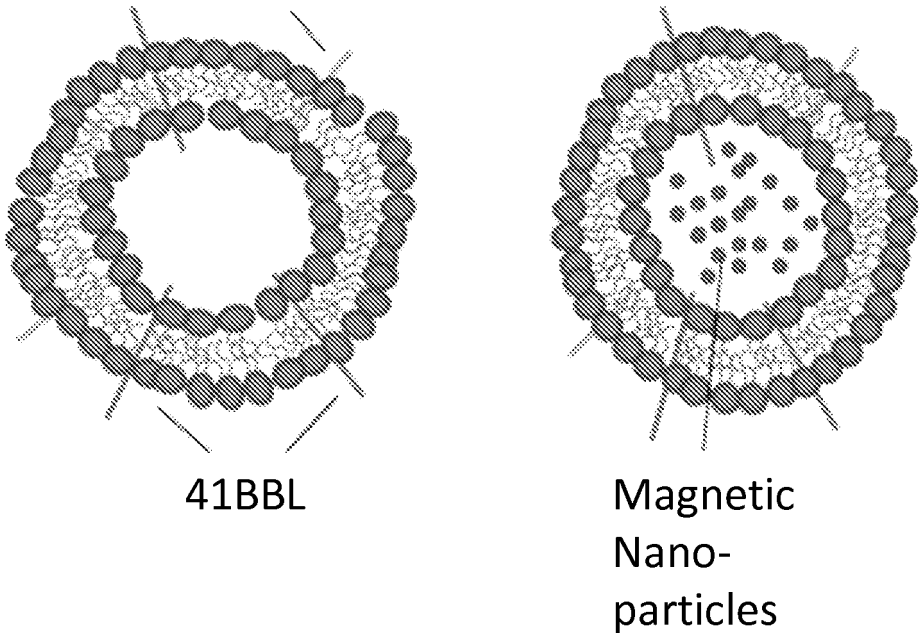
PM-mb15-41BBL 1/14



PM-mb15-41BBL coated microparticles

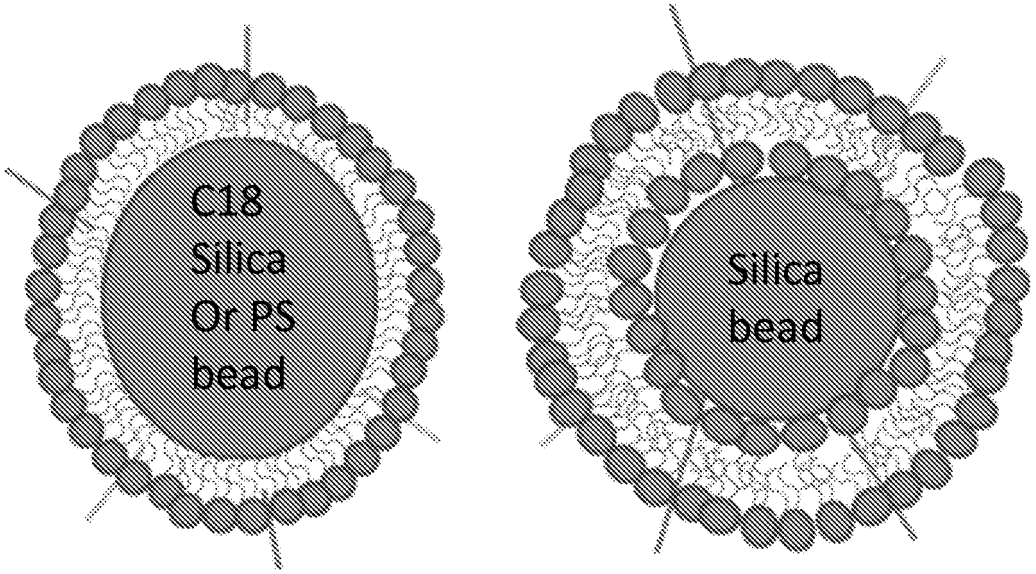
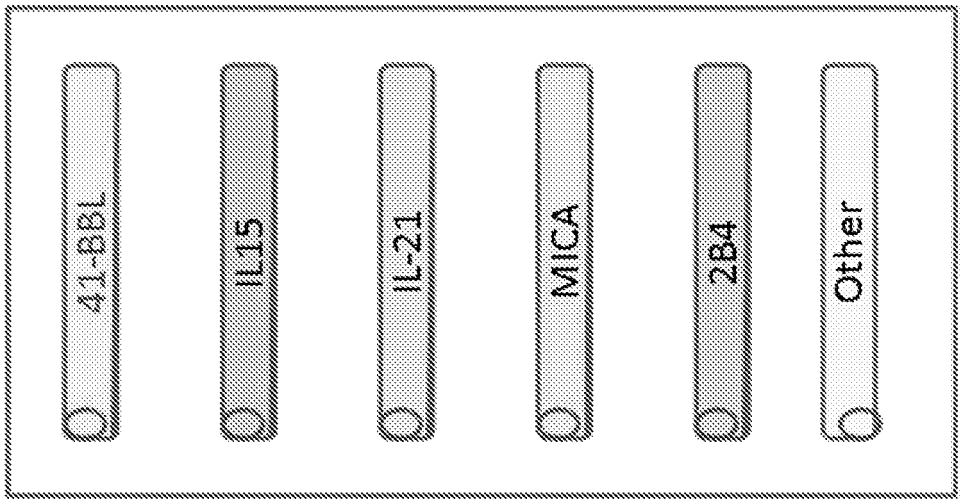


