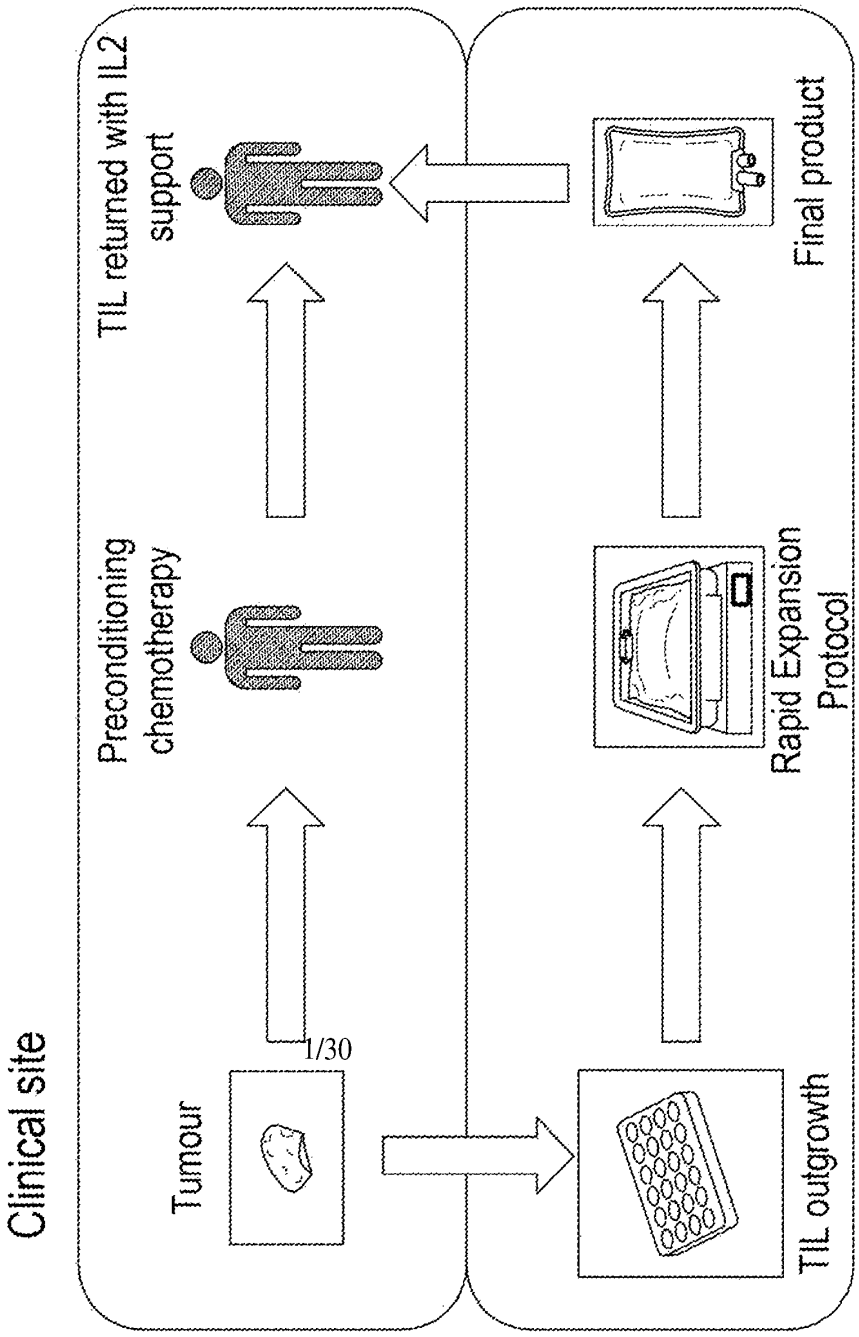

Clinical site
Tumour
1/30
Preconditioning chemotherapy
TIL returned with IL2 support
Manufacturing site
TIL outgrowth
Rapid Expansion Protocol
Final product

Fig. 1

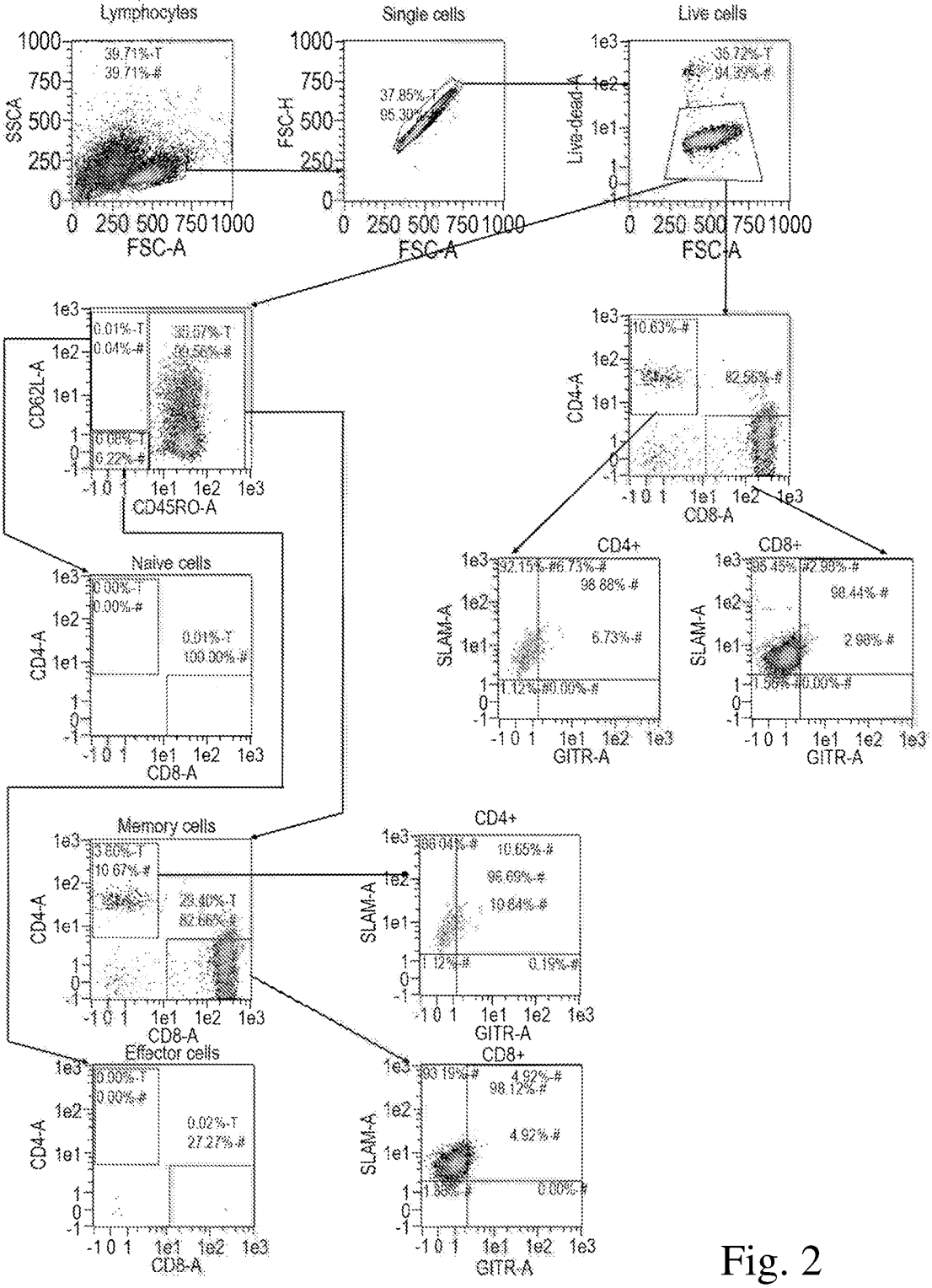
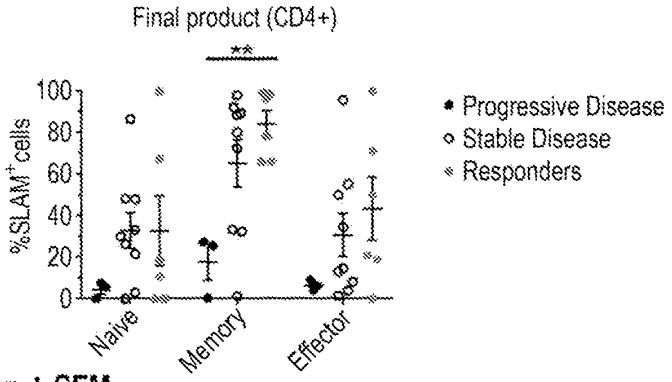

Lymphocytes
Single cells
Live cells
SSC-A
FSC-H
Live-dead-A
FSC-A
CD62L-A
CD45RO-A
CD4-A
CD8-A
Naive cells
CD4+
CD8+
SLAM-A
GITR-A
Memory cells
Effector cells

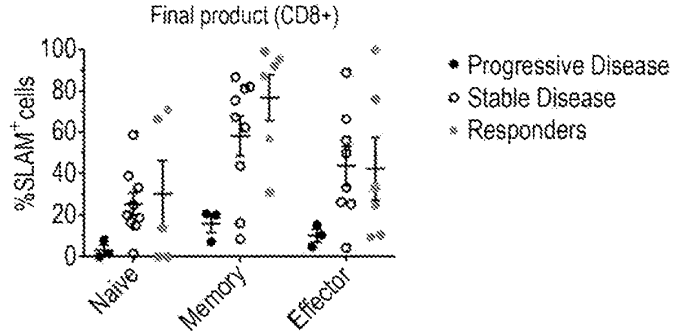
Fig. 2



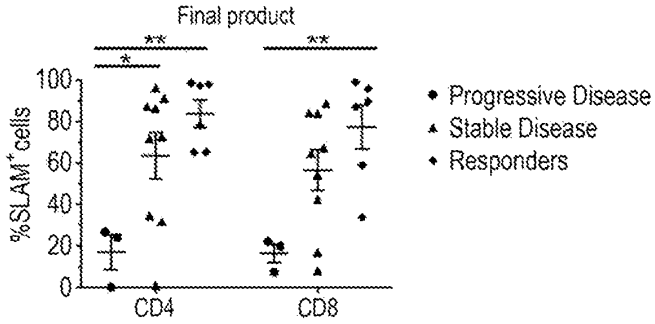
Mean ± SEM

Significance determined using 2-way ANOVA, followed by Sidak's multiple comparison test

Memory: PD vs R, **p = 0.009



Mean ± SEM



Mean ± SEM

Significance determined using 2-way ANOVA, followed by Sidak's multiple comparison test

