FIG. 1

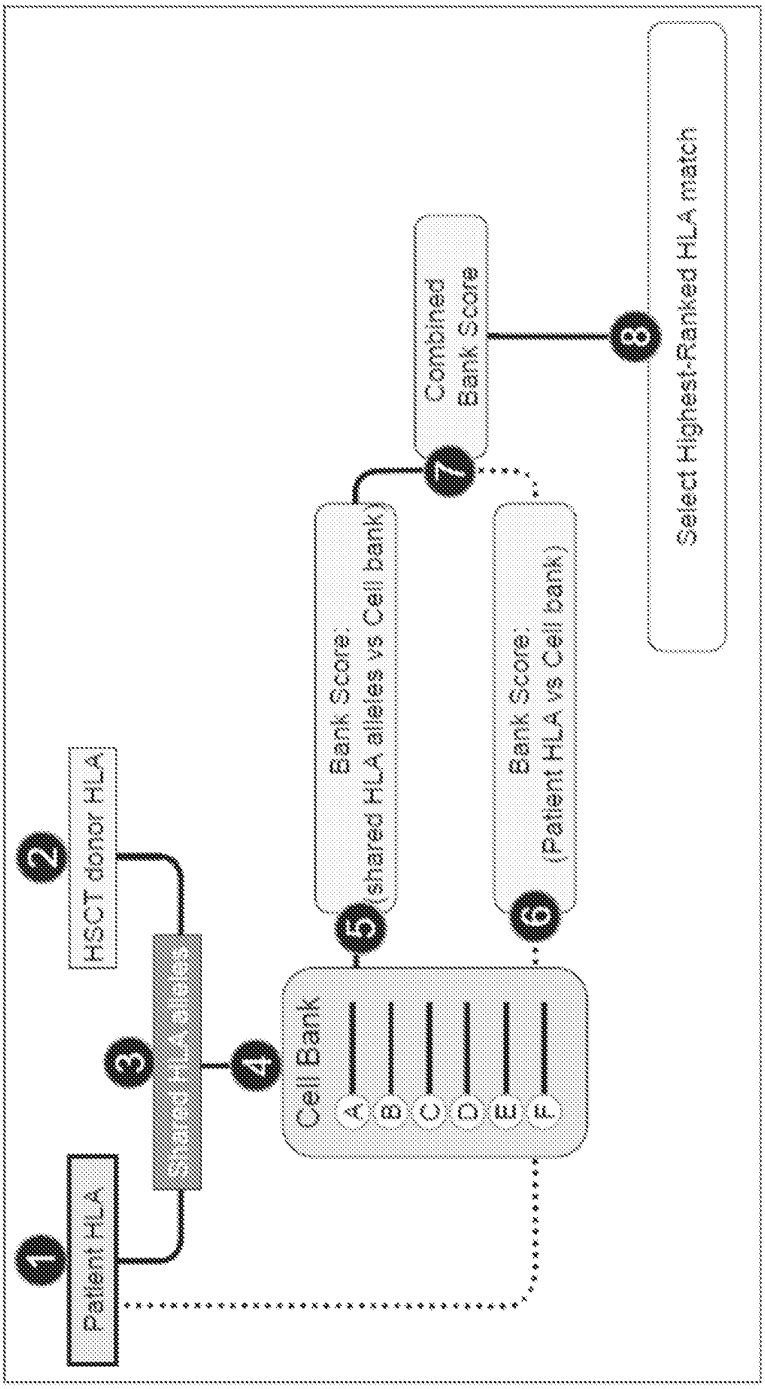

1
Patient HLA
2
HSCT donor HLA
3
Search Algorithm
4
Cell Bank
A
B
C
D
E
F
5
Bank Score:
shared HLA alleles vs Cell bank)
6
Bank Score:
(Patient HLA vs Cell bank)
7
Combined
Bank Score
8
Select Highest-Ranked HLA match

FIG. 2

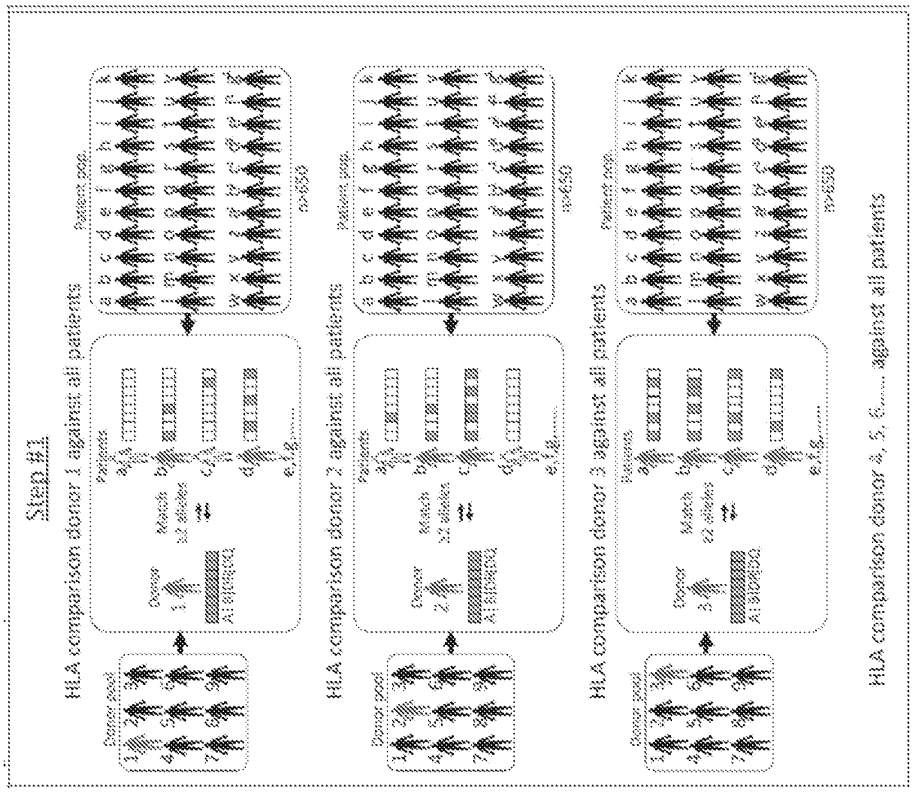

Step #1
HLA comparison donor 1 against all patients
HLA comparison donor 2 against all patients
HLA comparison donor 3 against all patients
HLA comparison donor 4, 5, 6,.... against all patients
Donor pool
Patient pool
Donor
Match
≥2 alleles
n>650

FIG. 3

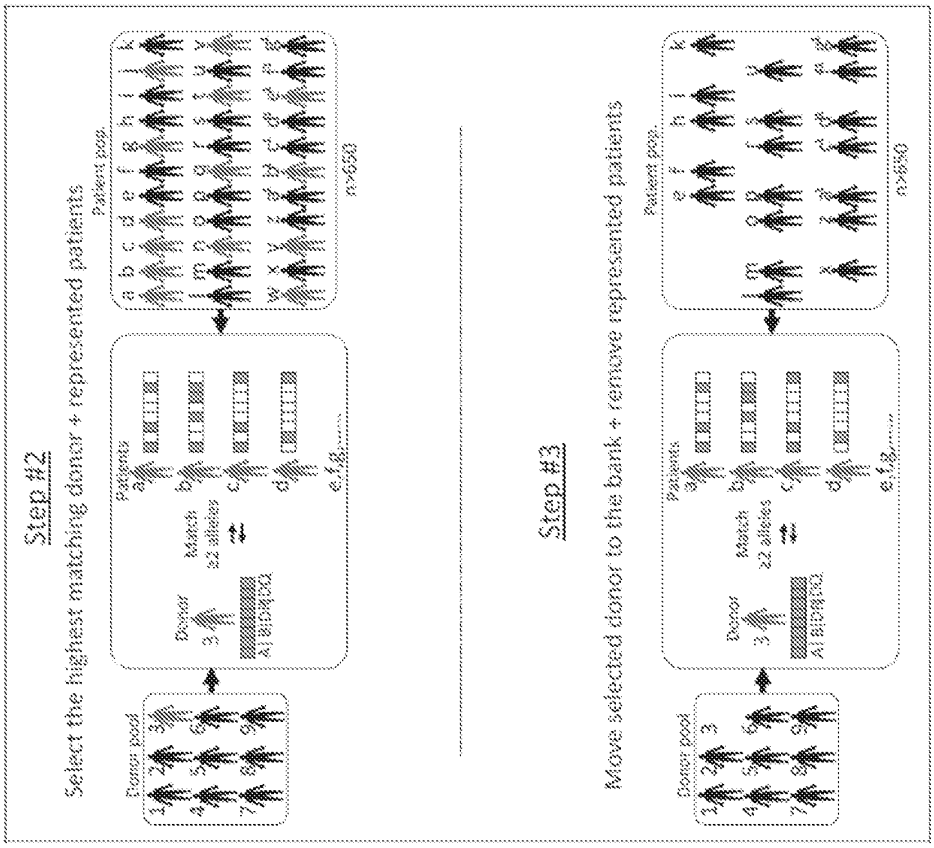

Step #2
Select the highest matching donor + represented patients
Donor pool
Patient pop.
Patients
Donor
Match
≥2 alleles
n>650
Step #3
Move selected donor to the bank + remove represented patients

FIG. 4

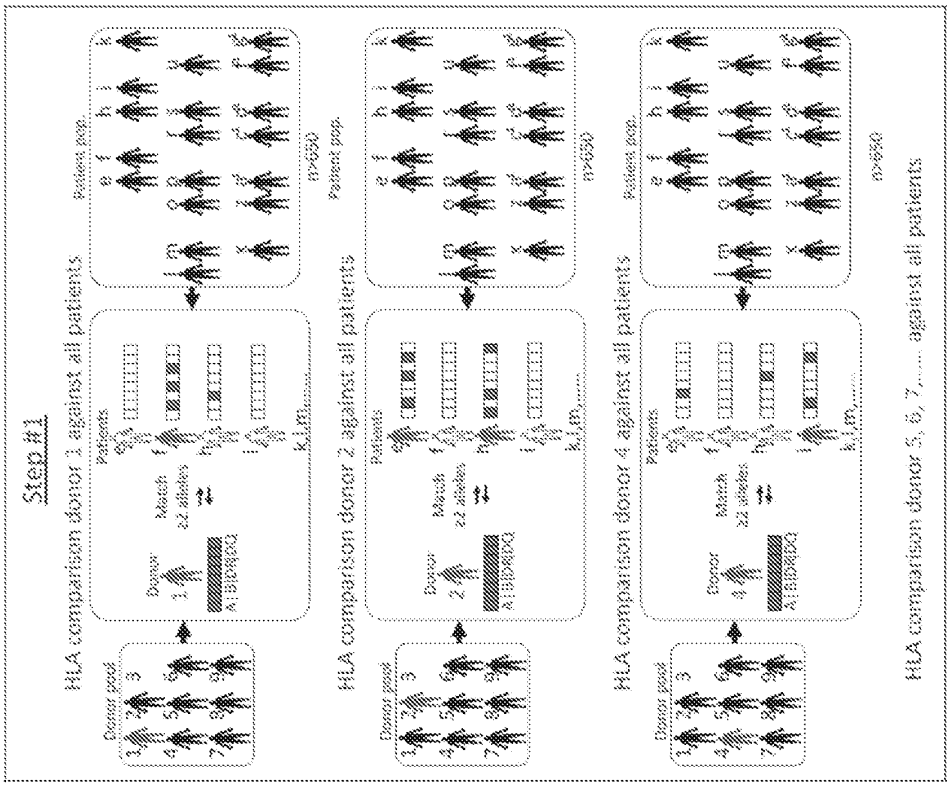

Step #1
HLA comparison donor 1 against all patients
HLA comparison donor 2 against all patients
HLA comparison donor 4 against all patients
HLA comparison donor 5, 6, 7,..... against all patients
Donor pool
Donor 1
Donor 2
Donor 4
Match
22 alleles
Patients
Patient pop.
n=650

FIG. 5

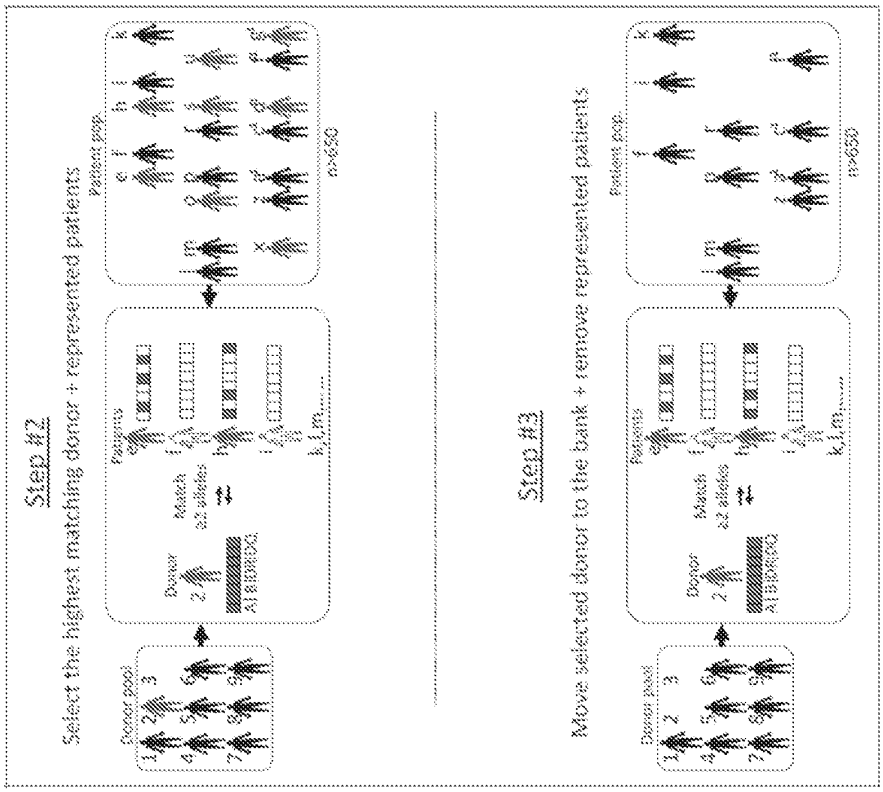

Step #2
Select the highest matching donor + represented patients
Donor pool
Donor
Match
≥2 alleles
Patients
Patient pop.
n×650
Step #3
Move selected donor to the bank + remove represented patients
Donor pool
Donor
Match
≥2 alleles
Patients
Patient pop.
n×650

