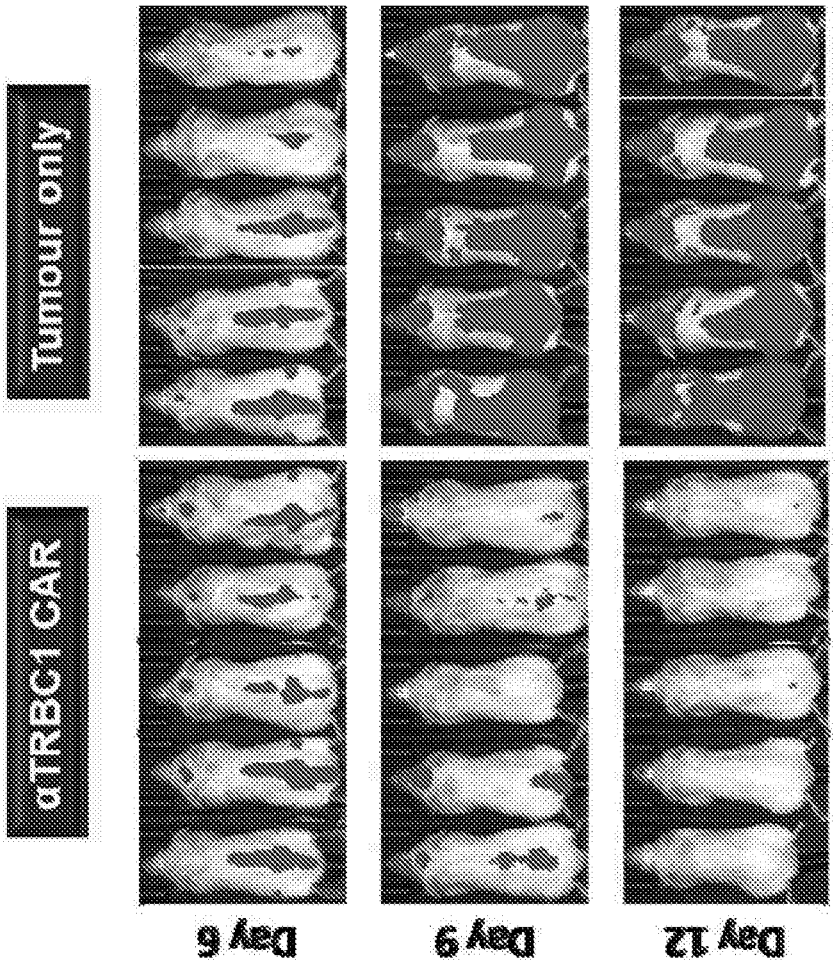
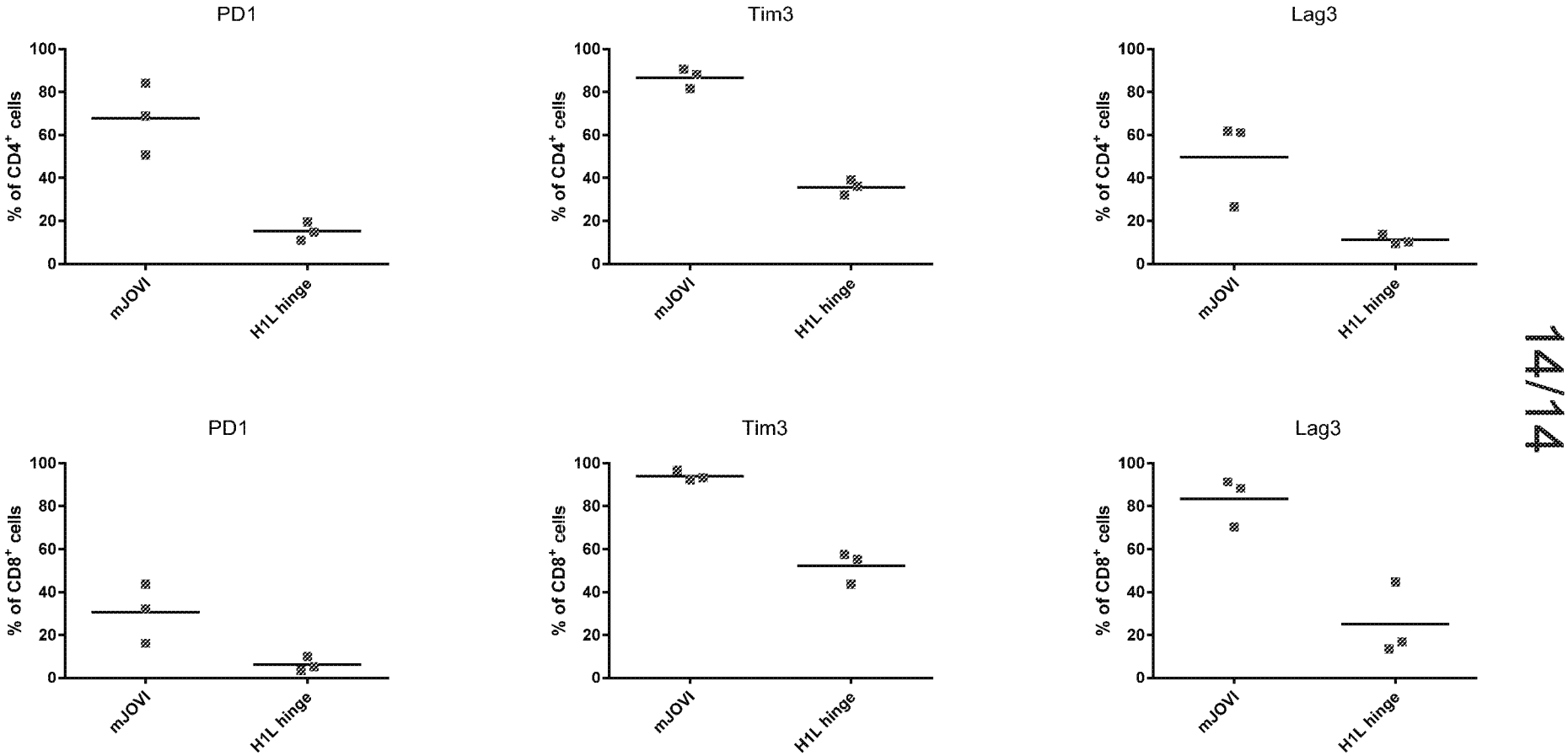


FIGURE 13

FIGURE 14


PD1
Tim3
Lag3
% of CD4+ cells
% of CD8+ cells
0
20
40
60
80
100
mJOVI
H1L hinge