CD4: PD vs SD, *p = 0.037; PD vs R, **p = 0.004

CD8: PD vs R, **p = 0.008

Fig. 3A

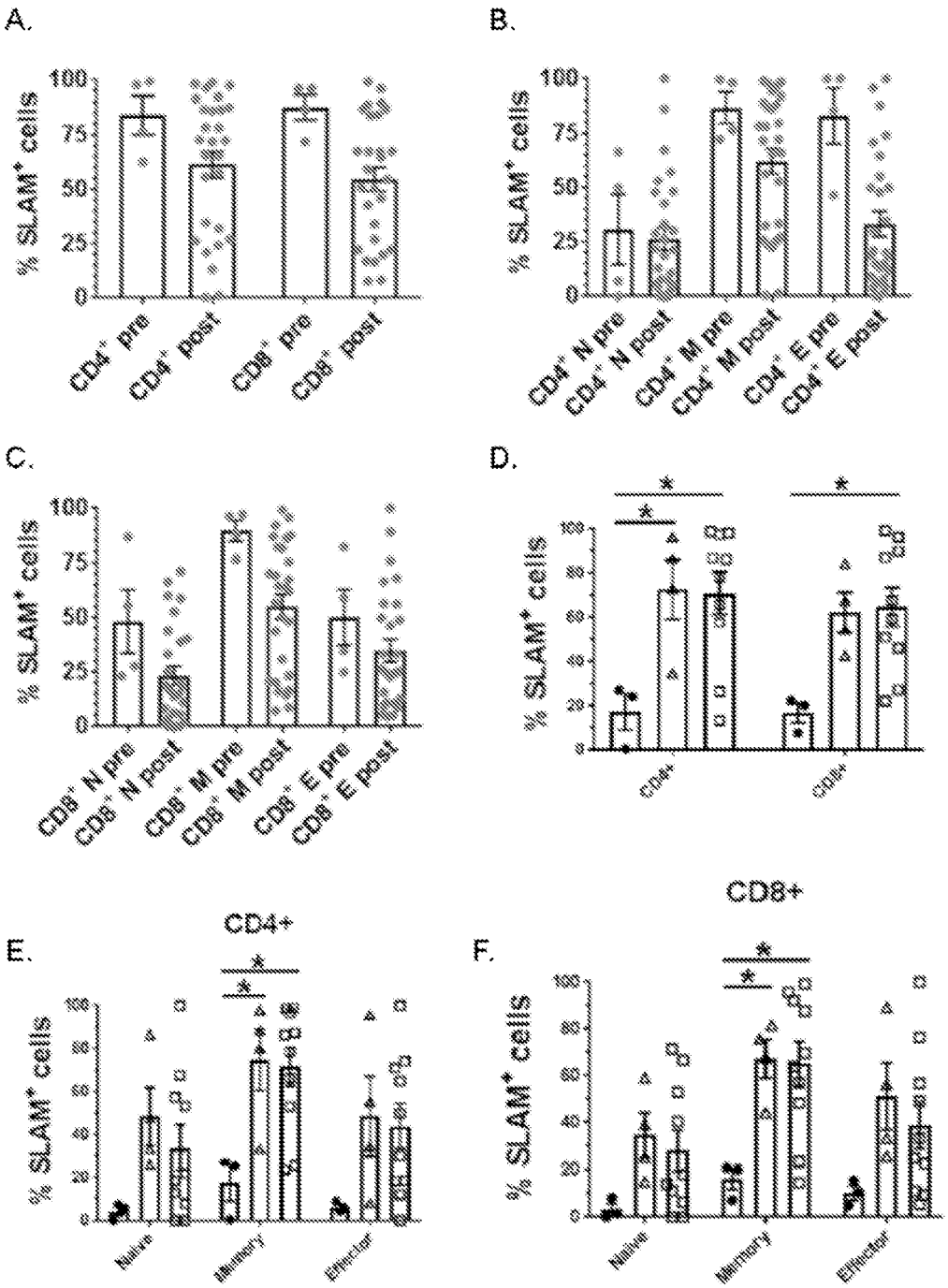
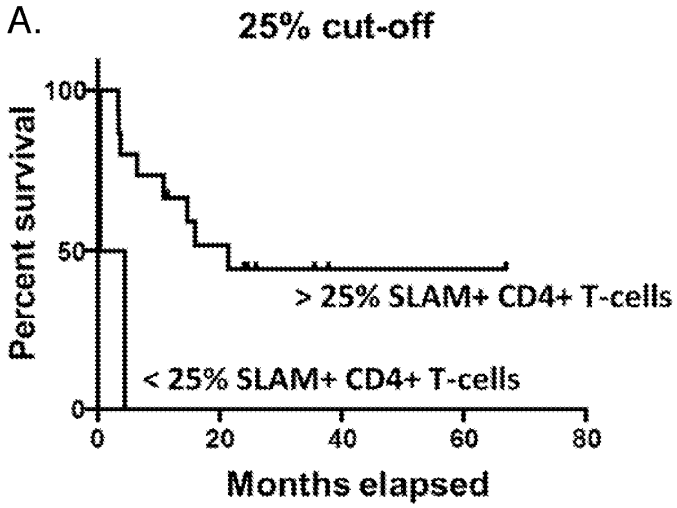
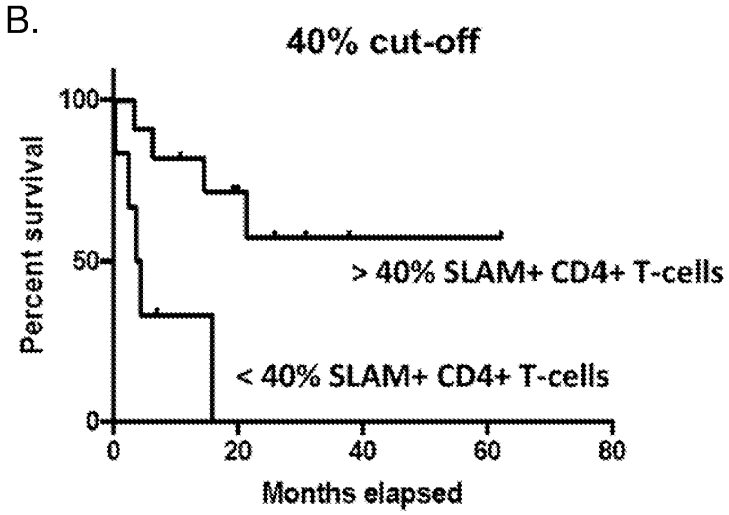

A.
B.
C.
D.
E.
F.
% SLAM+ cells
CD4+ pre
CD4+ post
CD8+ pre
CD8+ post
CD4+ N pre
CD4+ N post
CD4+ M pre
CD4+ M post
CD4+ E pre
CD4+ E post
CD8+ N pre
CD8+ N post
CD8+ M pre
CD8+ M post
CD8+ E pre
CD8+ E post
CD4+
CD8+
Naive
Memory
Effector

Fig. 3B



Median = 2.4 v 21.3 months
p- = 0.009 (Wilcoxon)
Plateau = 44%



Median = 4 v NR months
p- = 0.027 (Wilcoxon)
Plateau = 55%

Fig. 4A-4B

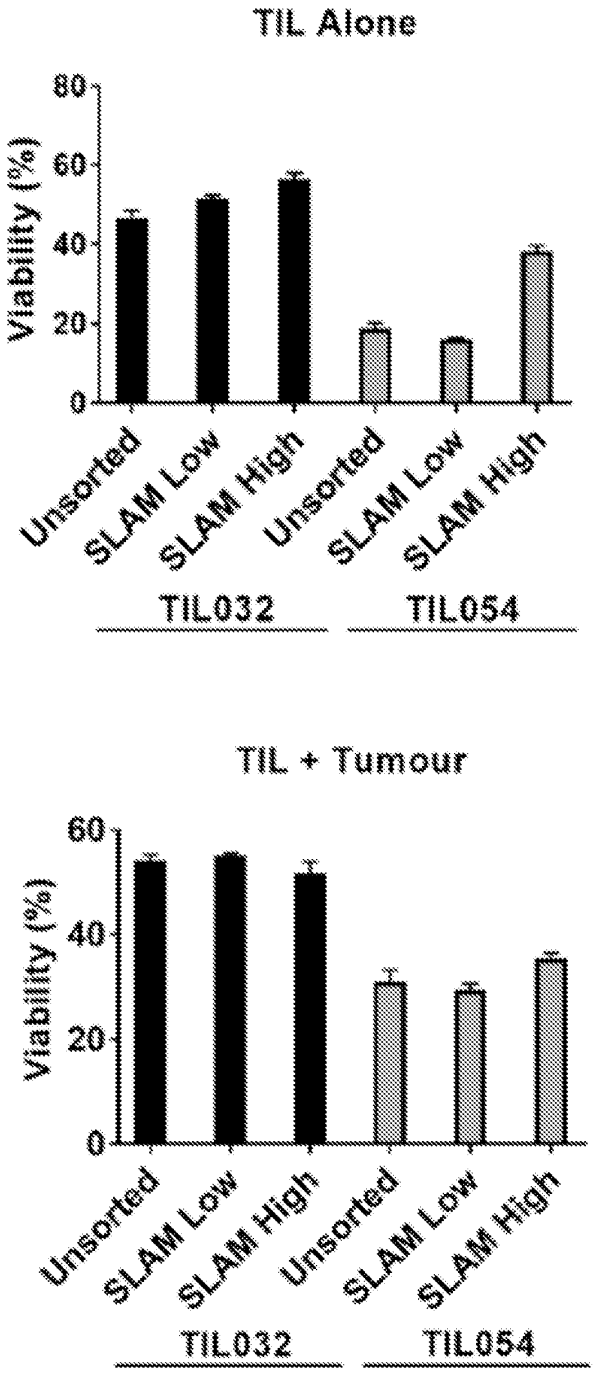

TIL Alone
Viability (%)
80
60
40
20
0
Unsorted
SLAM Low
SLAM High
Unsorted
SLAM Low
SLAM High
TIL032
TIL054
TIL + Tumour
Viability (%)
60
40
20
0
Unsorted
SLAM Low
SLAM High
Unsorted
SLAM Low
SLAM High
TIL032
TIL054