FIG. 6

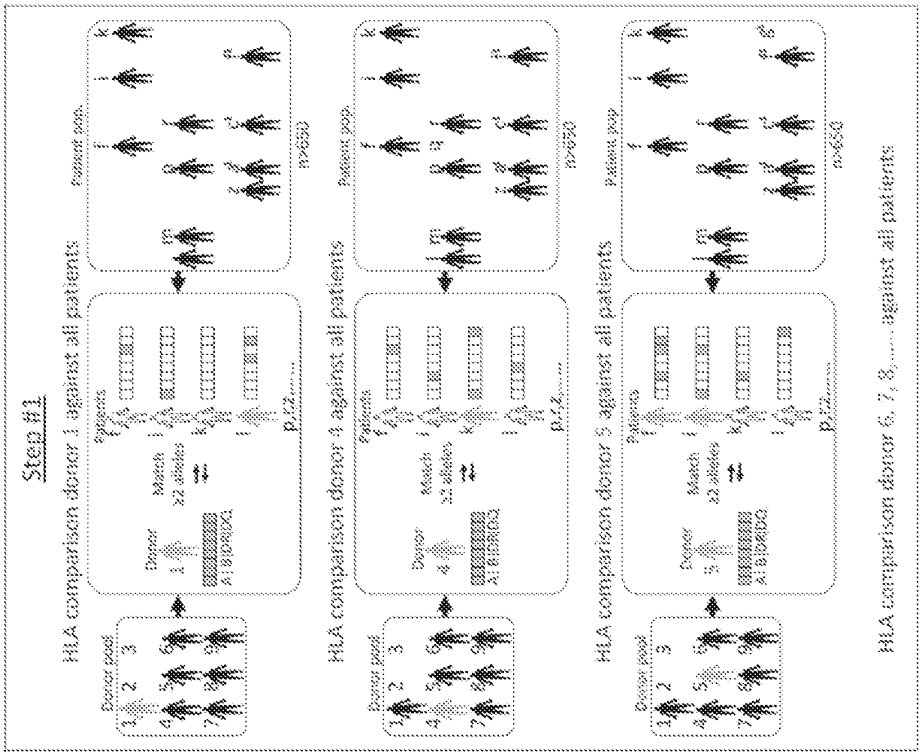

Step #1
HLA comparison donor 1 against all patients
HLA comparison donor 4 against all patients
HLA comparison donor 5 against all patients
HLA comparison donor 6, 7, 8,..... against all patients
Donor pool
Donor
Match ≥2 alleles
Patients
Patient pop.
n=650

FIG. 7

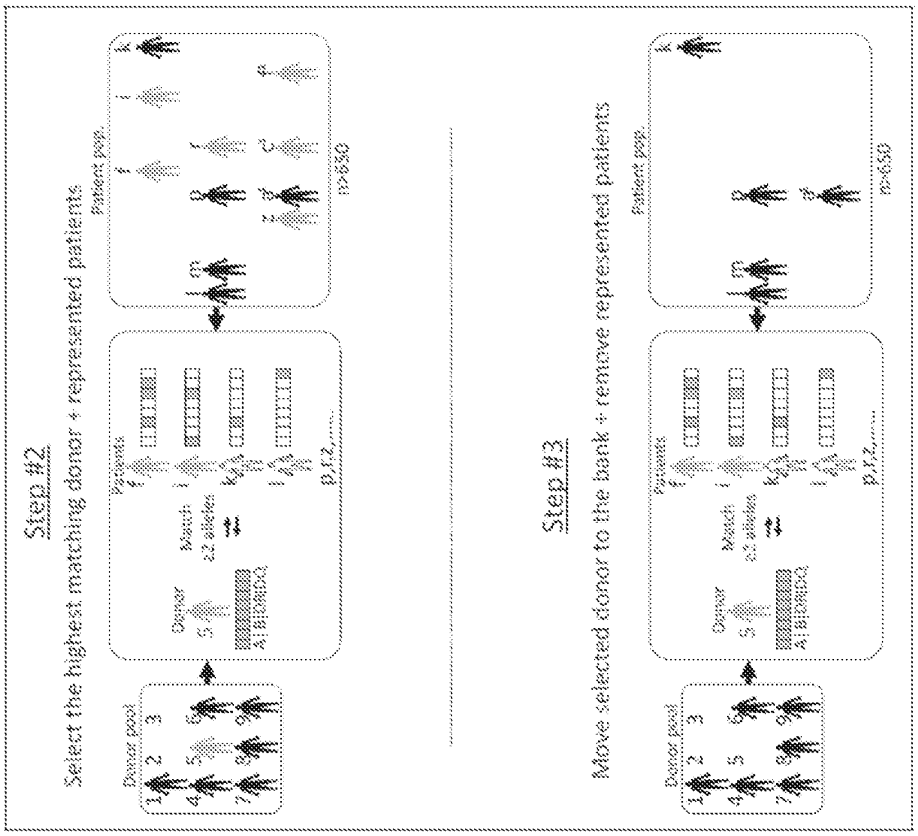

Step #2
Select the highest matching donor + represented patients
Donor pool
Donor
Match
Patients
Patient pop.
n>650
Step #3
Move selected donor to the bank + remove represented patients

FIG. 8

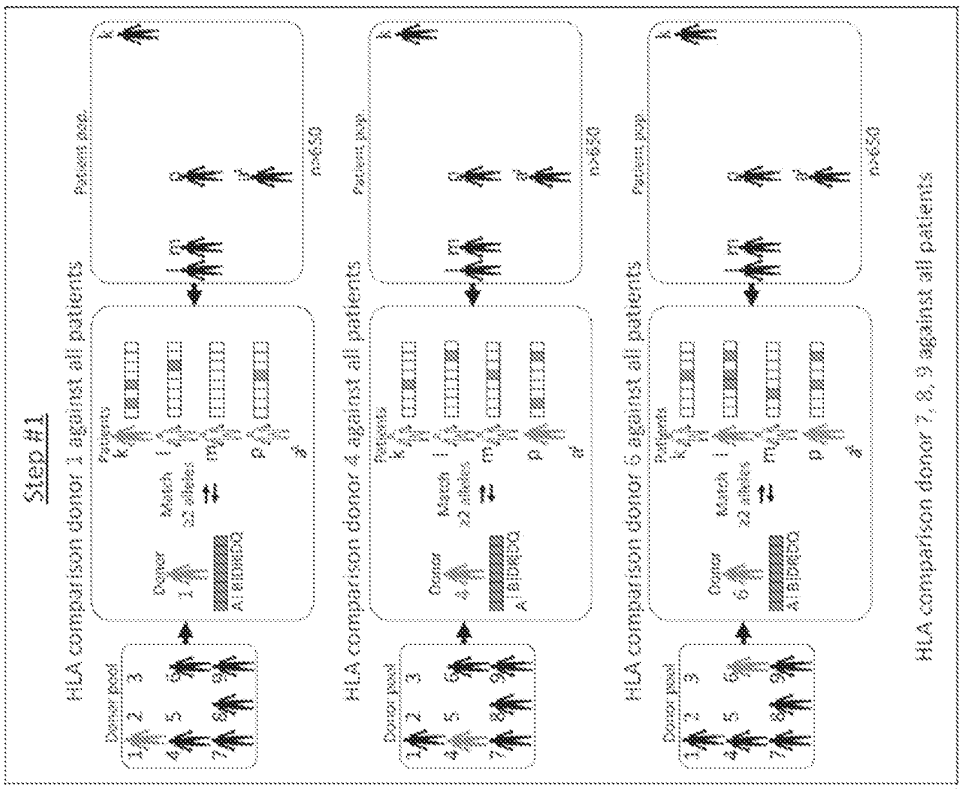

Step #1
HLA comparison donor 1 against all patients
Donor pool
Donor 1
Match ≥3 alleles
Patients
Patient pop.
n=650
HLA comparison donor 4 against all patients
Donor 4
HLA comparison donor 6 against all patients
Donor 6
HLA comparison donor 7, 8, 9 against all patients

FIG. 9

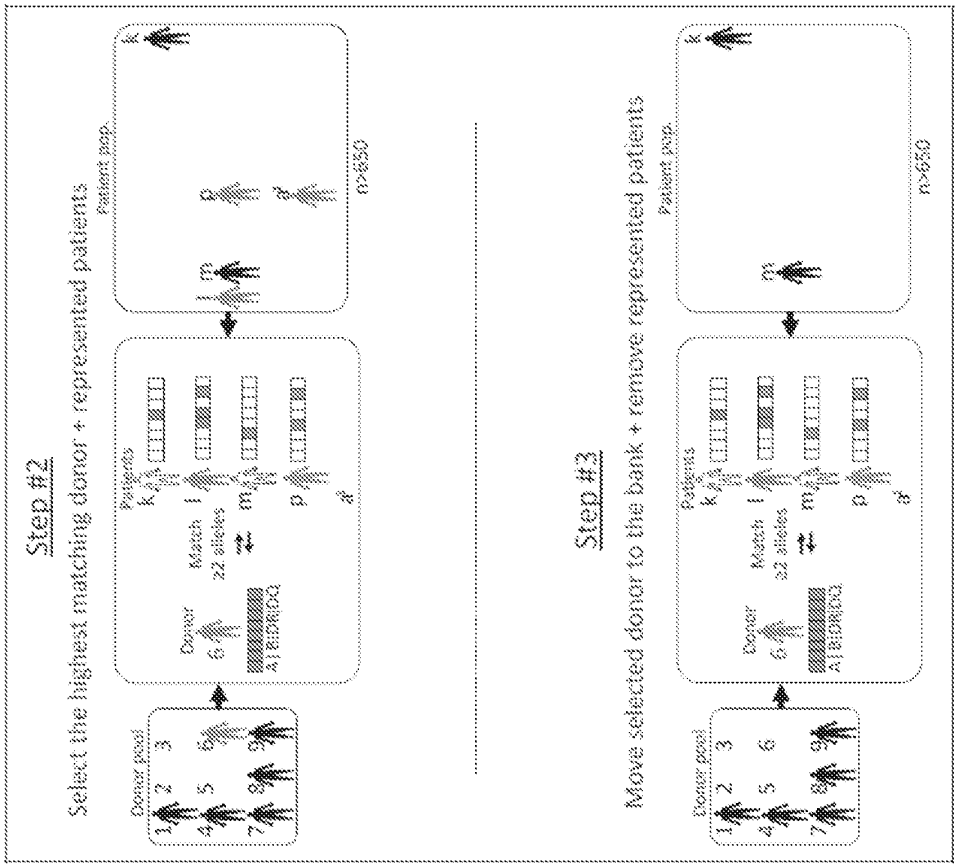

Step #2
Select the highest matching donor + represented patients
Donor pool
Donor
Match ≥2 alleles
Patients
Patient pop.
n>650
Step #3
Move selected donor to the bank + remove represented patients
Donor pool
Donor
Match ≥2 alleles
Patients
Patient pop.
n>650