FIG. 1


41-BBL
IL15
IL-21
MICA
2B4
Other

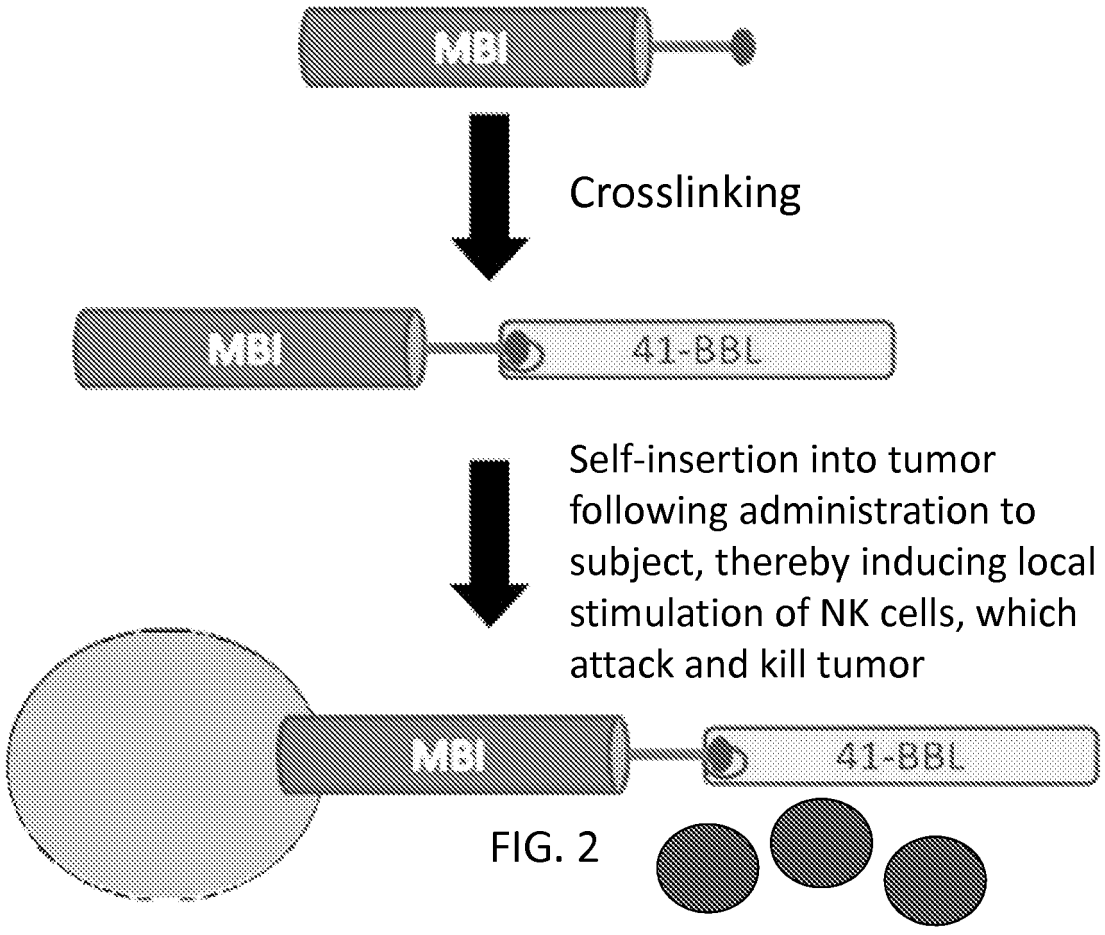

MBI
Crosslinking
MBI
41-BBL
Self-insertion into tumor following administration to subject, thereby inducing local stimulation of NK cells, which attack and kill tumor
MBI
41-BBL