Fig. 5A

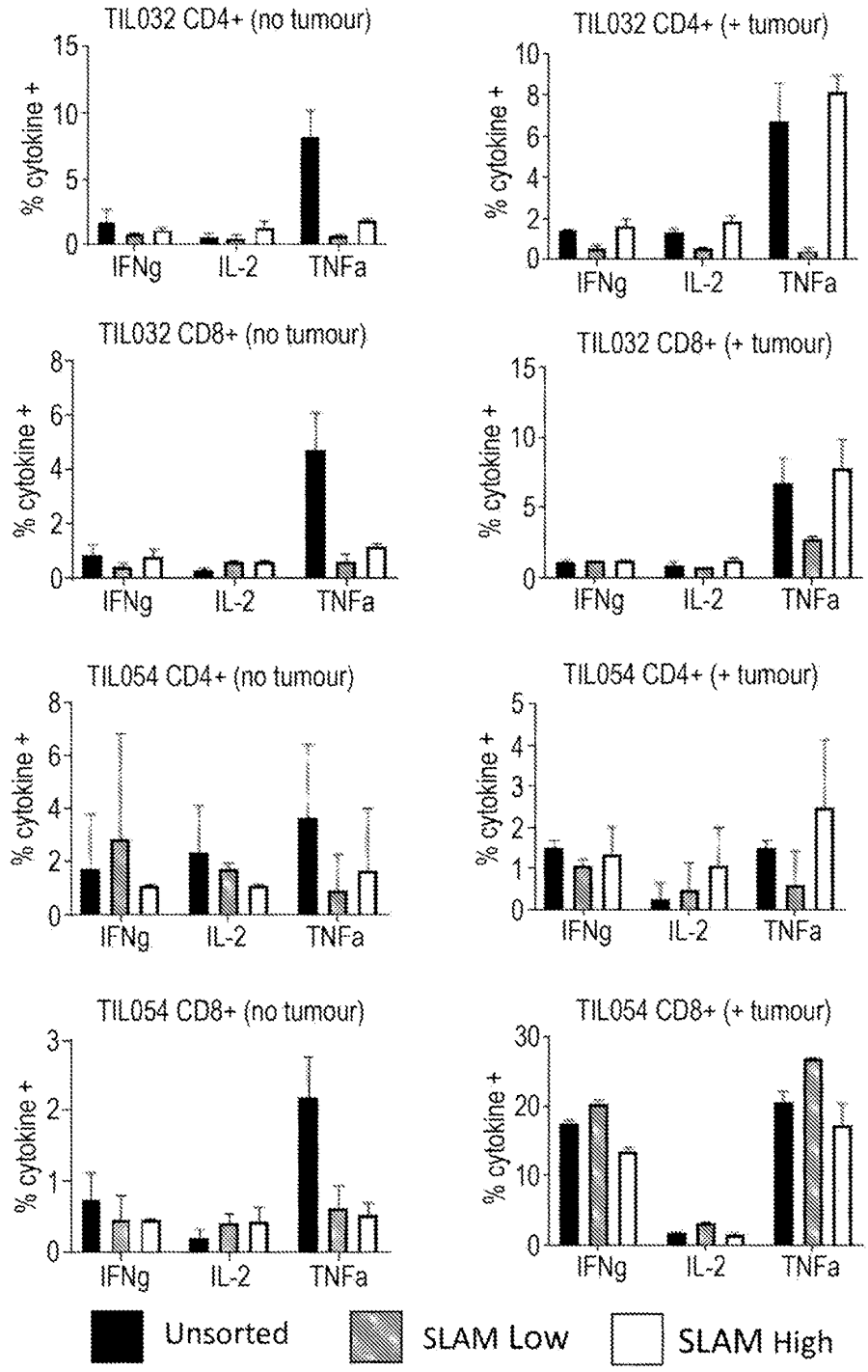

TIL032 CD4+ (no tumour)
TIL032 CD4+ (+ tumour)
TIL032 CD8+ (no tumour)
TIL032 CD8+ (+ tumour)
TIL054 CD4+ (no tumour)
TIL054 CD4+ (+ tumour)
TIL054 CD8+ (no tumour)
TIL054 CD8+ (+ tumour)
% cytokine +
IFNg
IL-2
TNFa
Unsorted
SLAM Low
SLAM High

Fig. 5B

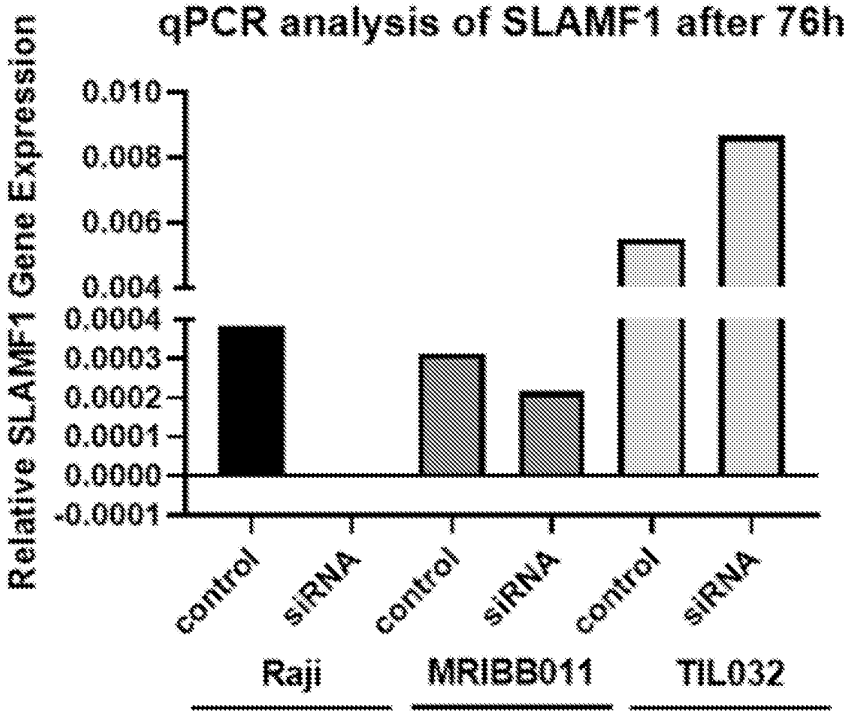

qPCR analysis of SLAMF1 after 76h
Relative SLAMF1 Gene Expression
0.010
0.008
0.006
0.004
0.0004
0.0003
0.0002
0.0001
0.0000
-0.0001
control
siRNA
control
siRNA
control
siRNA
Raji
MRIBB011
TIL032

Fig. 6A

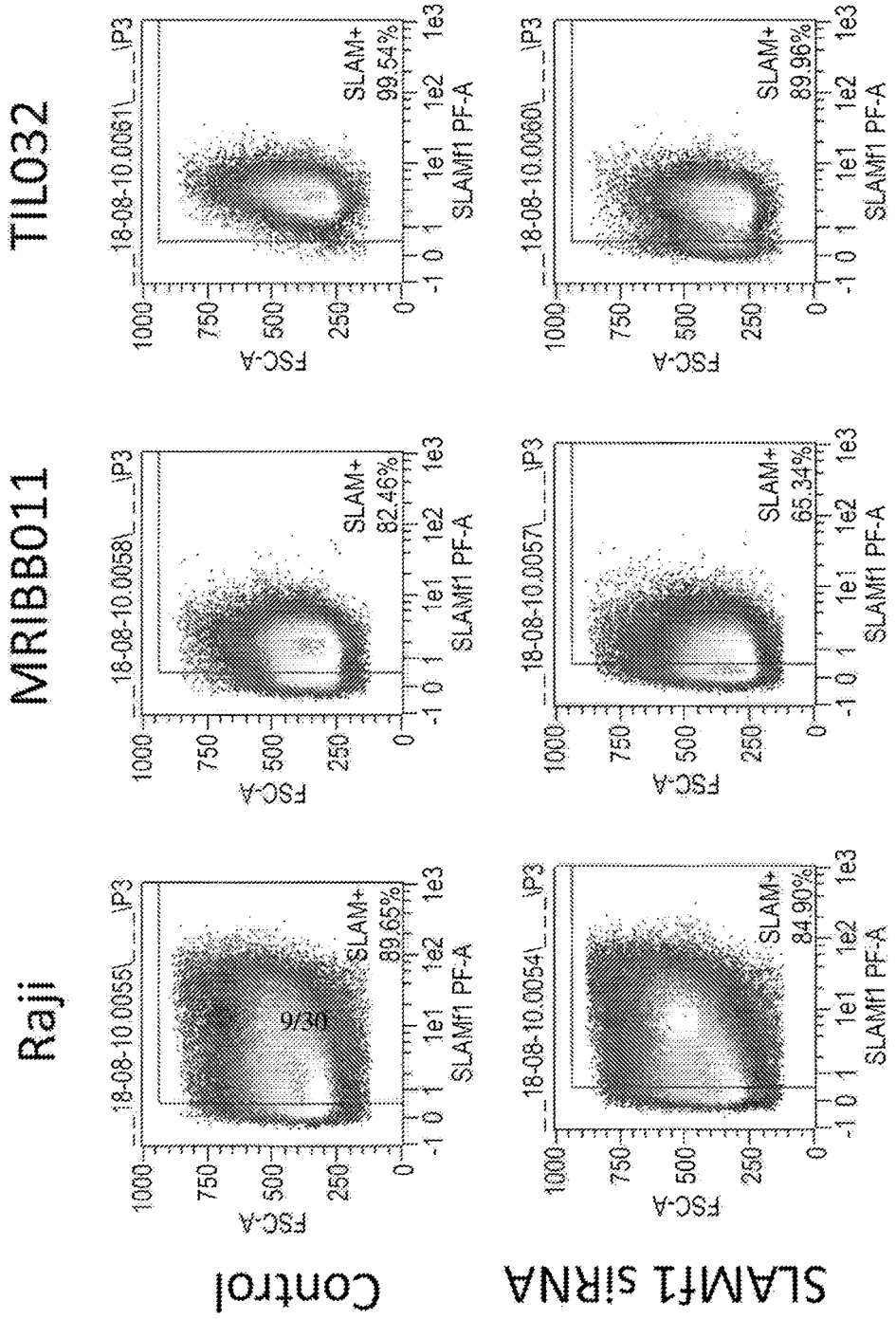

Raji
MRIBB011
TIL032
Control
SLAMf1 siRNA
18-08-10.0055_ _\P3
18-08-10.0058_ _\P3
18-08-10.0061_ _\P3
18-08-10.0054_ _\P3
18-08-10.0057_ _\P3
18-08-10.0060_ _\P3
SLAM+
89.65%
82.46%
99.54%
84.90%
65.34%
89.96%
FSC-A
SLAMf1 PF-A
9/30

Fig. 6B

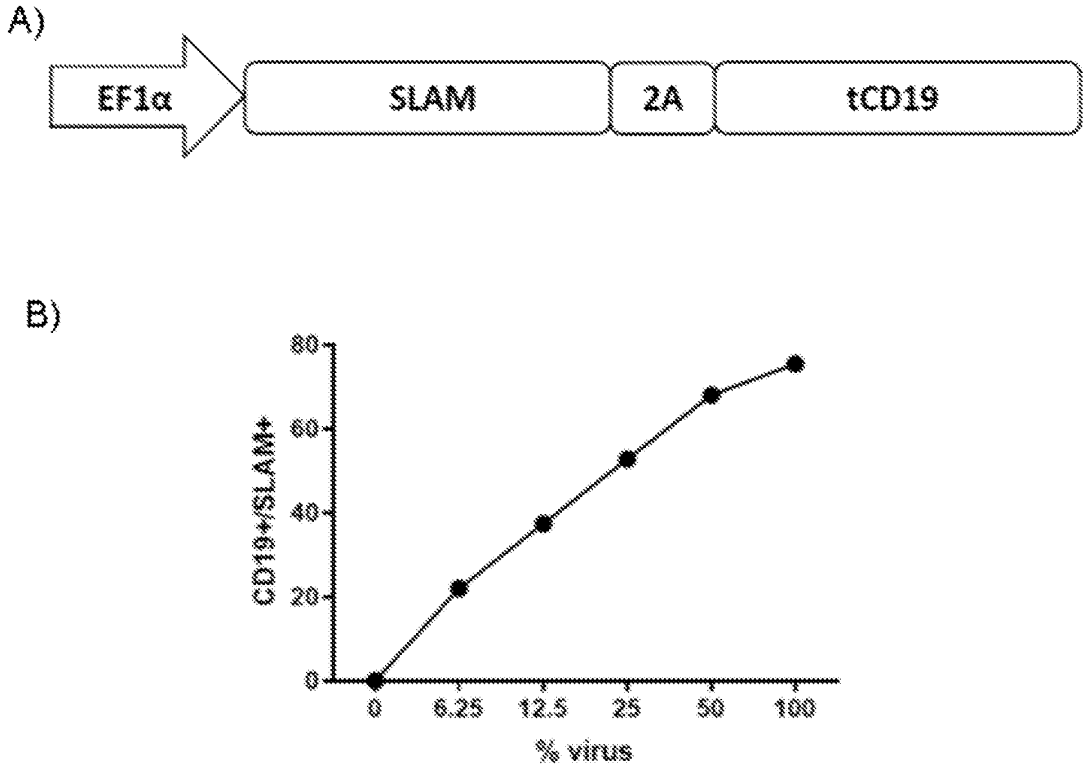
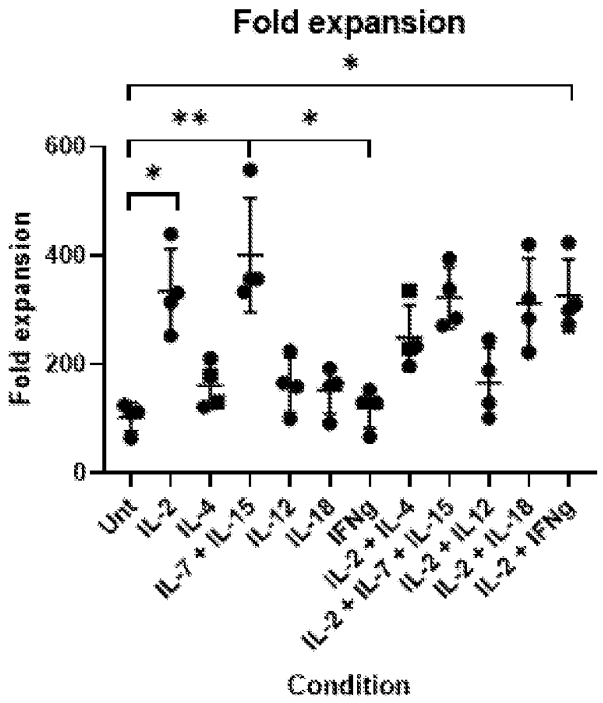