FIG. 10

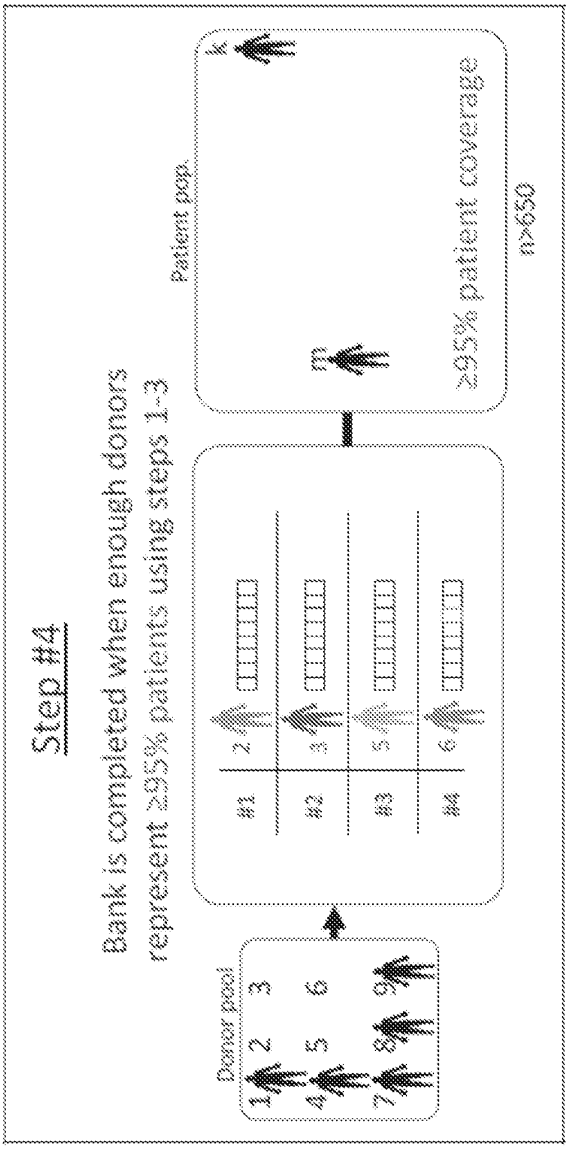
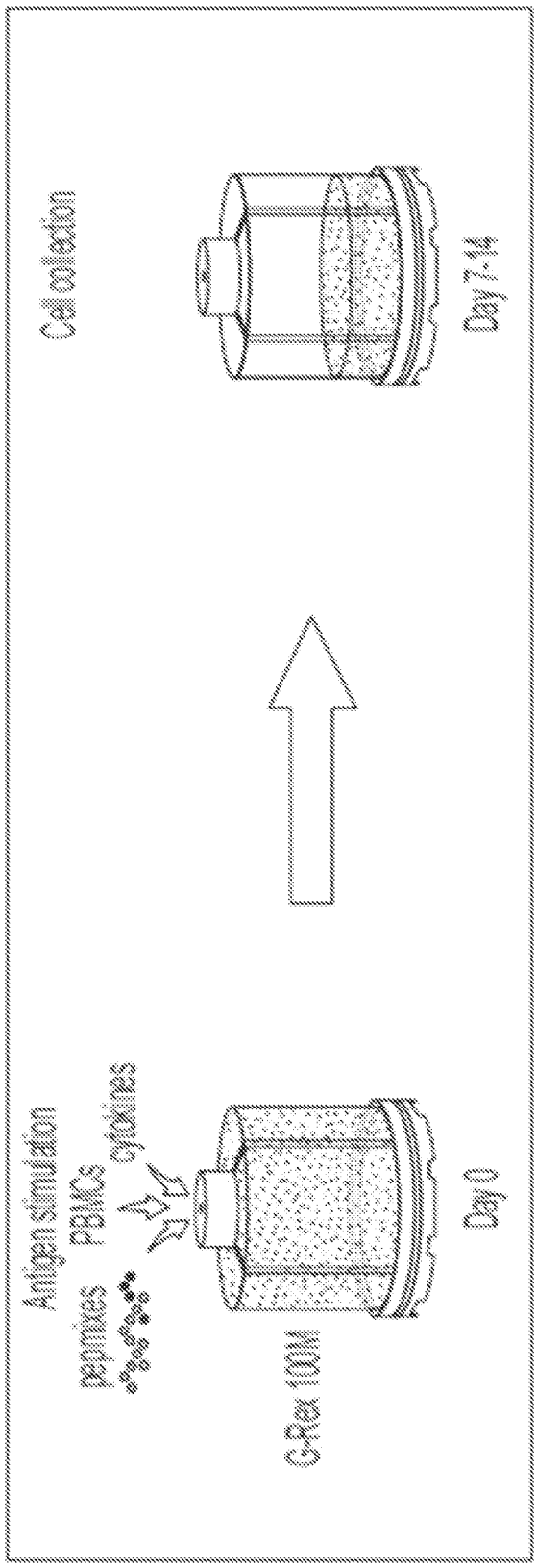

Step #4
Bank is completed when enough donors represent ≥95% patients using steps 1-3
Donor pool
1 2 3 4 5 6 7 8 9
#1
#2
#3
#4
Patient pop.
k
m
≥95% patient coverage
n>650

FIG. 11


Cell collection
Day 7-14
Antigen stimulation
peptides
PBMCs
cytokines
Day 0
G-Rex 100M

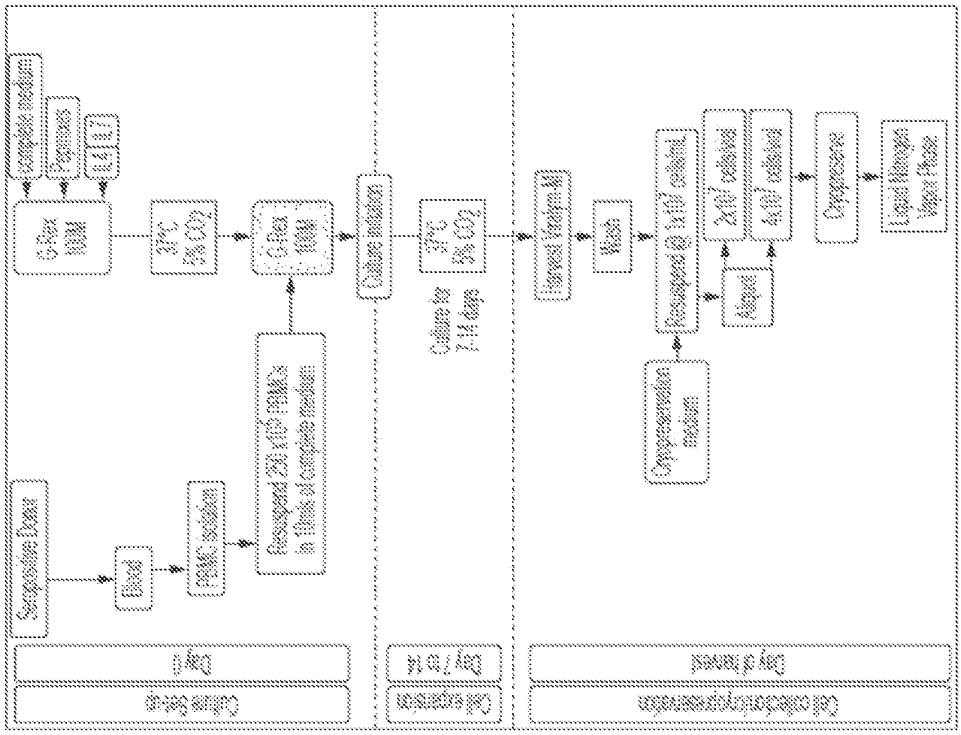

Day 0
Day 0 to 14
Day 14 to Day 21
Day 21 harvest
Cell culture
Cell expansion
Cell collection/cryopreservation
Sorted cells
Beads
Add to
Resuspend Ab (nb BMA
in thaw kit complete media
Culture initiation
Culture for
7-14 days
Harvest cells
Wash
Resuspend @ 1x10^7 cells/mL
Aliquot
2x10^7 cells/vial
4x10^7 cells/vial
Cryopreserve
Liquid Nitrogen
Vapor Phase

FIG. 12

FIG. 13

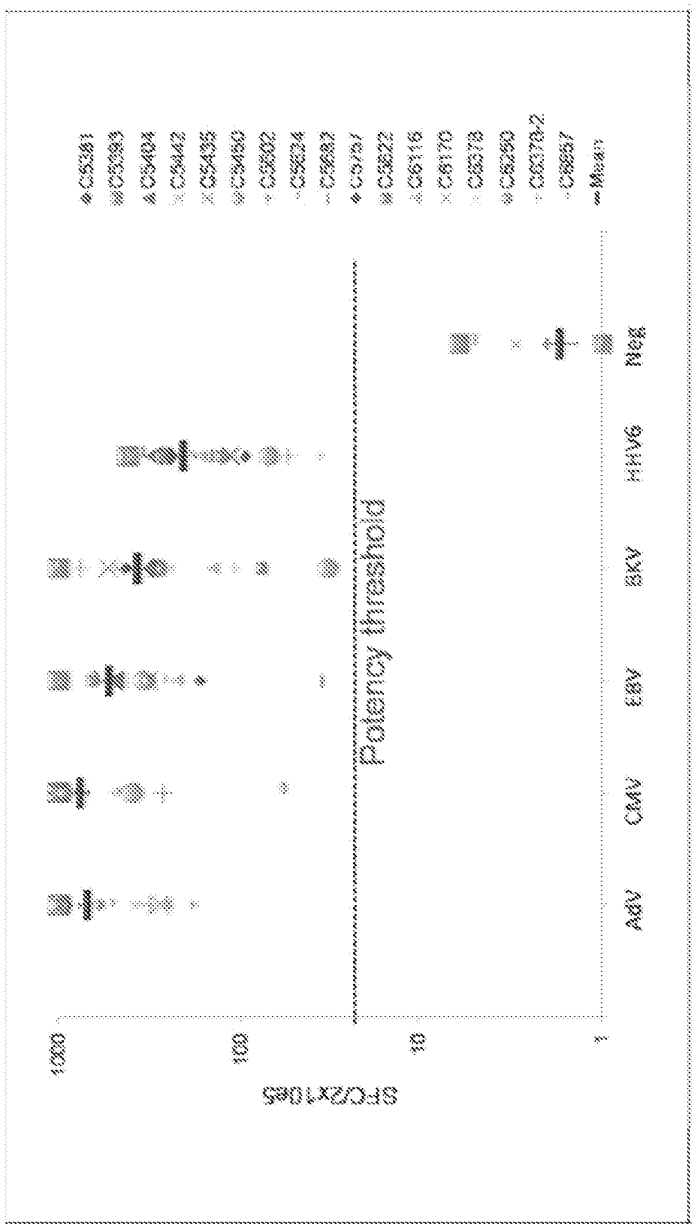

C5381
C5393
C5404
C5442
C5455
C5460
C5602
C5624
C5683
C5751
C5822
C6116
C6170
C6378
C6260
C6378-2
C6557
Mean
Potency threshold
SFC/2x10^5
1000
100
10
1
AdV
CMV
EBV
BKV
HHV6
Mock

FIG. 14

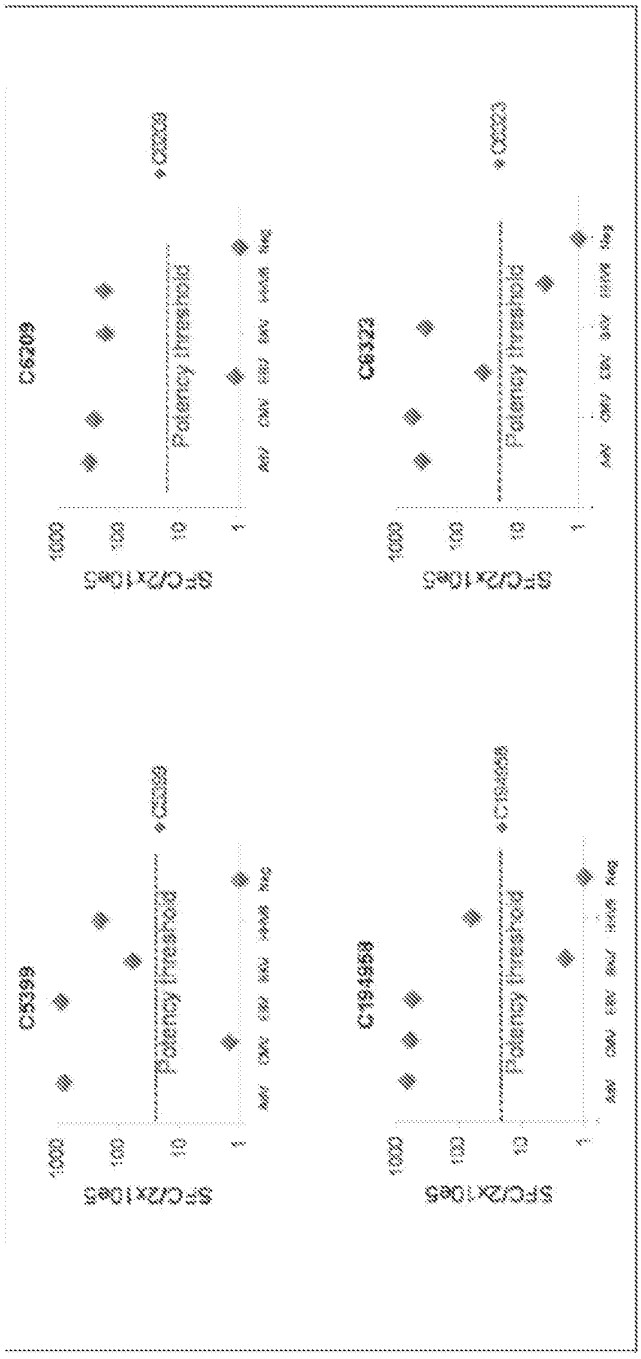

C6209
C6209
Potency Threshold
SFC/2x10e5
1000
100
10
1
Ave
C6322
C6322
Potency Threshold
C5399
C5399
Potency Threshold
C1944658
C1944658
Potency Threshold