FIG. 2

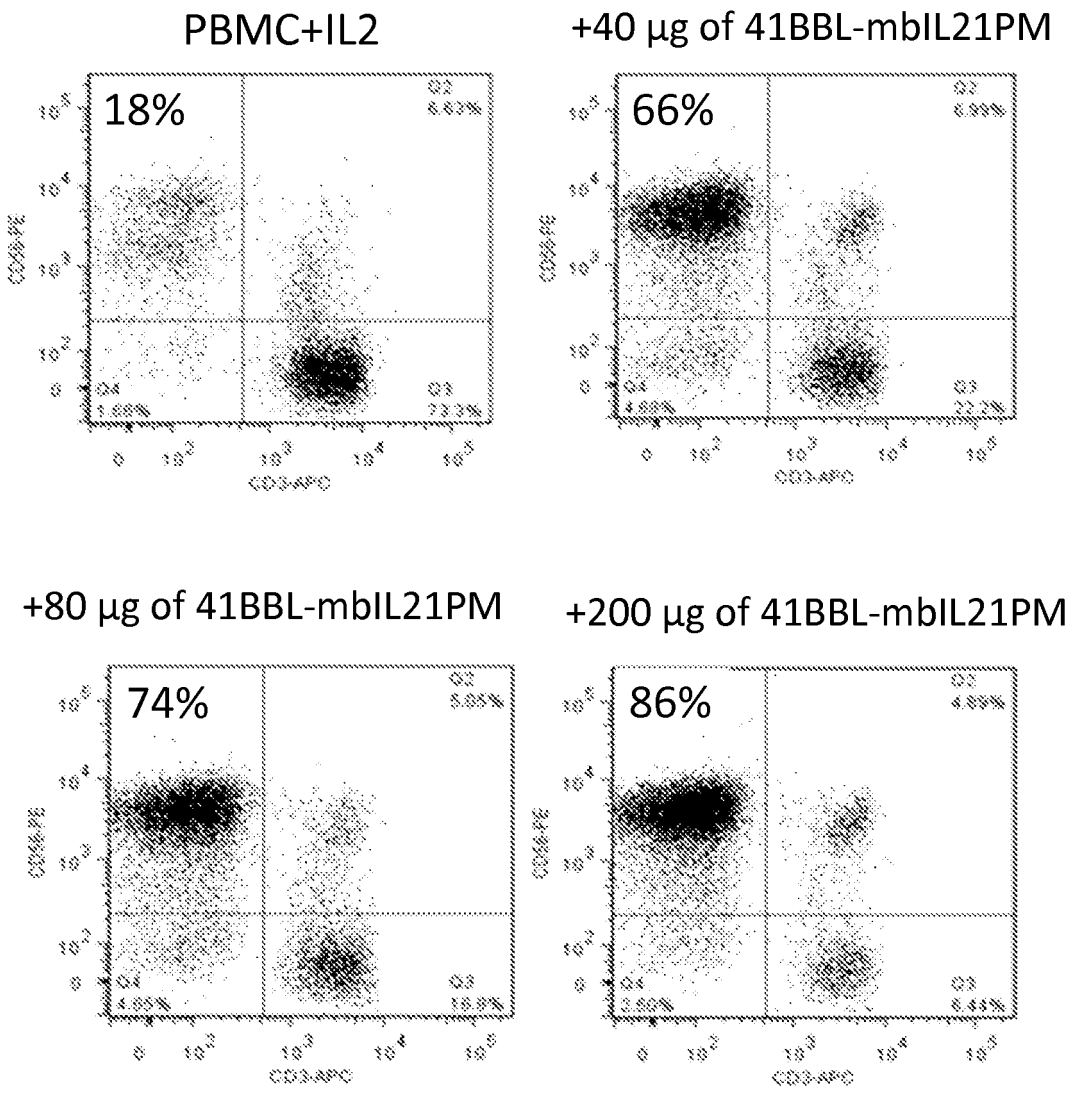

PBMC+IL2
18%
+40 µg of 41BBL-mbIL21PM
66%
+80 µg of 41BBL-mbIL21PM
74%