A)
EF1α
SLAM
2A
tCD19
B)
CD19+/SLAM+
80
60
40
20
0
0
6.25
12.5
25
50
100
% virus

Fig. 7

A.


Fold expansion
*
**
*
*
600
400
200
0
Fold expansion
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL-12
IL-2 + IL-18
IL-2 + IFNg
Condition

B.

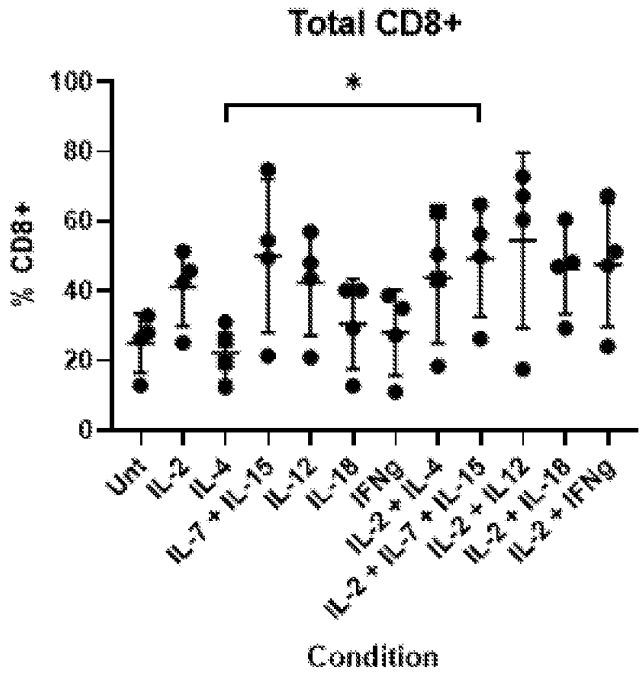
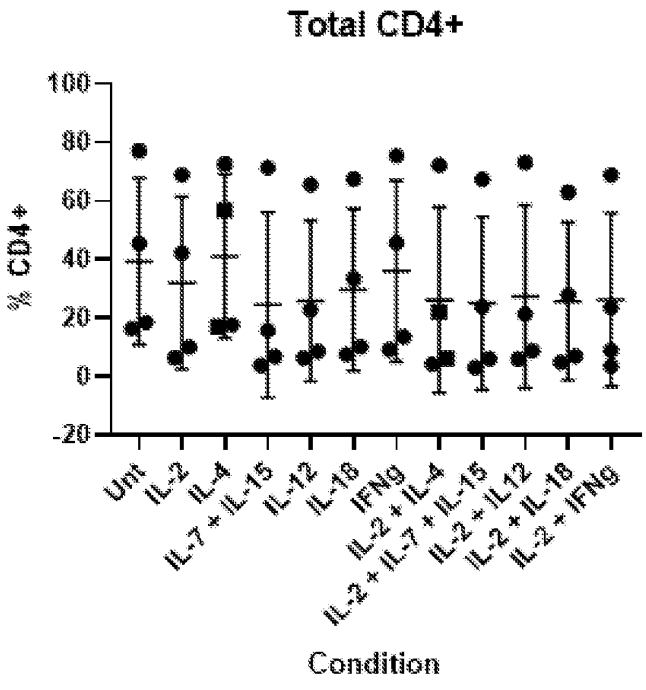

Total CD8+
*
100
80
60
40
20
0
% CD8+
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL-12
IL-2 + IL-18
IL-2 + IFNg
Condition

Fig. 8A-8B

C.


Total CD4+
% CD4+
100
80
60
40
20
0
-20
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL-12
IL-2 + IL-18
IL-2 + IFNg
Condition

D.

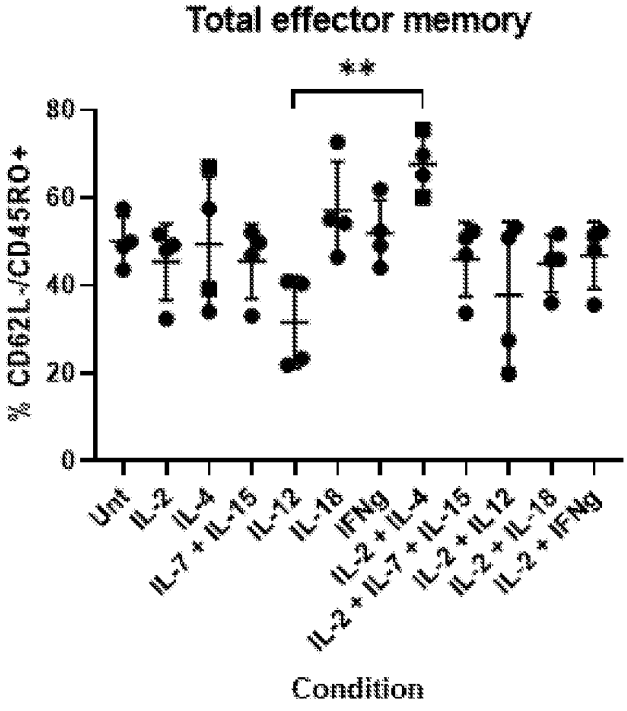

Total effector memory
**
% CD62L-/CD45RO+
80
60
40
20
0
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL-12
IL-2 + IL-18
IL-2 + IFNg
Condition

Fig. 8C-8D

E.

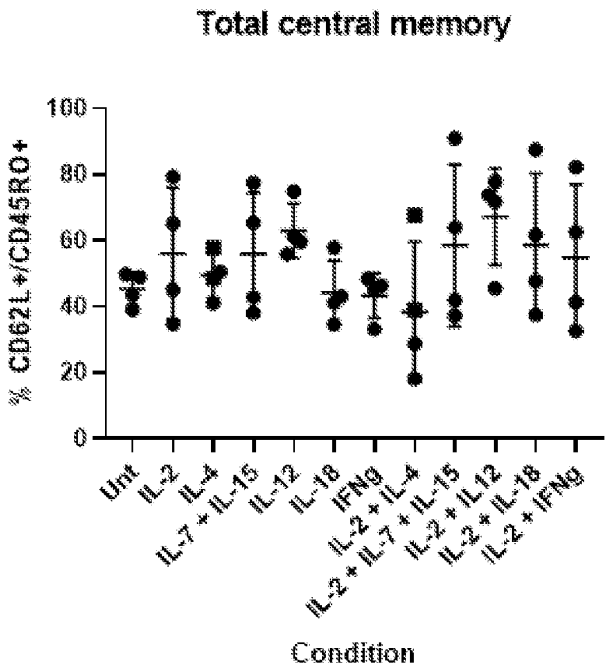
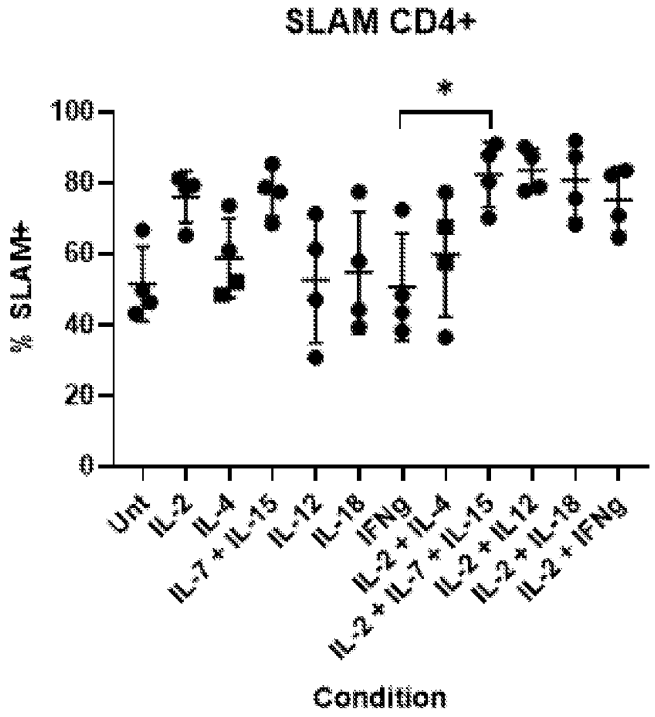

Total central memory
% CD62L+/CD45RO+
100
80
60
40
20
0
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL12
IL-2 + IL-18
IL-2 + IFNg
Condition

Fig. 8E

A.


SLAM CD4+
*
100
80
60
40
20
0
% SLAM+
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL12
IL-2 + IL-18
IL-2 + IFNg
Condition

B.