FIG. 15

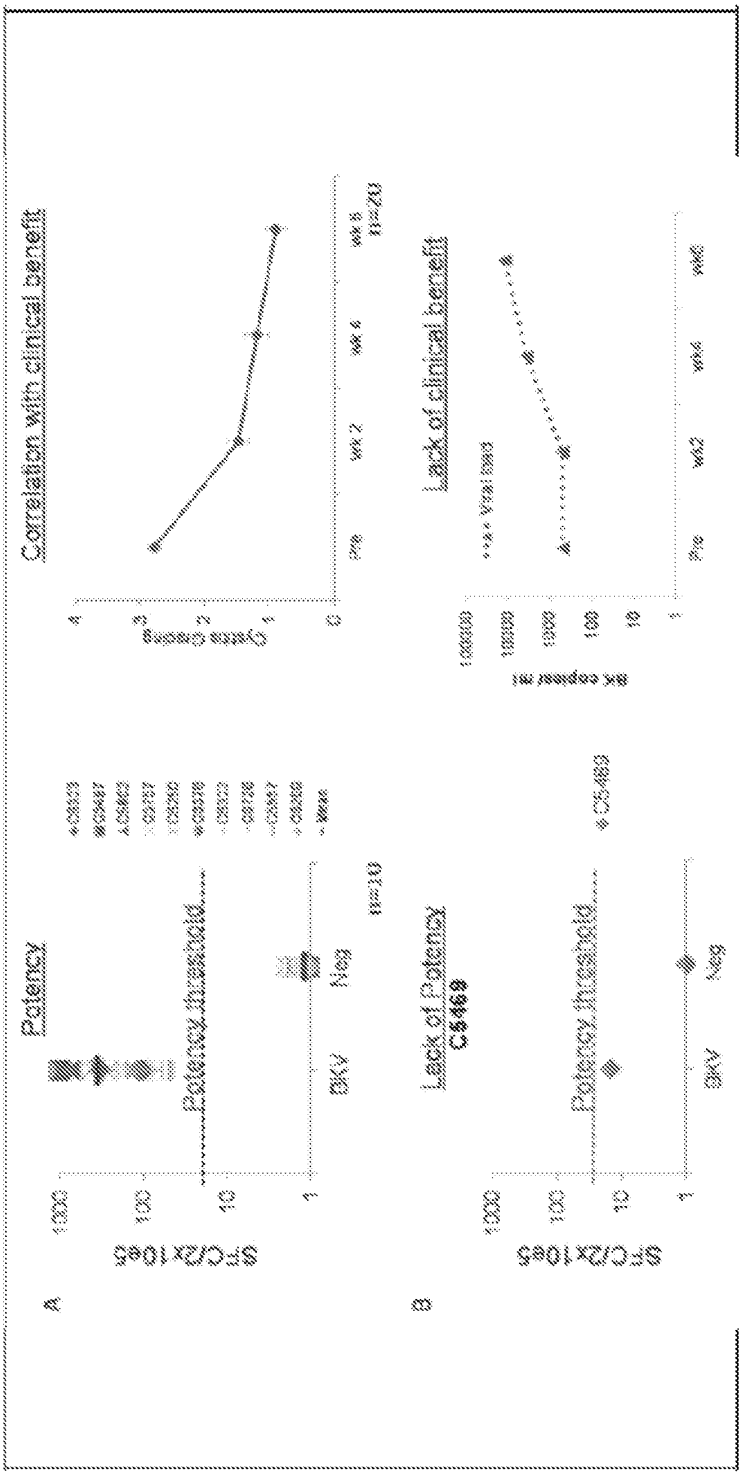

Correlation with clinical benefit
Lack of clinical benefit
Potency
Potency threshold
BKV
Neg
Lack of Potency
C5469
SFC/2x10e5
A
B

FIG. 16

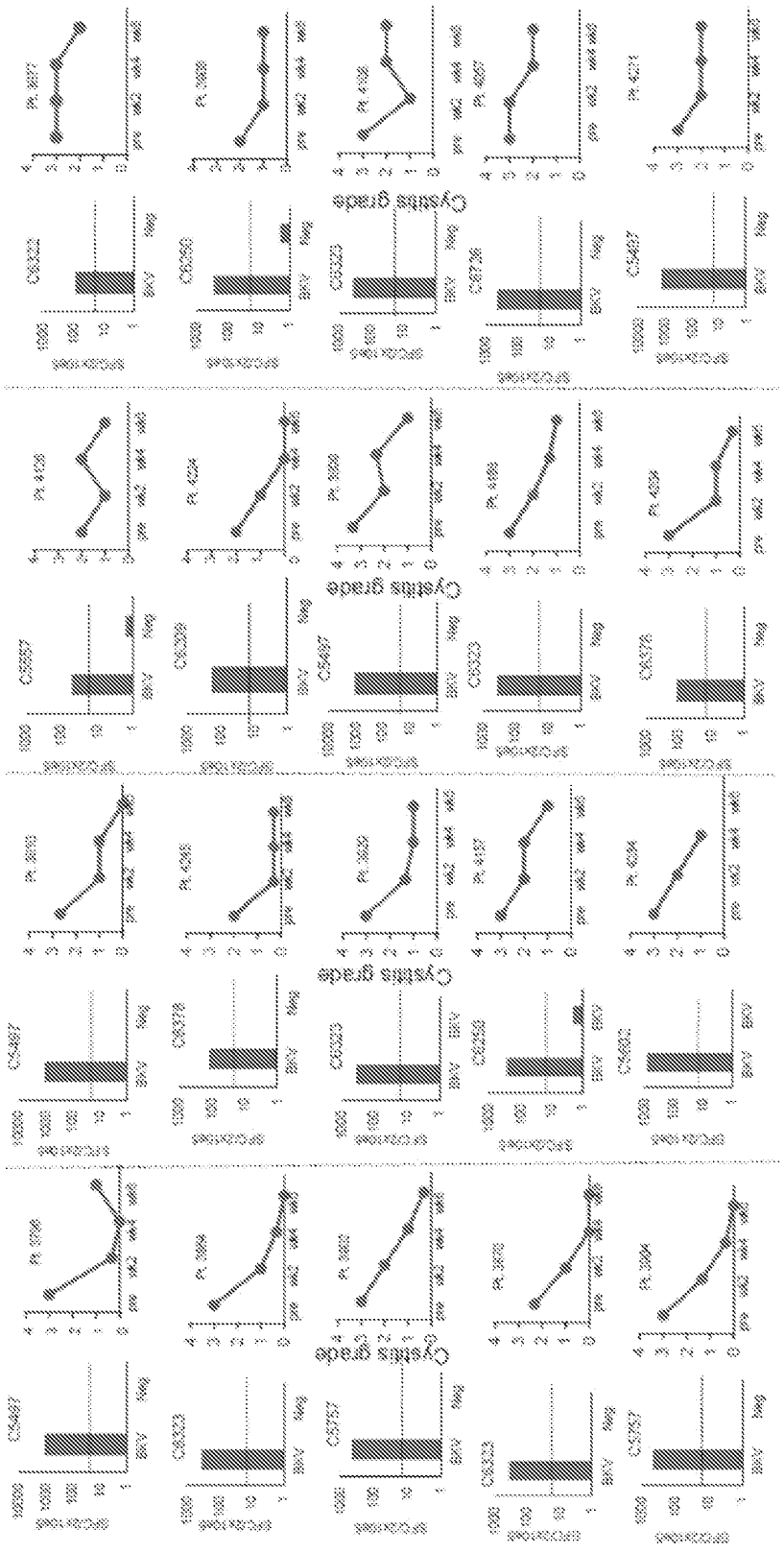


FIG. 17A

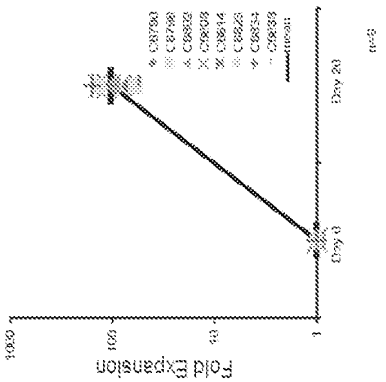


FIG. 17B

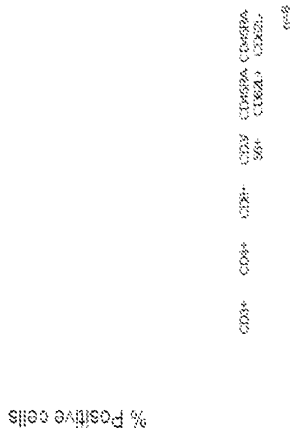


FIG. 17C

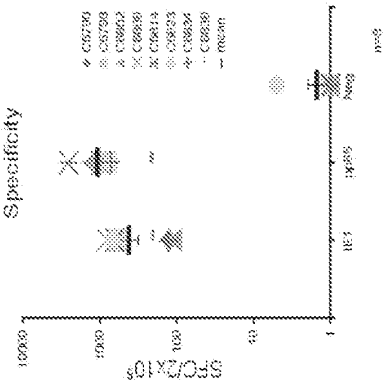


FIG. 17D

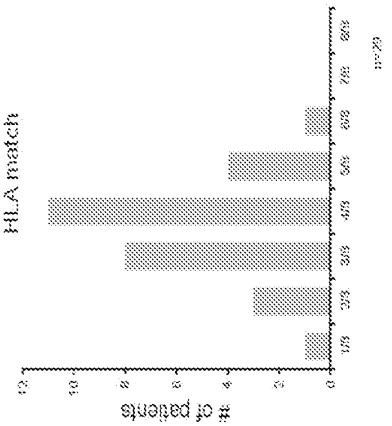
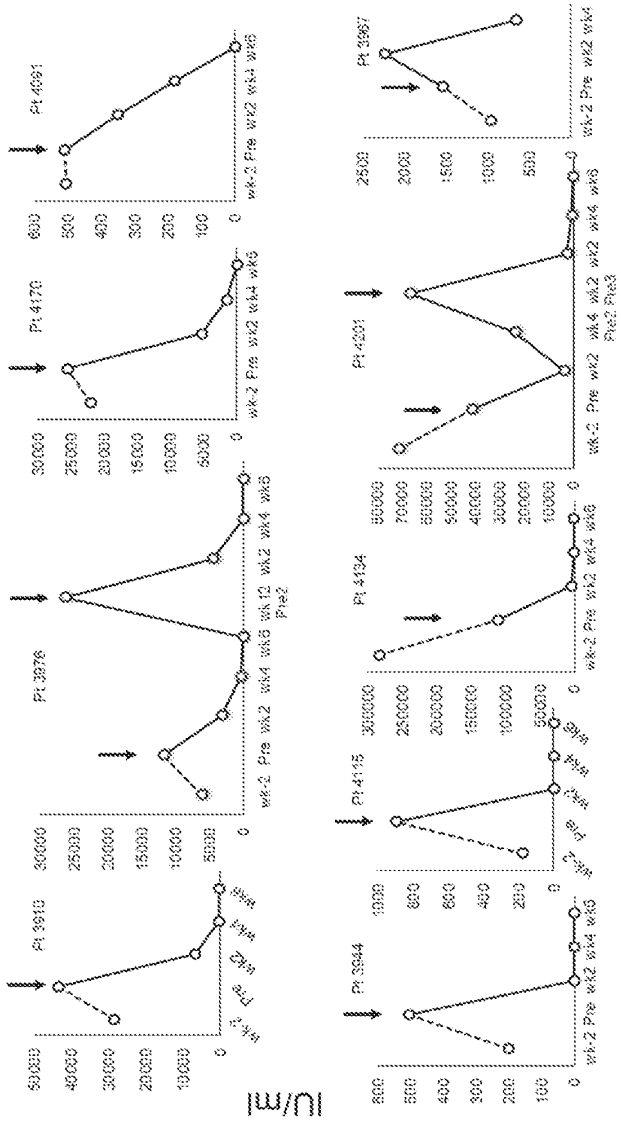


FIG. 18


IU/ml
Pt 3844
Pt 3910
Pt 3976
Pt 4041
Pt 4105
Pt 4170
Pt 4234
Pt 4297
wk-2 Pre wk2 wk4 wk6
wk-2 Pre wk2 wk4 wk6 wk12 wk24
Phe2
wk-2 Pre wk2 wk4 wk6
Phe2 Phe3