+200 µg of 41BBL-mbIL21PM
86%
CD3-APC

FIG. 3

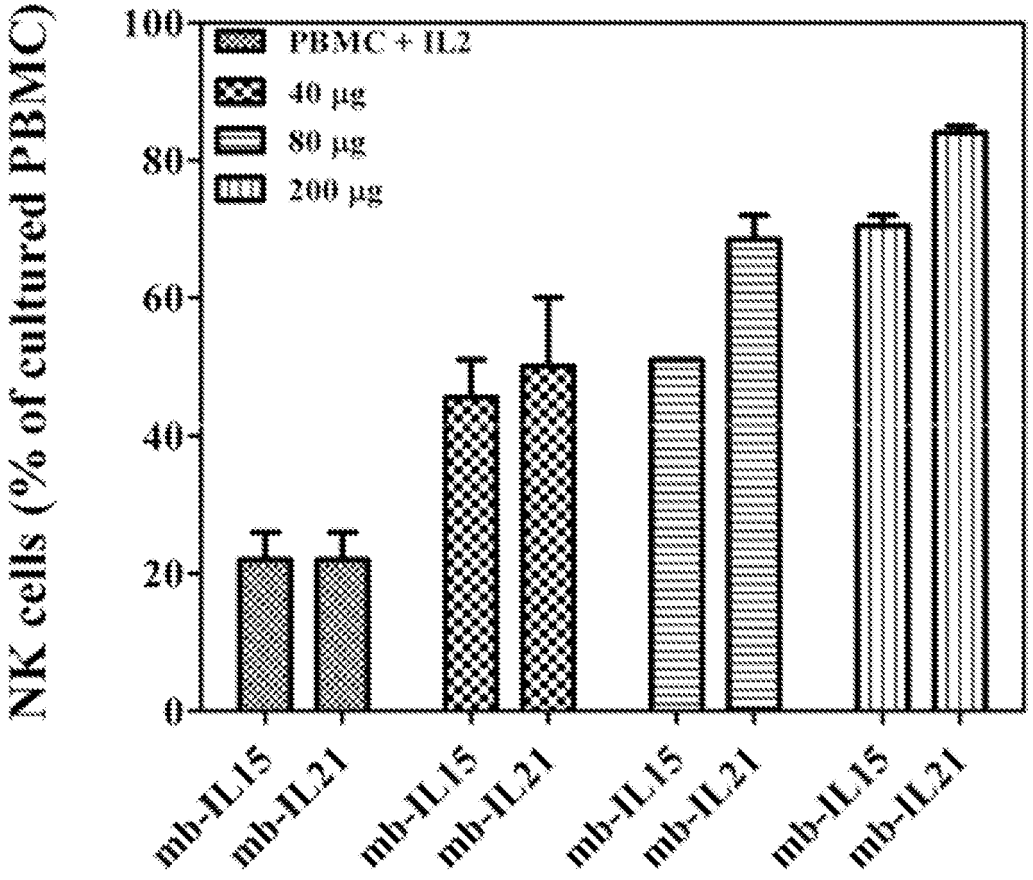
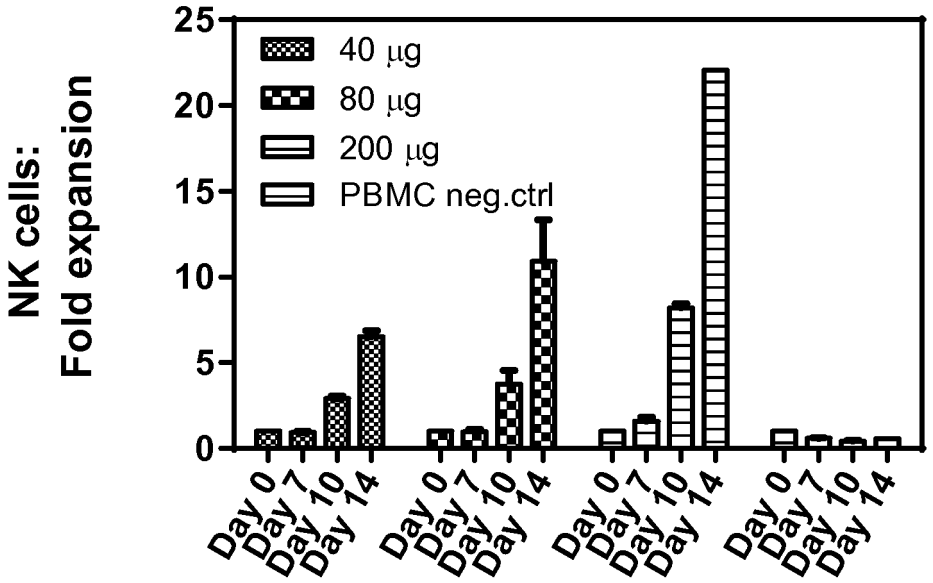