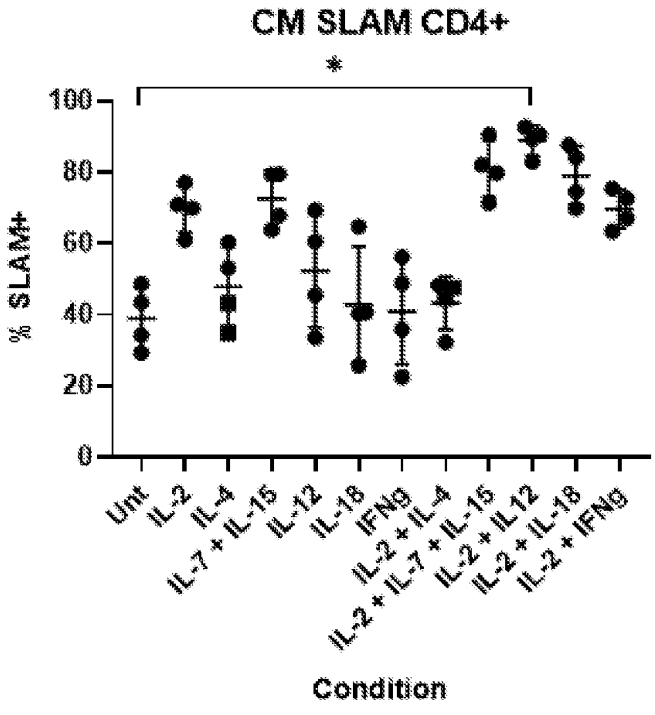
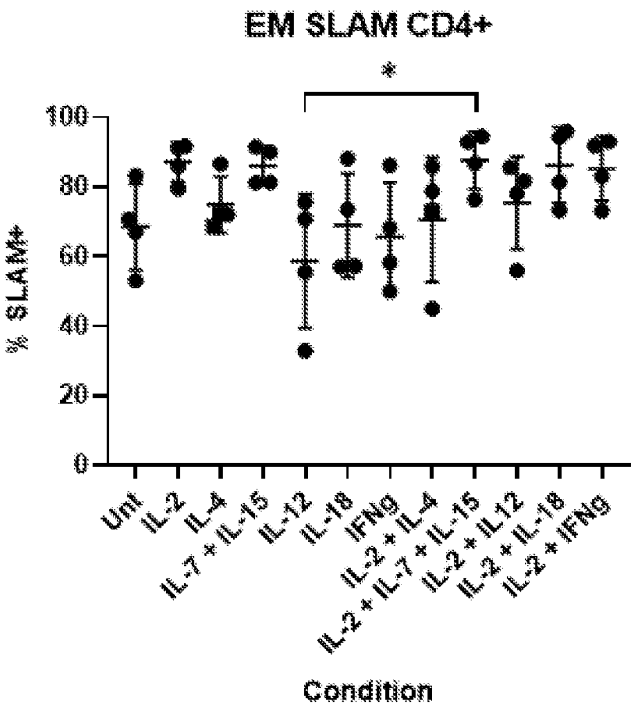

CM SLAM CD4+
*
100
80
60
40
20
0
% SLAM+
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL12
IL-2 + IL-18
IL-2 + IFNg
Condition

Fig. 9A-9B

C.


EM SLAM CD4+
*
% SLAM+
100
80
60
40
20
0
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL12
IL-2 + IL-18
IL-2 + IFNg
Condition

D.

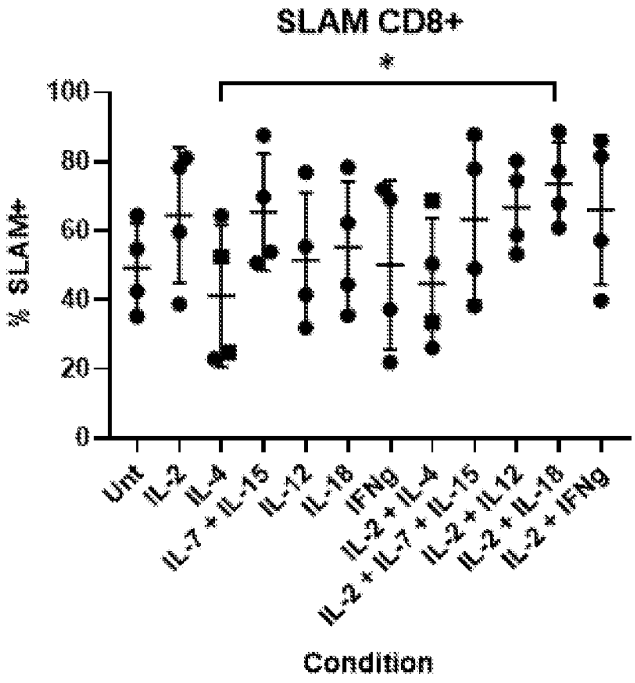
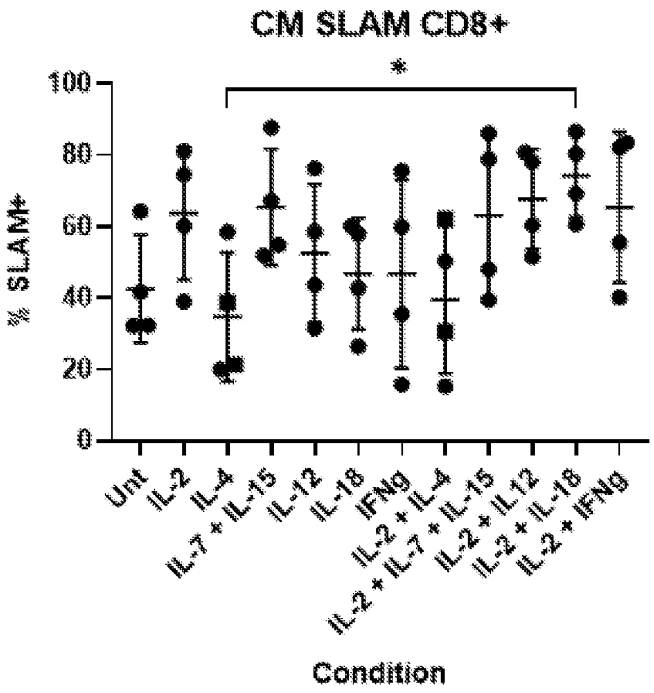

SLAM CD8+
*
% SLAM+
100
80
60
40
20
0
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL12
IL-2 + IL-18
IL-2 + IFNg
Condition

Fig. 9C-9D

E.


CM SLAM CD8+
*
% SLAM+
100
80
60
40
20
0
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL-12
IL-2 + IL-18
IL-2 + IFNg
Condition

F.

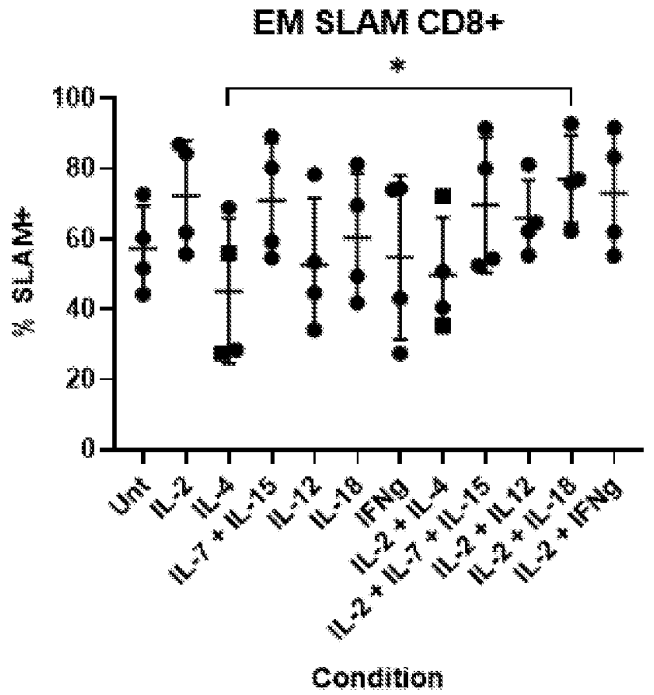
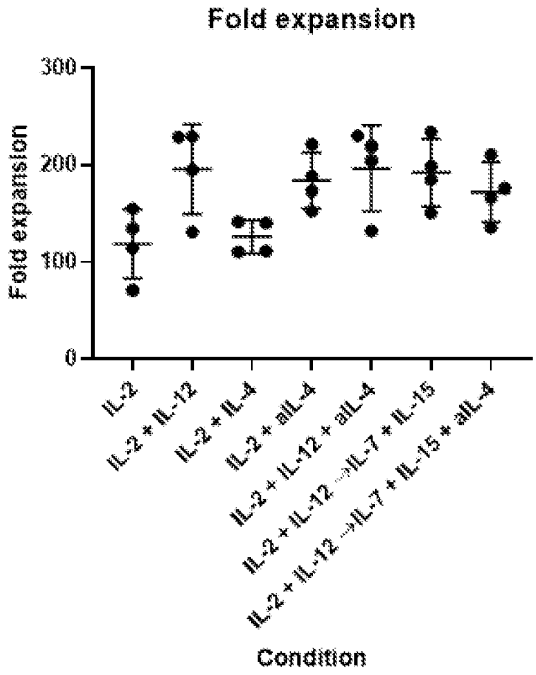

EM SLAM CD8+
*
% SLAM+
100
80
60
40
20
0
Unt
IL-2
IL-4
IL-7 + IL-15
IL-12
IL-18
IFNg
IL-2 + IL-4
IL-2 + IL-7 + IL-15
IL-2 + IL-12
IL-2 + IL-18
IL-2 + IFNg
Condition

Fig. 9E-9F

A.



B.

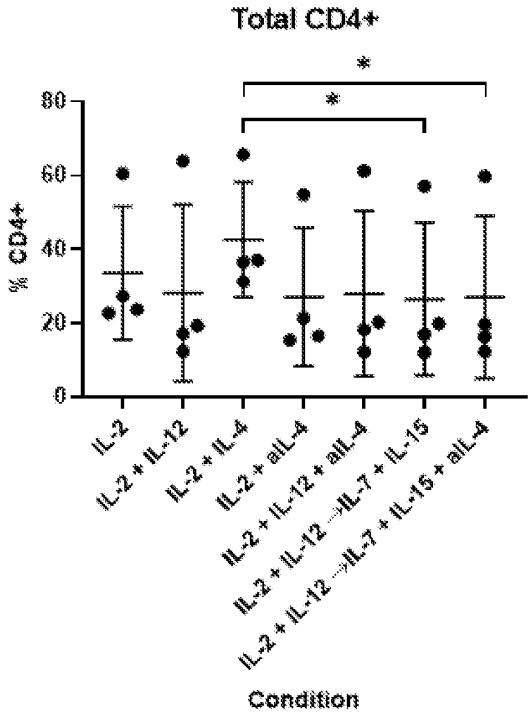
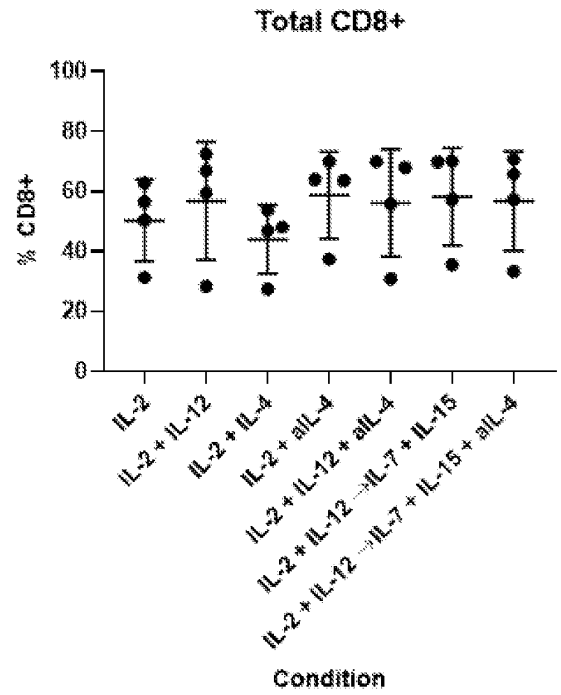


Fig. 10A-10B

C.