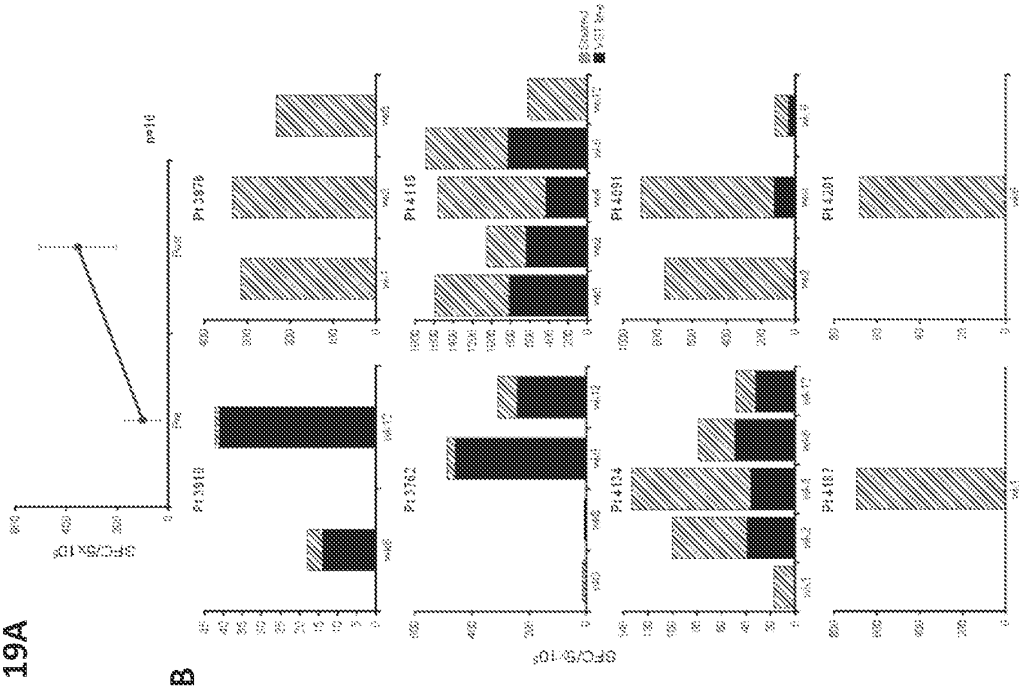


FIG. 19A

FIG. 19B

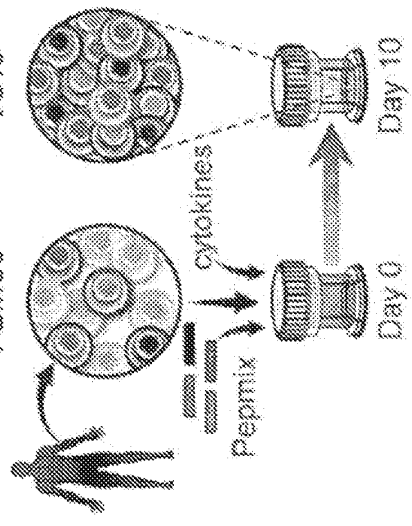


FIG. 20A

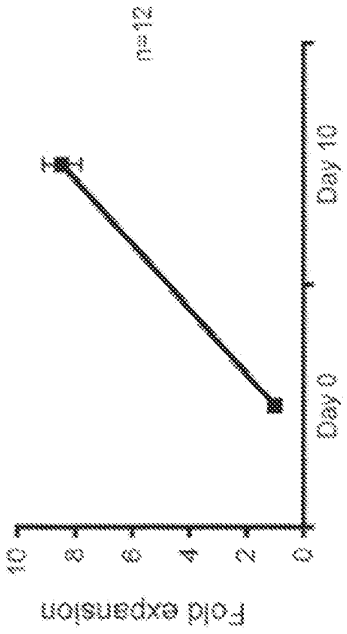


FIG. 20B

FIG. 20C

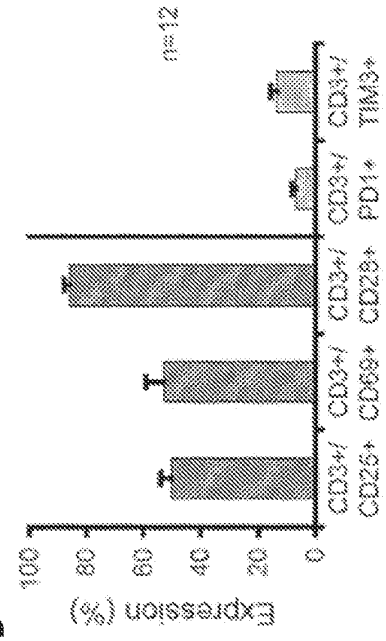
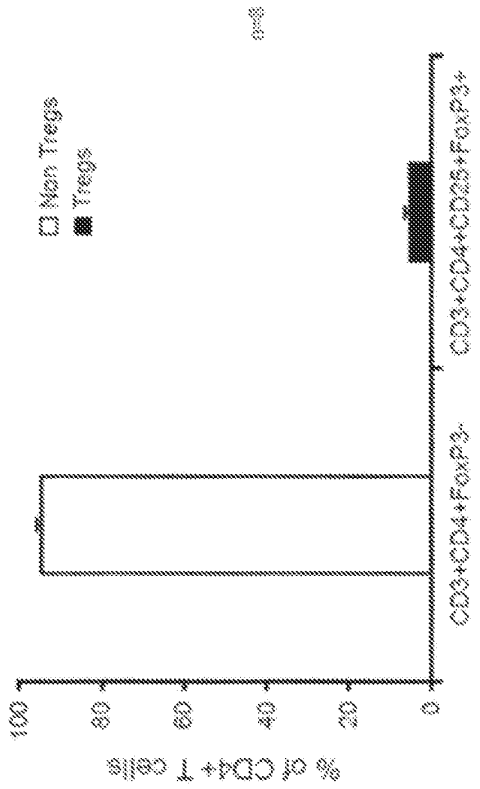


FIG. 20D

FIG. 21


Non Tregs
Tregs
% of CD4+ T cells
100
80
60
40
20
0
CD3+CD4+FoxP3-
CD3+CD4+CD25+FoxP3+

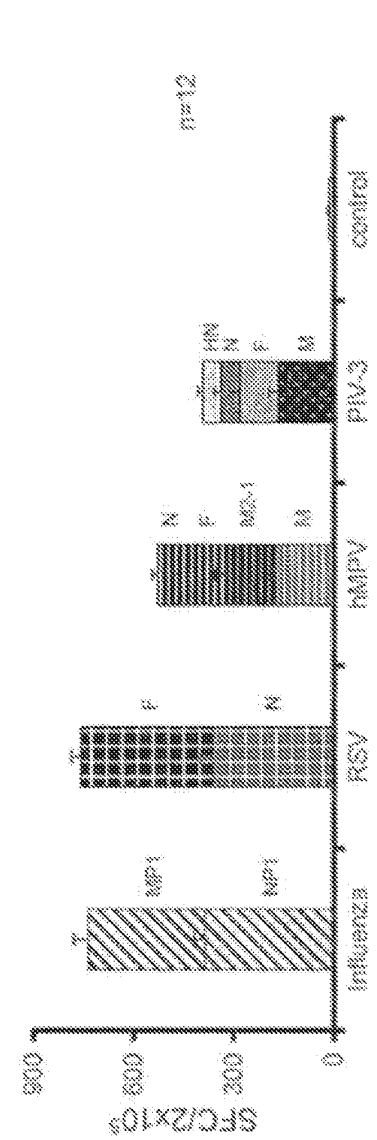


FIG. 22A

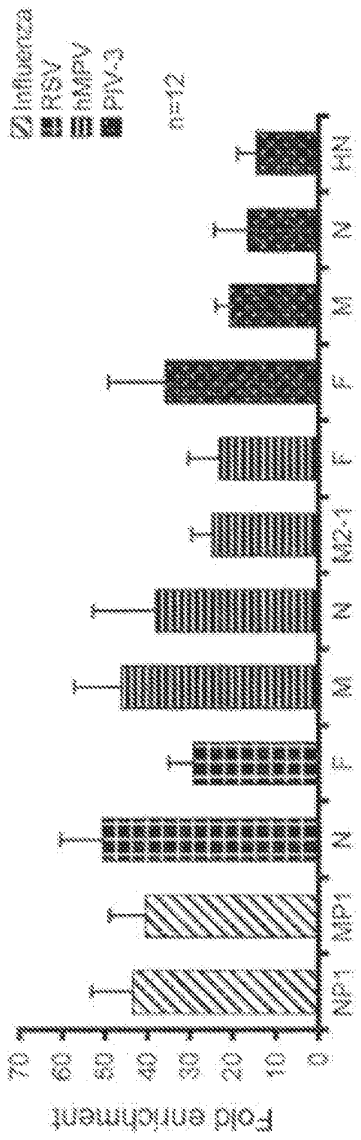


FIG. 22B

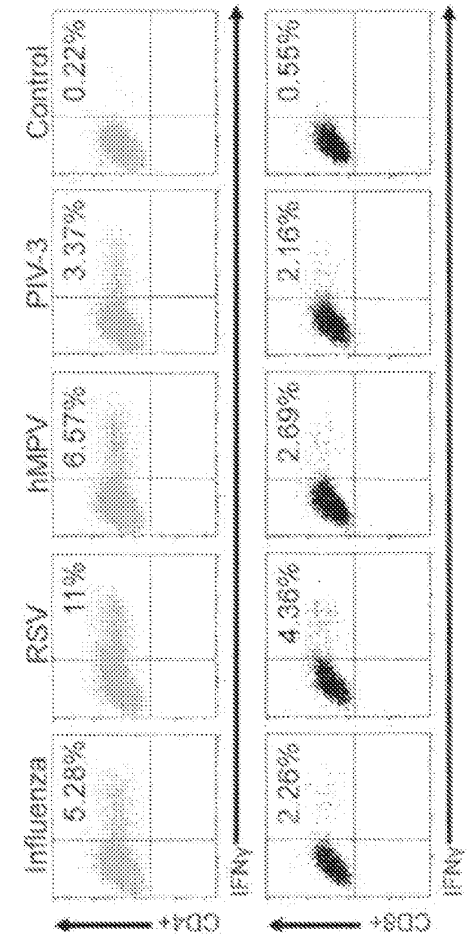


FIG. 22C

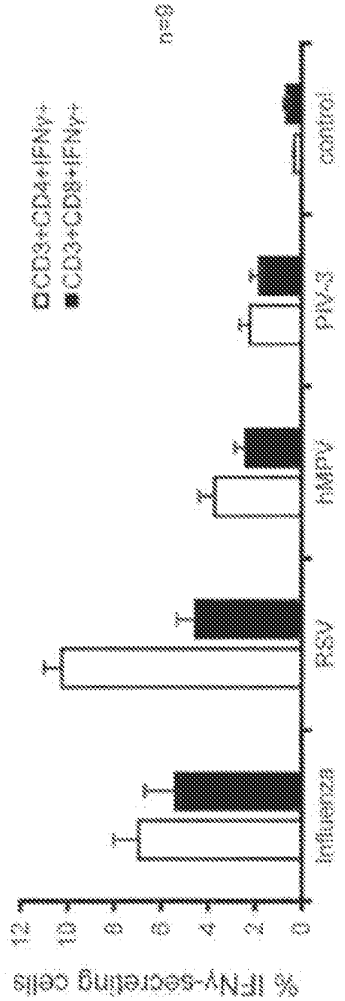


FIG. 22D

FIG. 23

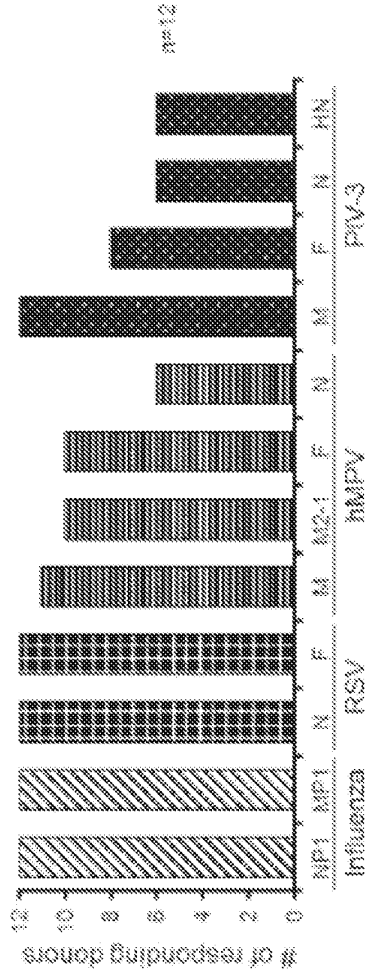

n=13
# of responding donors
0
2
4
6
8
10
12
NP1
M2-1
N
F
M
F
N
M
F
N
HN
Influenza
RSV
hMPV
PIV-3

FIG. 24

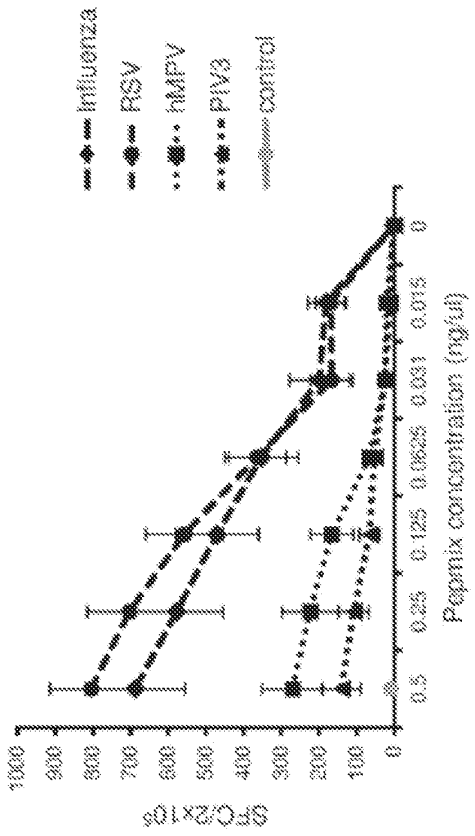

Influenza
RSV
hMPV
PIV3
control
SFC/2x10^5
1000
900
800
700
600
500
400
300
200
100
0
0.5
0.25
0.125
0.0625
0.031
0.015
0
Pepmix concentration (ng/µl)

FIG. 25

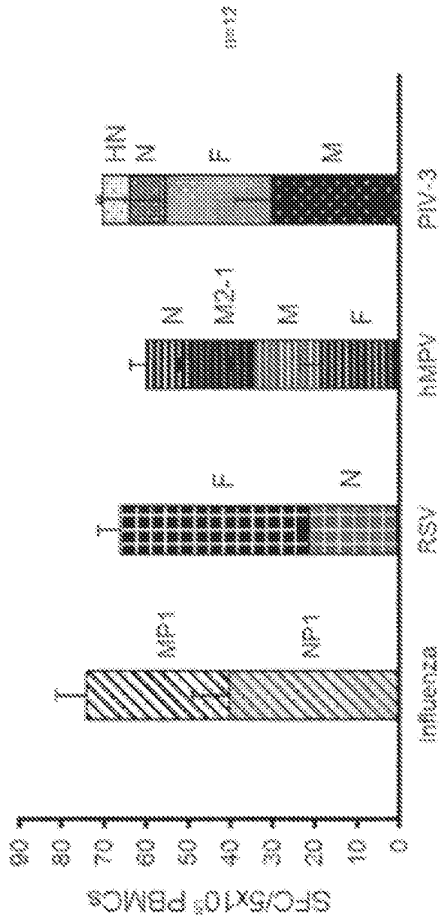
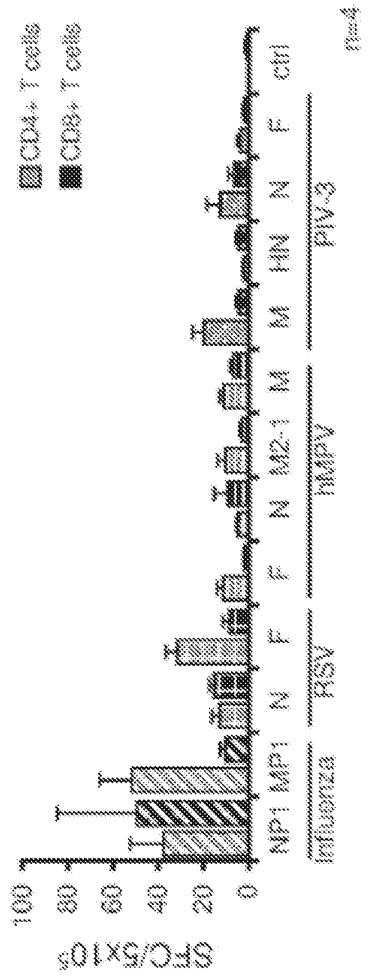

n=12
SFC/5x10^5 PBMCs
0
10
20
30
40
50
60
70
80
90
Influenza
NP1
MP1
RSV
F
N
hMPV
F
M
M2-1
N
PIV-3
F
M
HN
N