D.

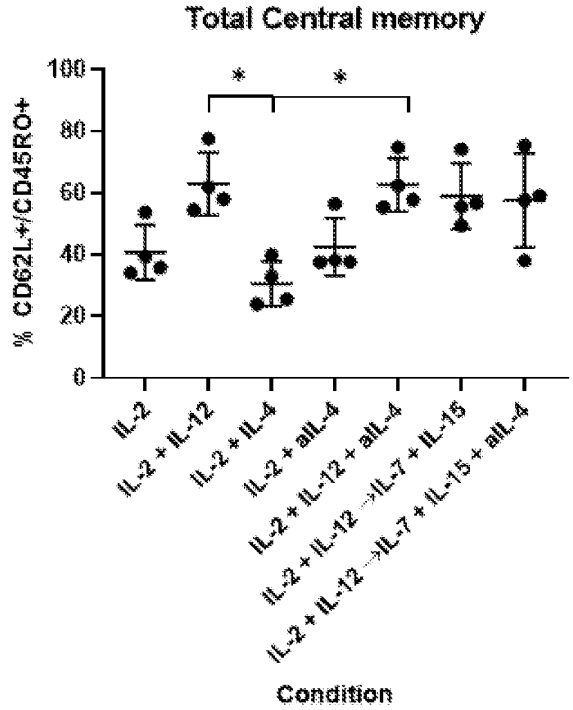


Fig. 10C-10D

E.

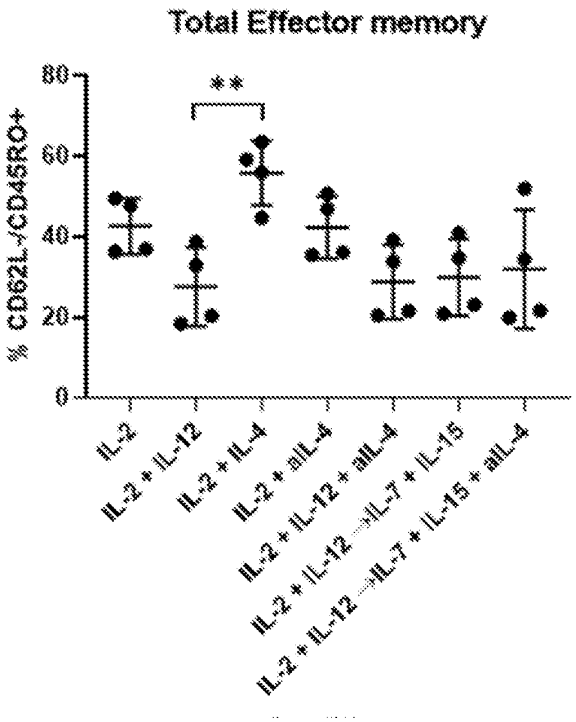
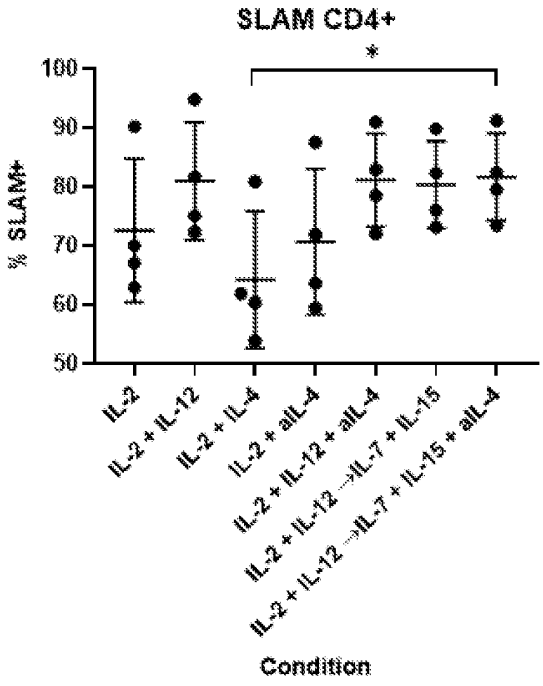

Total Effector memory
% CD62L-/CD45RO+
80
60
40
20
0
**
IL-2
IL-2 + IL-12
IL-2 + IL-4
IL-2 + αIL-4
IL-2 + IL-12 + αIL-4
IL-2 + IL-12 + IL-7 + IL-15
IL-2 + IL-12 + IL-7 + IL-15 + αIL-4

Fig. 10E

A.



B.

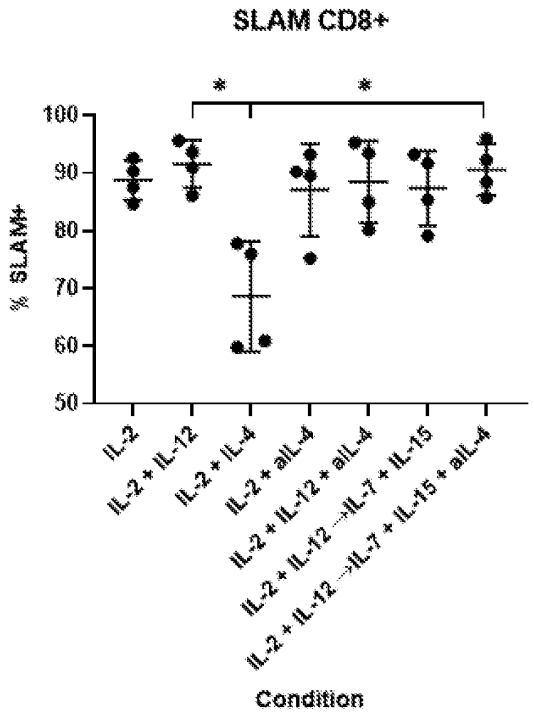
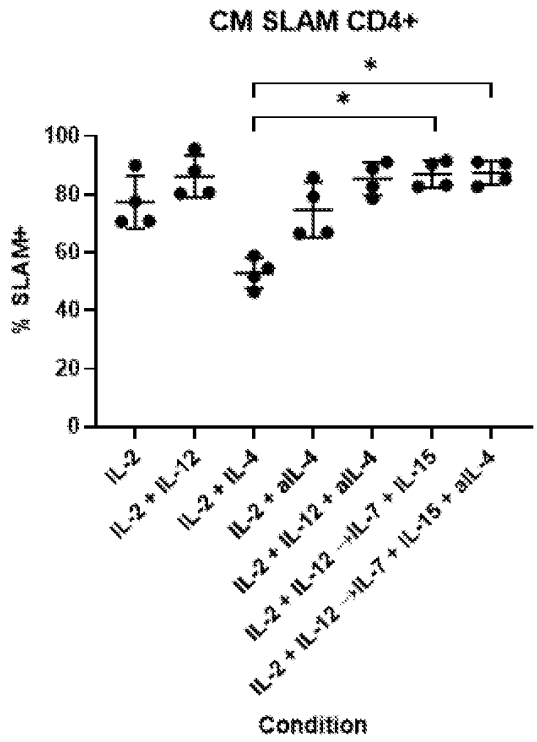


Fig. 11A-11B

C.



D.

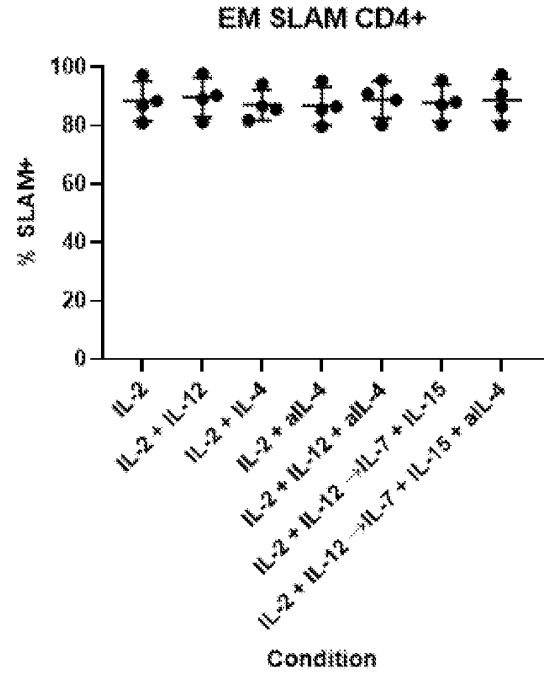
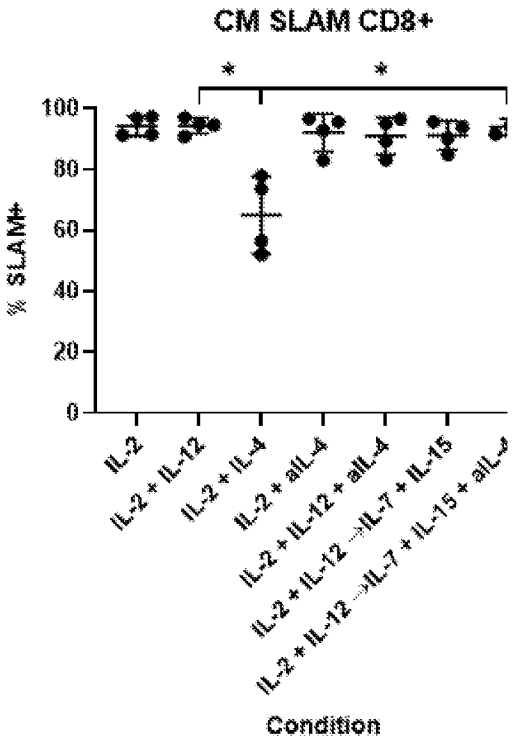


Fig. 11C-11D

E.



F.

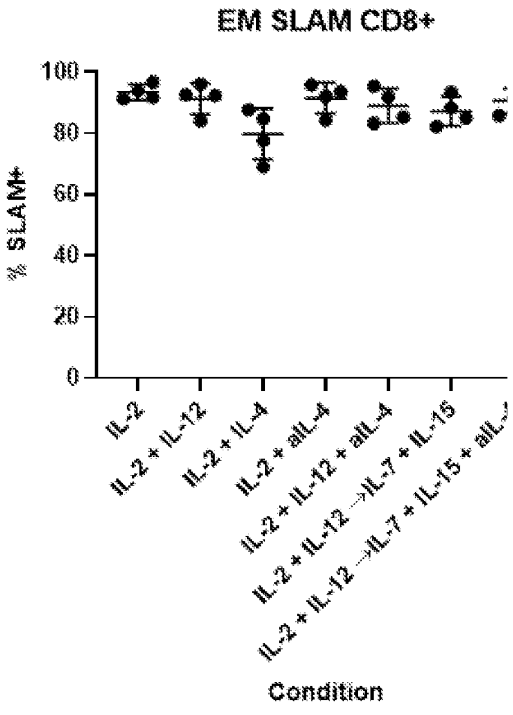
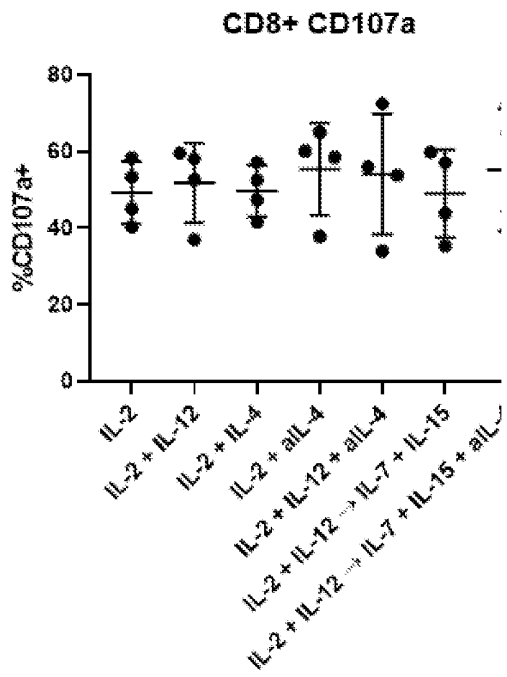


Fig. 11E-11F

A.