FIG. 26


CD4+ T cells
CD8+ T cells
SFC/5x10^5
100
80
60
40
20
0
NP1 MP1 N F F N M2-1 M M HN N F ctrl
Influenza
RSV
MMPV
PIV-3
n=4

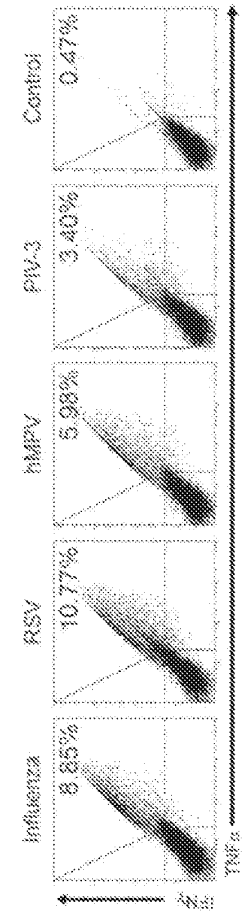


FIG. 27A

FIG. 27B

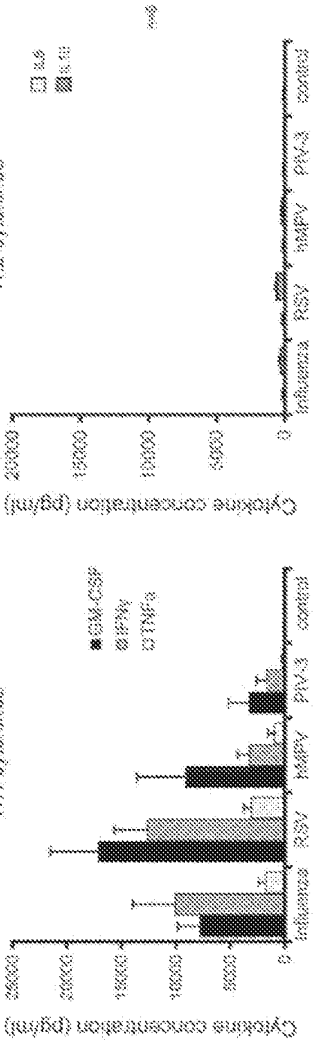


FIG. 27C

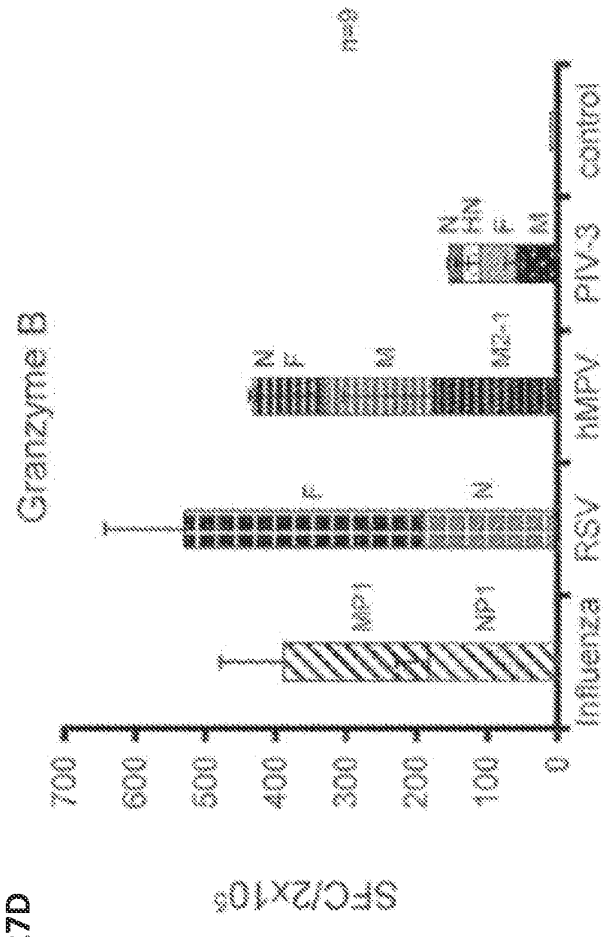

Granzyme B
SFC/2x10^5
700
600
500
400
300
200
100
0
Influenza
RSV
hMPV
PIV-3
control
NP1
M1
M2-1
N
F
M
HN
L

FIG. 27D

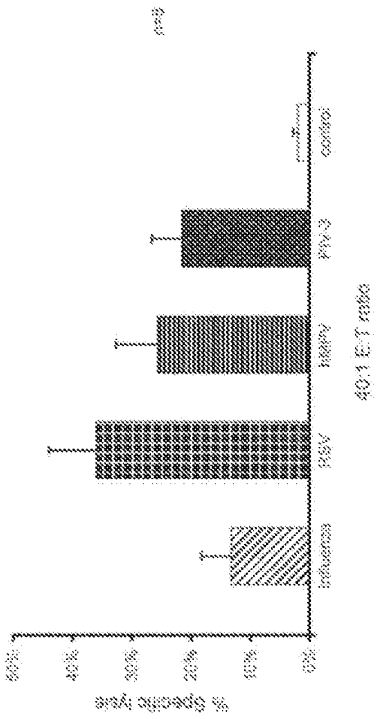


FIG. 28A

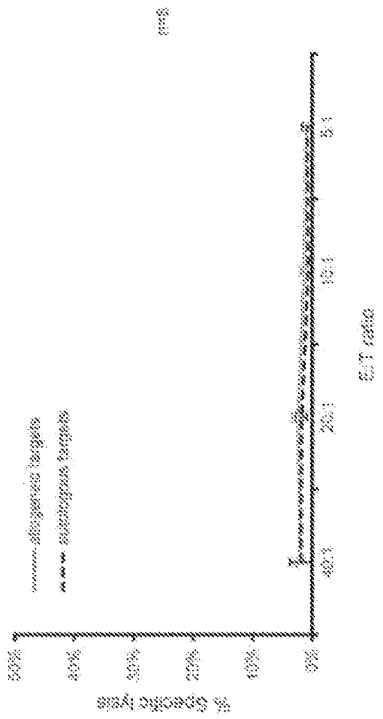
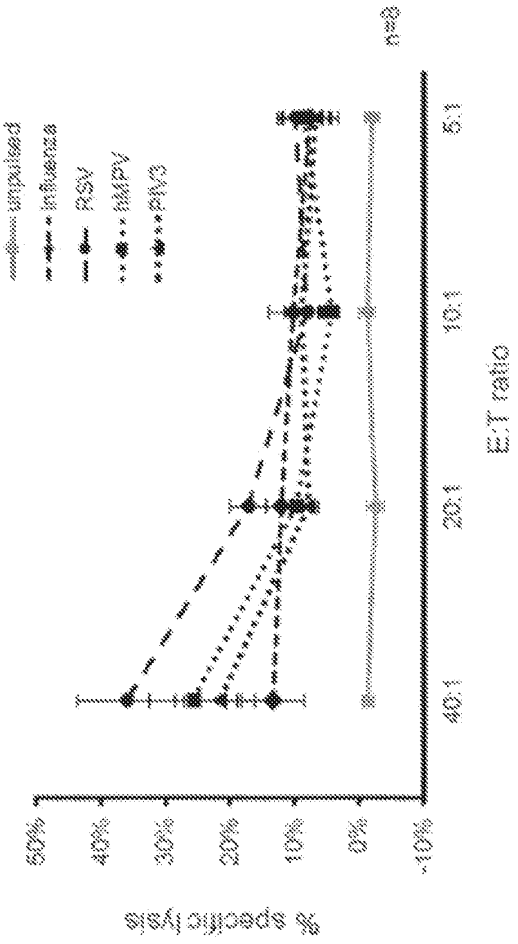


FIG. 28B

FIG. 29


unpulsed
Influenza
RSV
MPV
PIV3
n=8
% specific lysis
60%
40%
30%
20%
10%
0%
-10%
40:1
20:1
10:1
5:1
E:T ratio

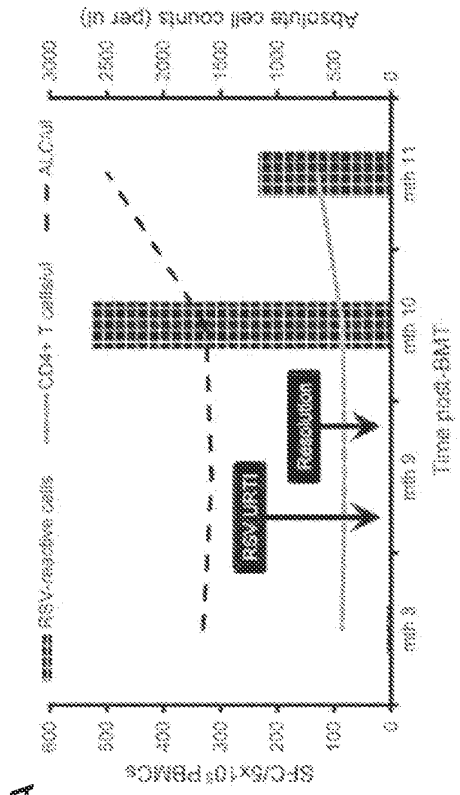


FIG. 30A

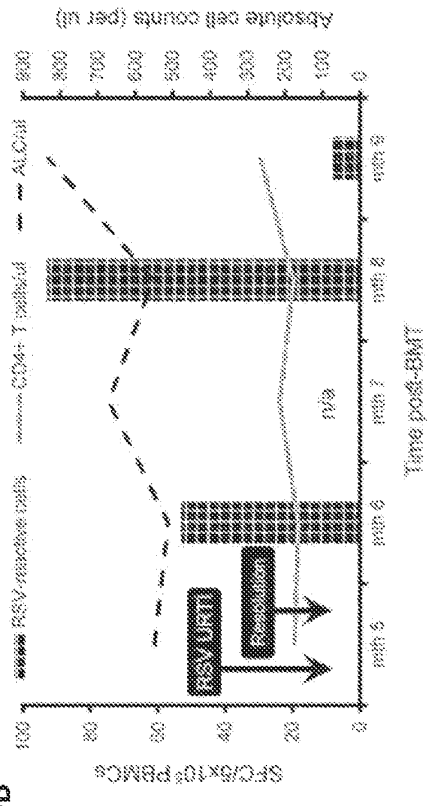


FIG. 30B

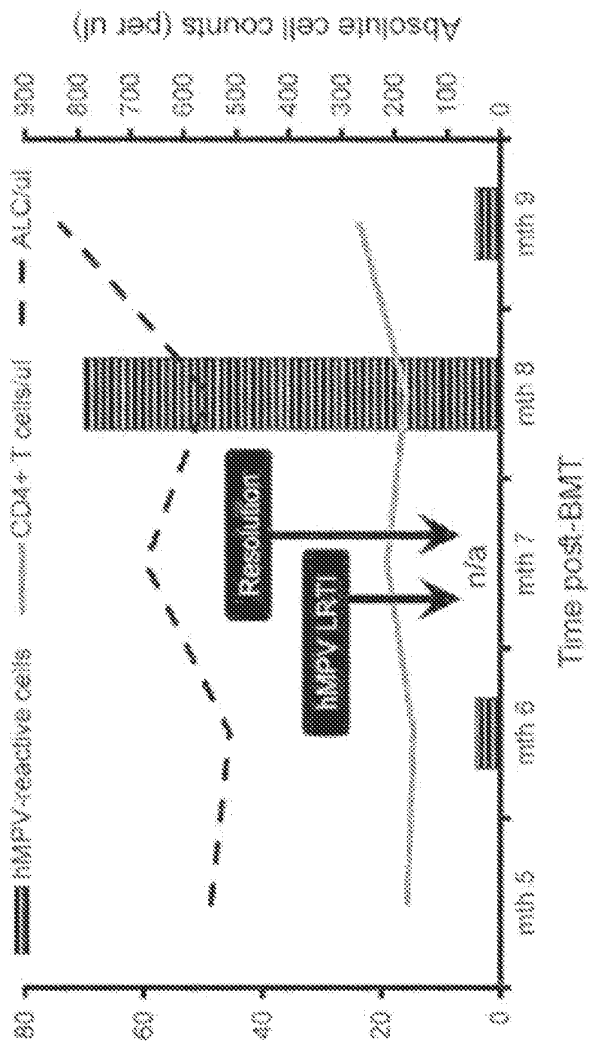

Absolute cell counts (per ul)
900
800
700
600
500
400
300
200
100
0
ALC/ul
CD4+ T cells/ul
hMPV-reactive cells
Recallion
hMPV LRTI
n/a
mth 9
mth 8
mth 7
mth 6
mth 5
Time post-BMT
SFC/5x10^5 PBMCs
80
60
40
20
0