B.

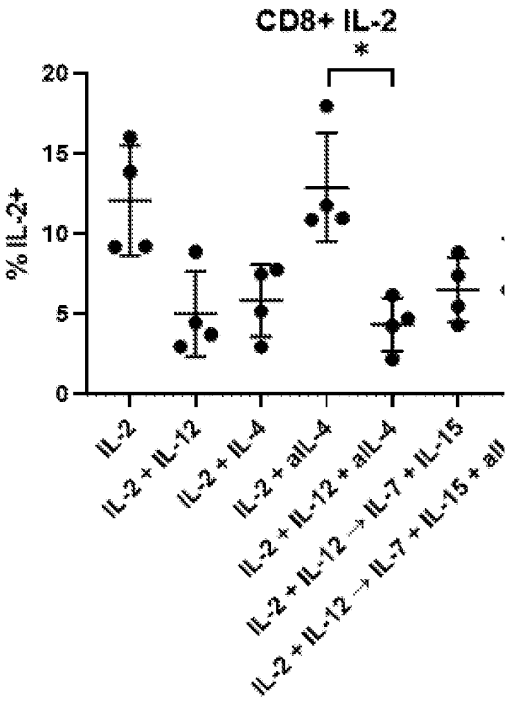
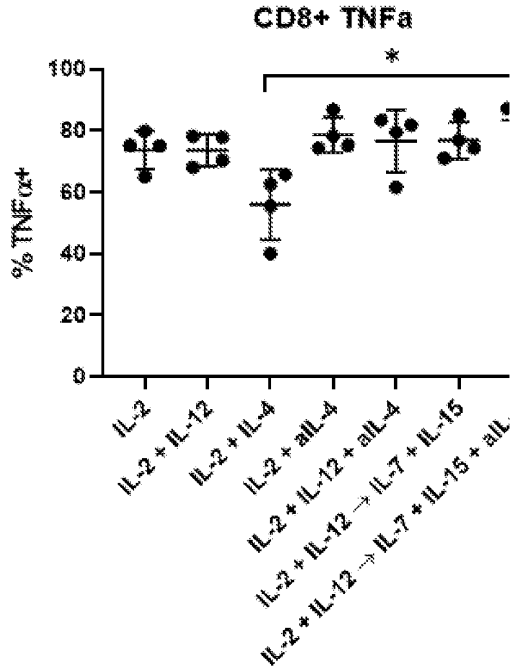


Fig. 12A-12B

C.



D.

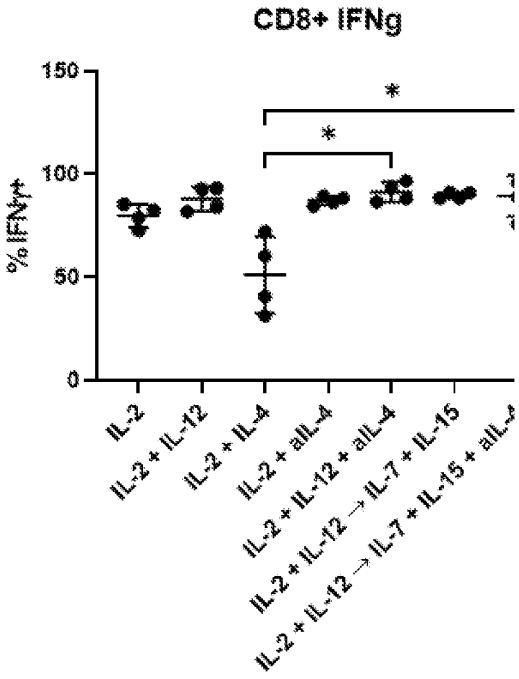
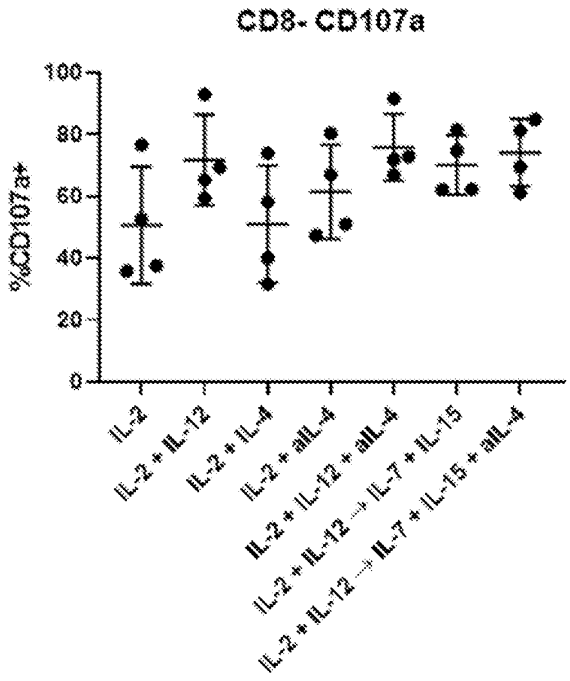


Fig. 12C-12D

A.



B.

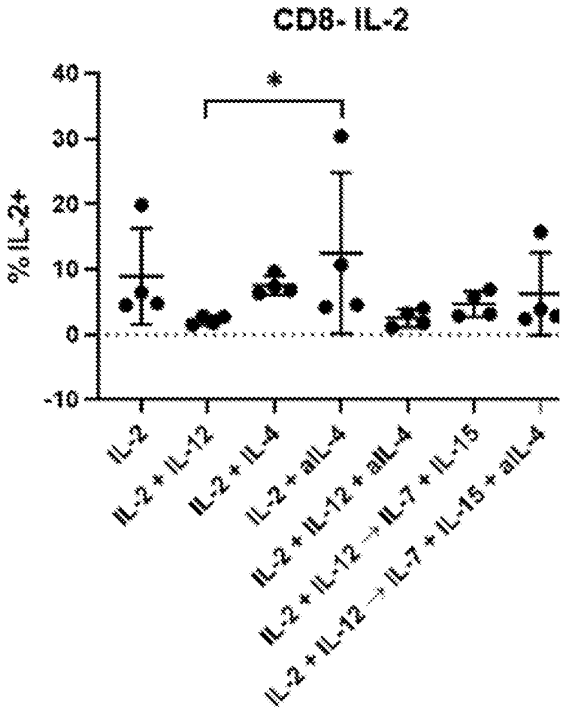
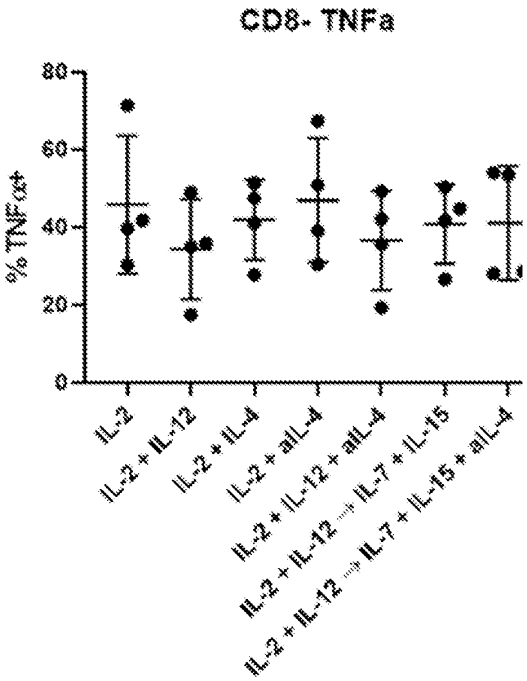


Fig. 13A-13B

C.



D.