FIG. 30C

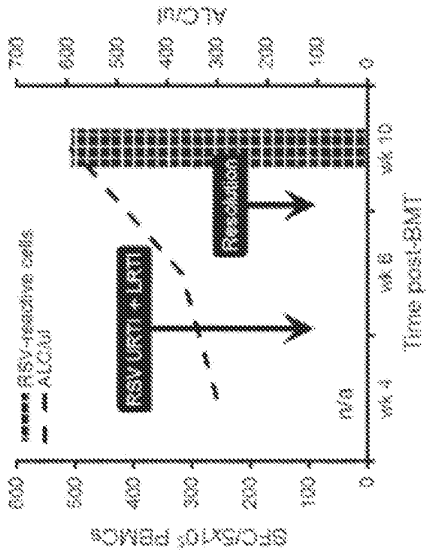


FIG. 31A

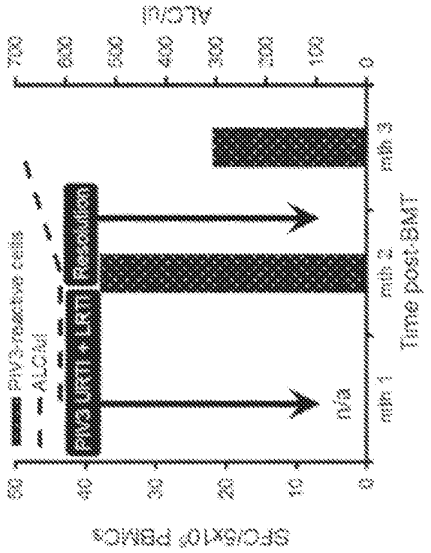


FIG. 31B

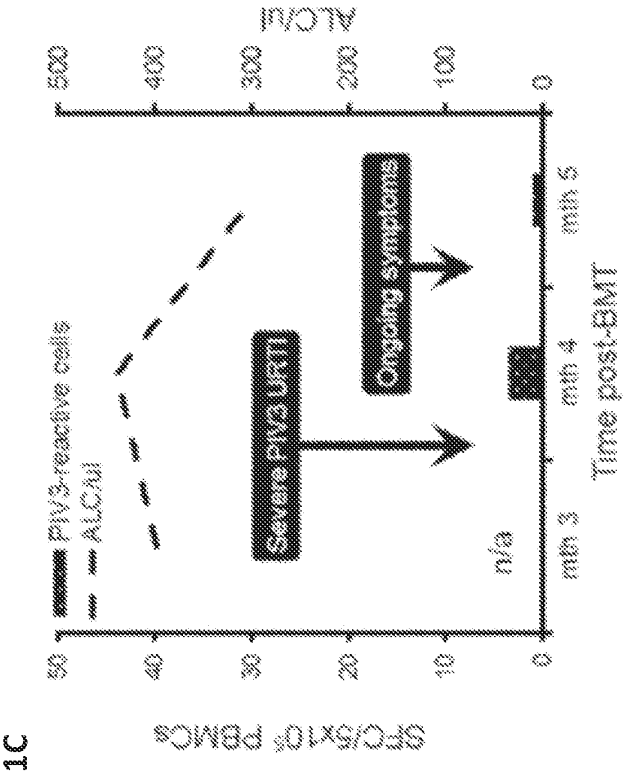

SFC/5x10⁵ PBMCs
ALC/ul
Time post-BMT
PIV3-reactive cells
ALC/ul
Severe PIV3 URTI
Ongoing symptoms
n/a
mth 3
mth 4
mth 5
0
10
20
30
40
50
0
100
200
300
400
500

FIG. 31C

FIG. 32

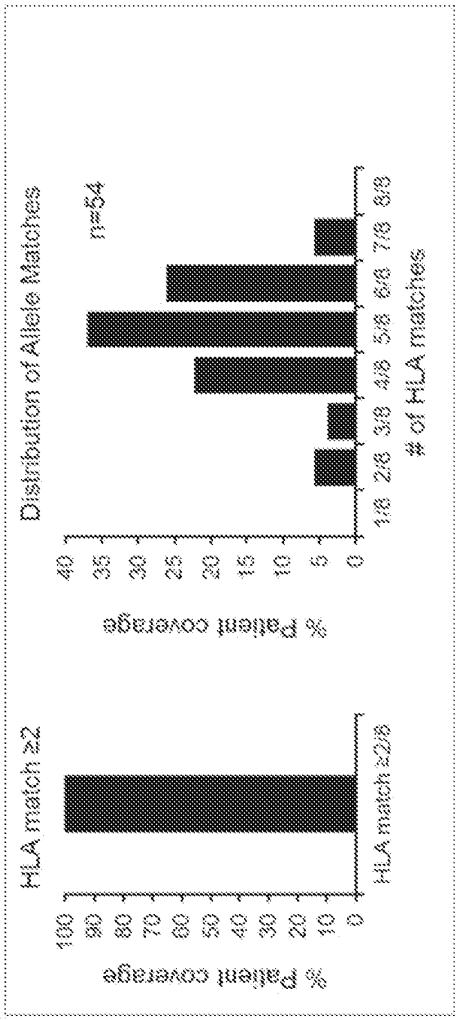

HLA match ≥2
% Patient coverage
100
90
80
70
60
50
40
30
20
10
0
HLA match ≥2/8
Distribution of Allele Matches
n=54
% Patient coverage
40
35
30
25
20
15
10
5
0
1/8 2/8 3/8 4/8 5/8 6/8 7/8 8/8
# of HLA matches

FIG. 33

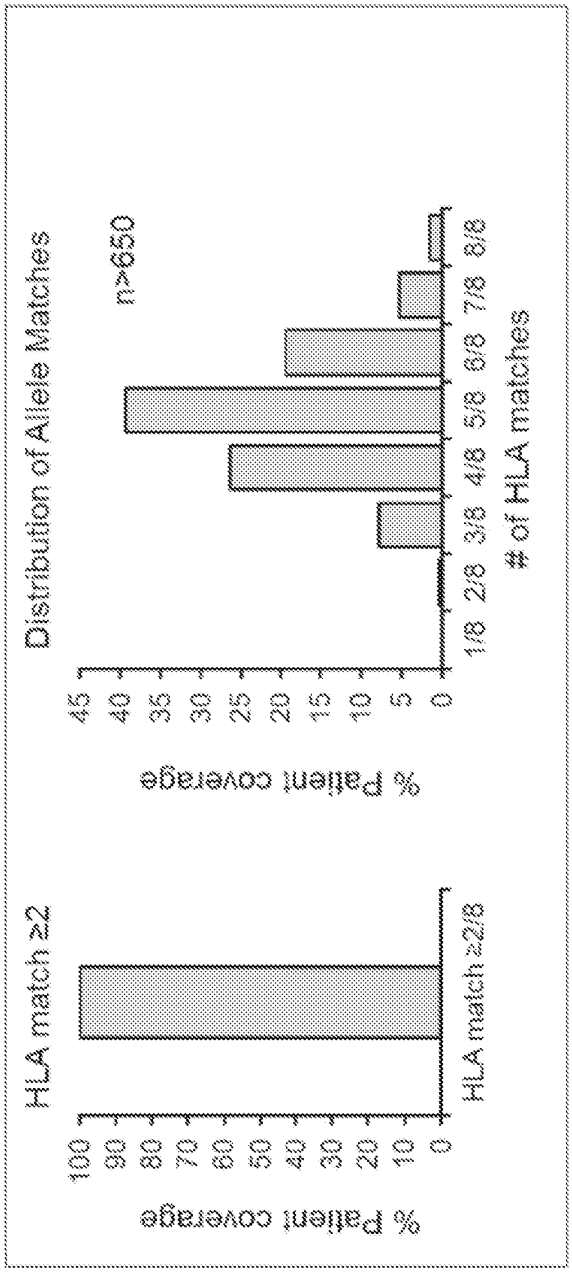

HLA match ≥2
% Patient coverage
100
90
80
70
60
50
40
30
20
10
0
HLA match ≥2/8
Distribution of Allele Matches
n>650
% Patient coverage
45
40
35
30
25
20
15
10
5
0
1/8 2/8 3/8 4/8 5/8 6/8 7/8 8/8
# of HLA matches

FIG. 34

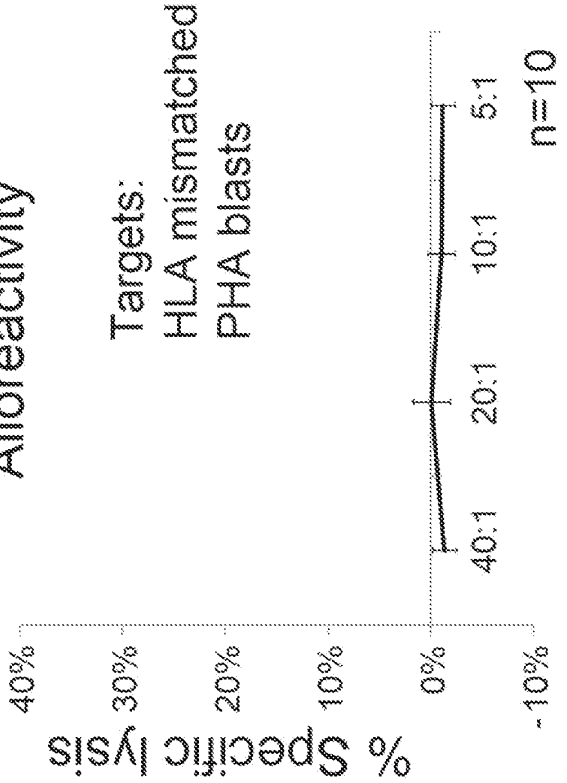

Alloreactivity
Targets:
HLA mismatched
PHA blasts
% Specific lysis
40%
30%
20%
10%
0%
-10%
40:1
20:1
10:1
5:1
n=10

FIG. 35

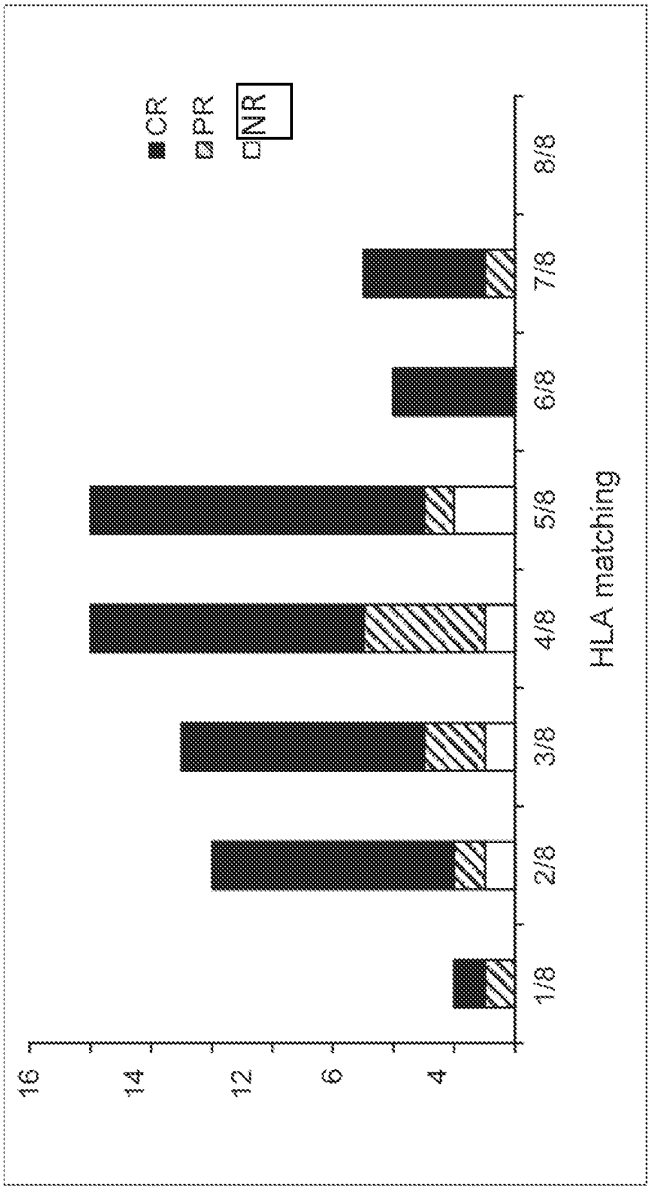


FIG. 36

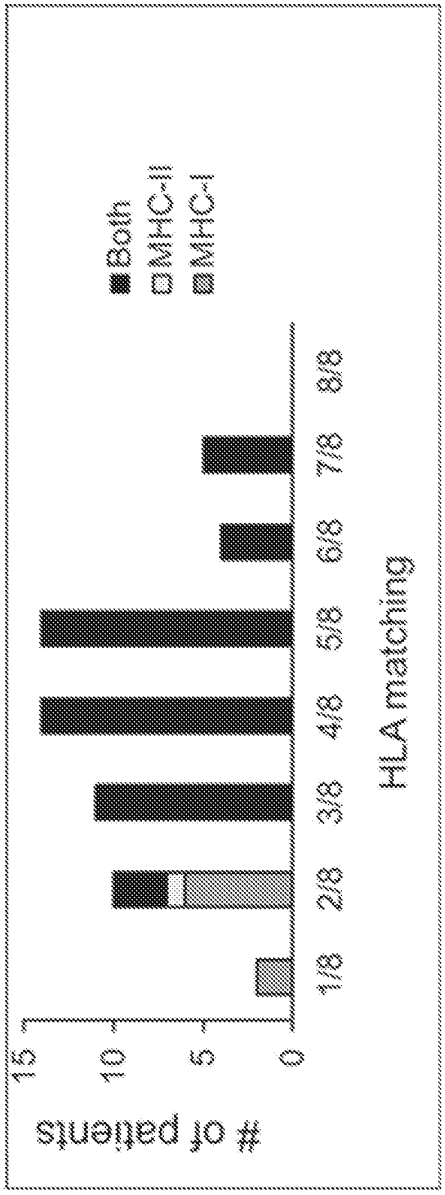

Both
MHC-II
MHC-I
# of patients
15
10
5
0
1/8
2/8
3/8
4/8
5/8
6/8
7/8
8/8
HLA matching

FIG. 37

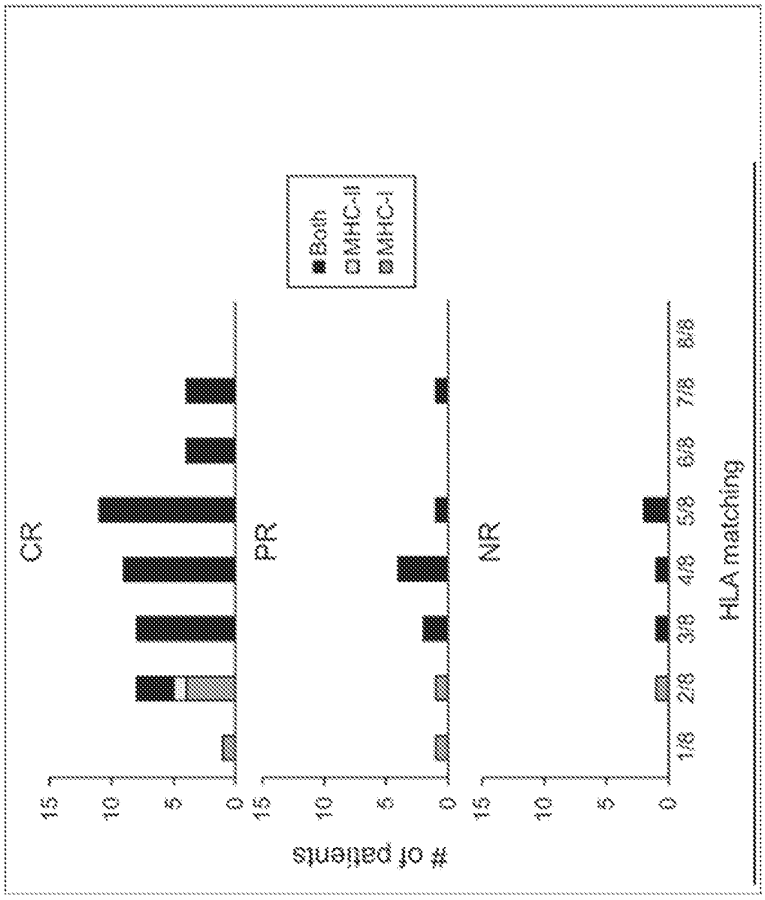

CR
PR
NR
Both
MHC-II
MHC-I
# of patients
0
5
10
15
1/8
2/8
3/8
4/8
5/8
6/8
7/8
8/8
HLA matching

FIG. 38

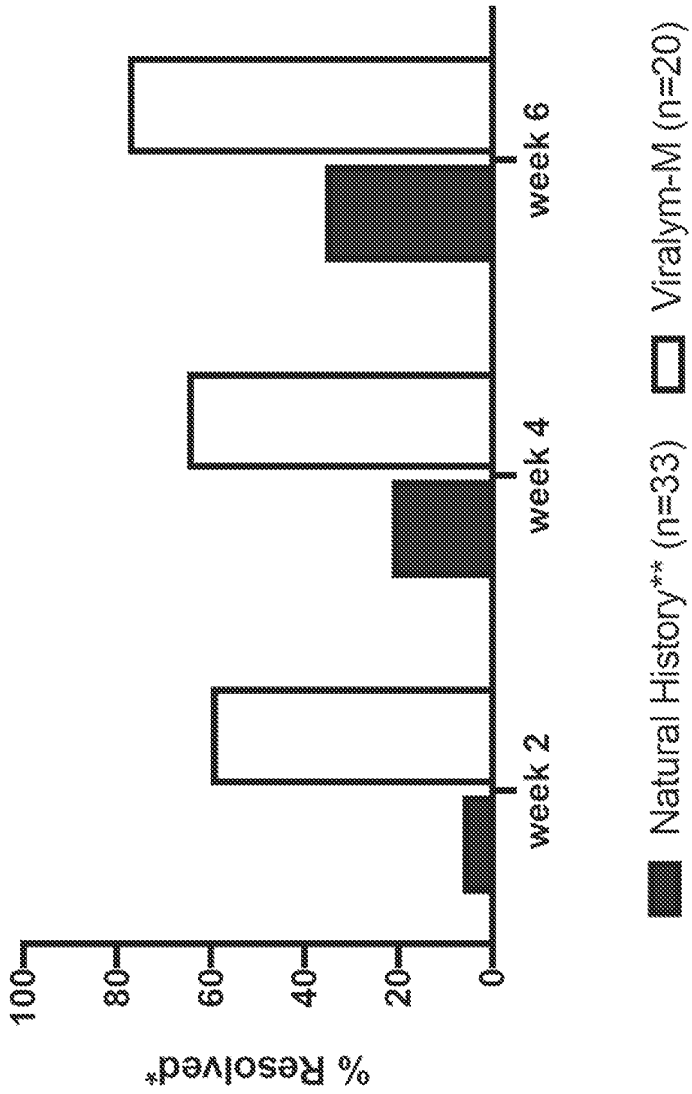

% Resolved*
100
80
60
40
20
0
week 2
week 4
week 6
Natural History** (n=33)
Viralym-M (n=20)

FIG. 39

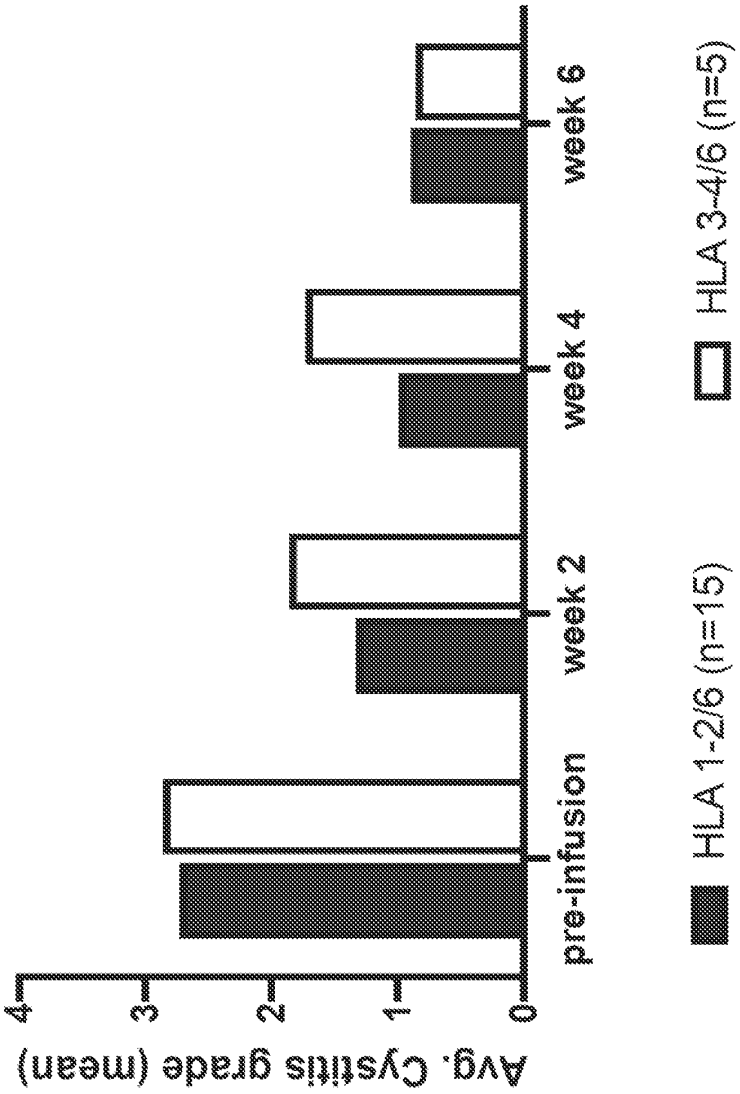

Avg. Cystitis grade (mean)
0
1
2
3
4
pre-infusion
week 2
week 4
week 6
HLA 1-2/6 (n=15)
HLA 3-4/6 (n=5)

FIG. 40

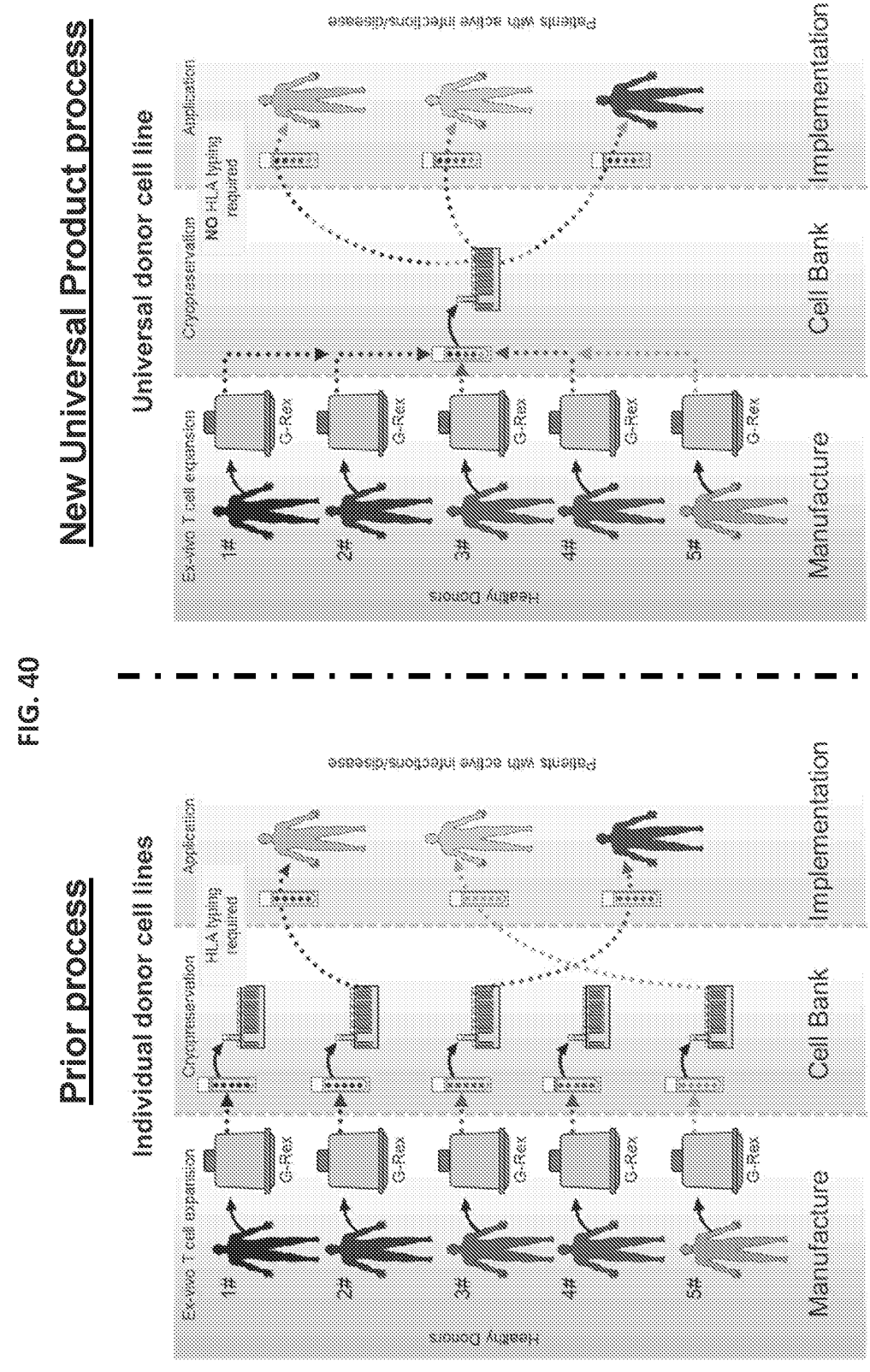
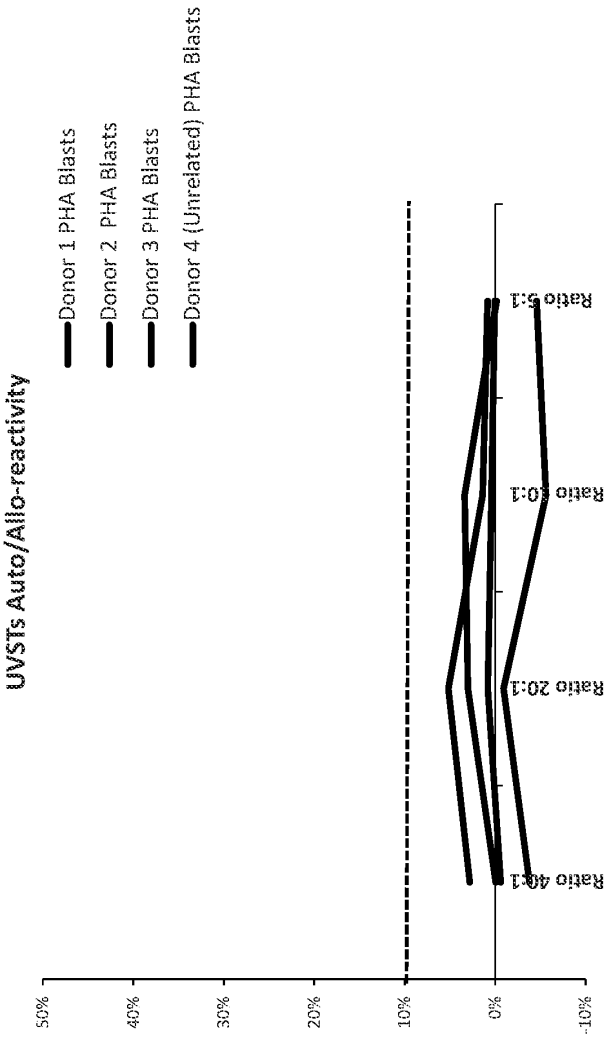

New Universal Product process
Universal donor cell line
Ex-vivo T cell expansion
Cryopreservation
NO HLA typing required
Application
Healthy Donors
Manufacture
Cell Bank
Implementation
Patients with active infections/disease
G-Rex
1#
2#
3#
4#
5#
Prior process
Individual donor cell lines
HLA typing required

FIG. 41


UVSTs Auto/Allo-reactivity
Donor 1 PHA Blasts
Donor 2 PHA Blasts
Donor 3 PHA Blasts
Donor 4 (Unrelated) PHA Blasts
50%
40%
30%
20%
10%
0%
-10%
Ratio 40:1
Ratio 20:1
Ratio 10:1
Ratio 5:1