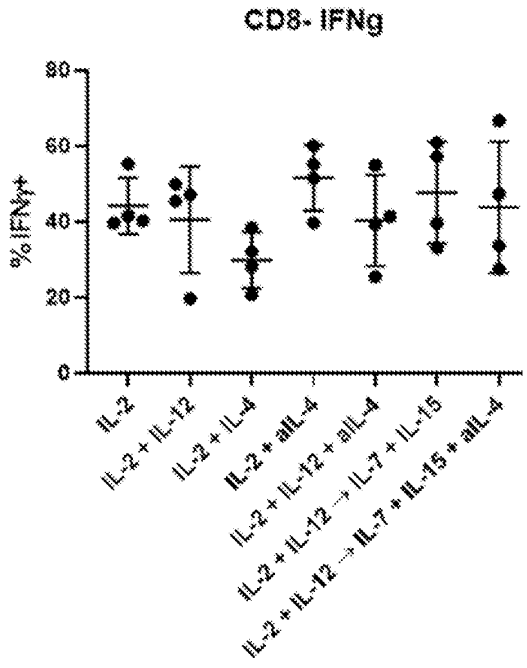


Fig. 13C-13D

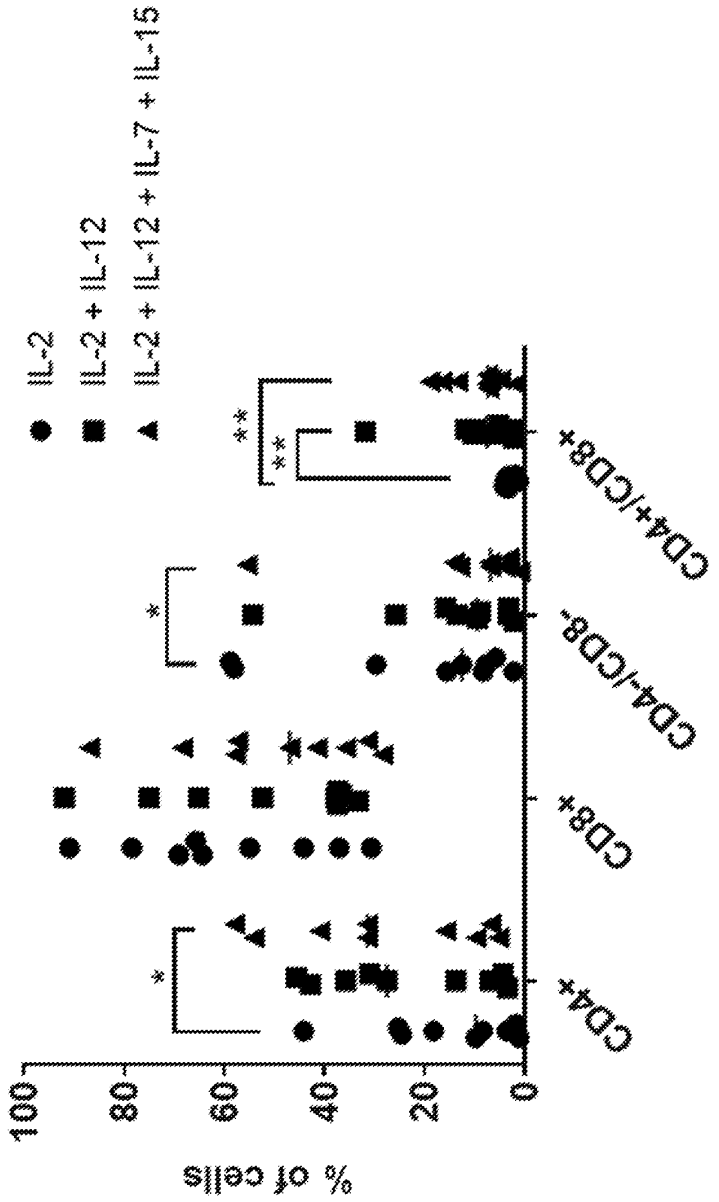
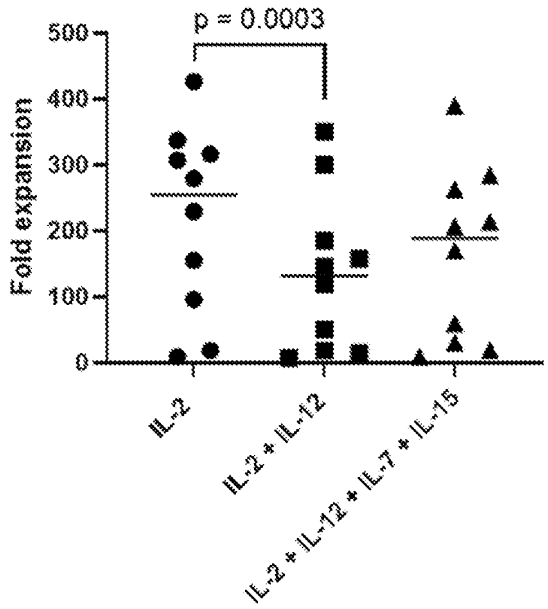

IL-2
IL-2 + IL-12
IL-2 + IL-12 + IL-7 + IL-15
% of cells
100
80
60
40
20
0
CD4+
CD8+
CD4-/CD8-
CD4+/CD8+
*
*
*
**
**

Fig. 14

A.



B.

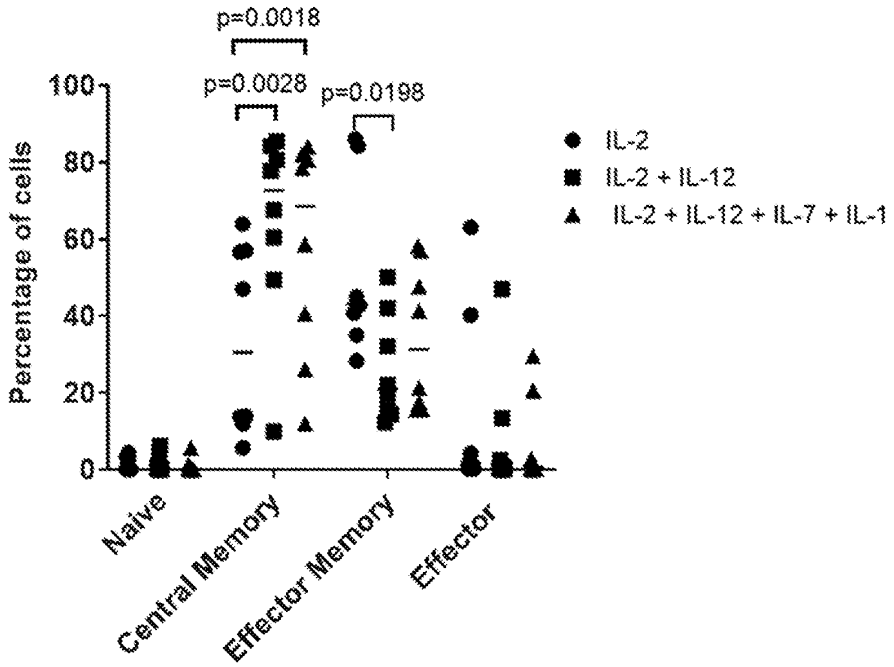
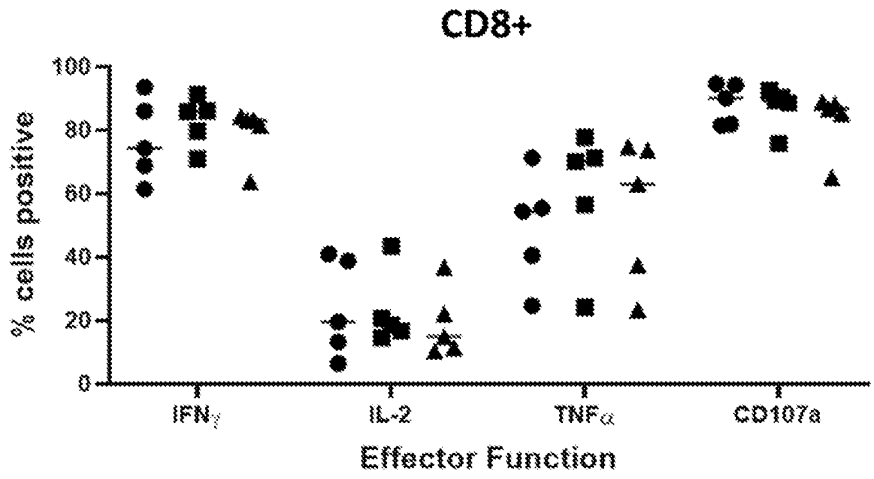


Fig. 15A-15B

A.



B.

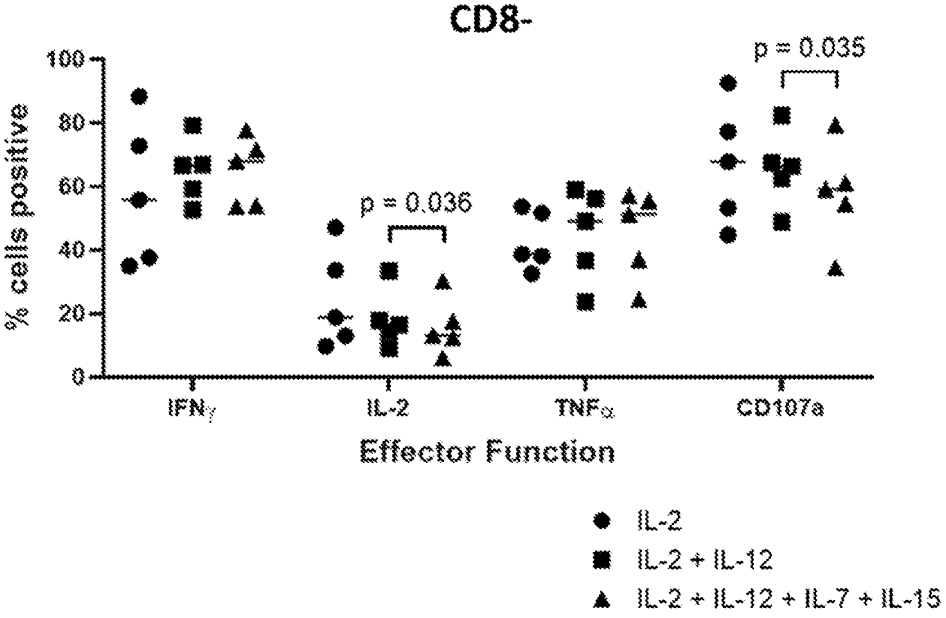
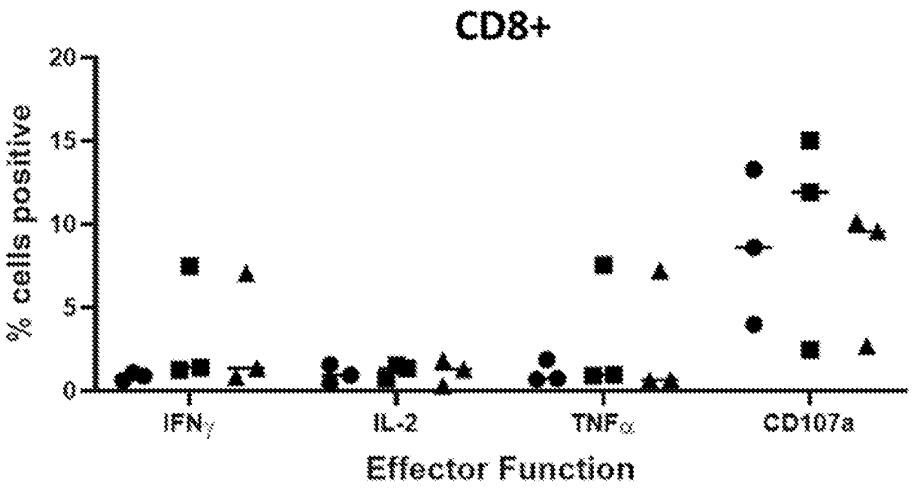


Fig. 16A-16B

A.



B.

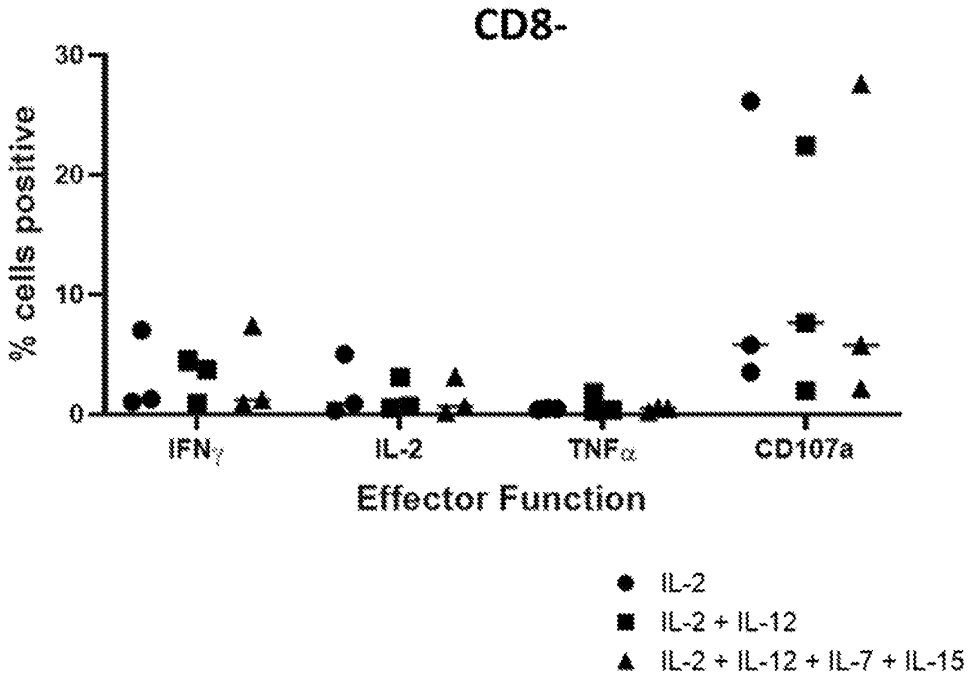


Fig. 17A-17B