NK cells (% of cultured PBMC)
100
80
60
40
20
0
PBMC + IL2
40 μg
80 μg
200 μg
mb-IL15
mb-IL21
mb-IL15
mb-IL21
mb-IL15
mb-IL21
mb-IL15
mb-IL21

FIG. 4

Expansion with purified PM vesicles 41BBL-mbIL15



Expansion with purified PM vesicles 41BBL-mbIL21

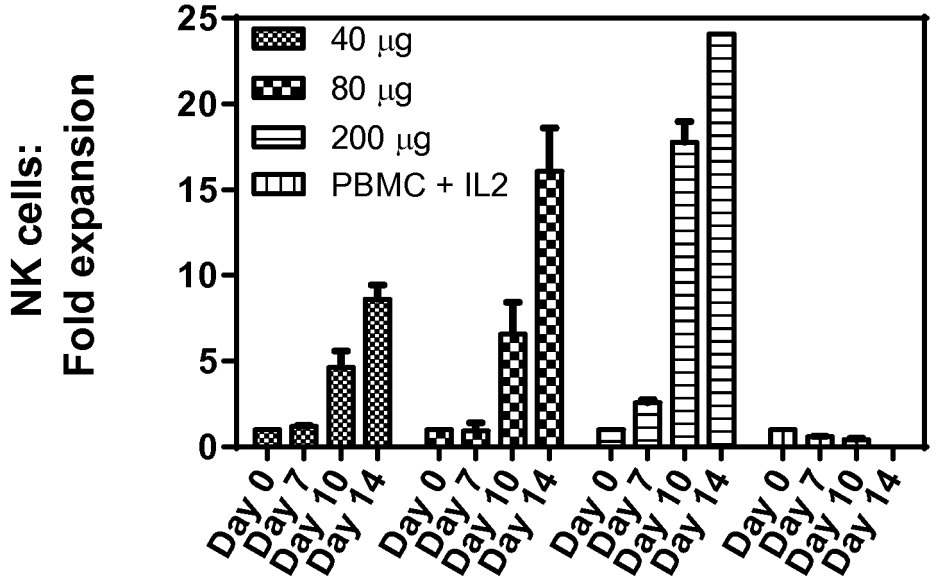


FIG. 5

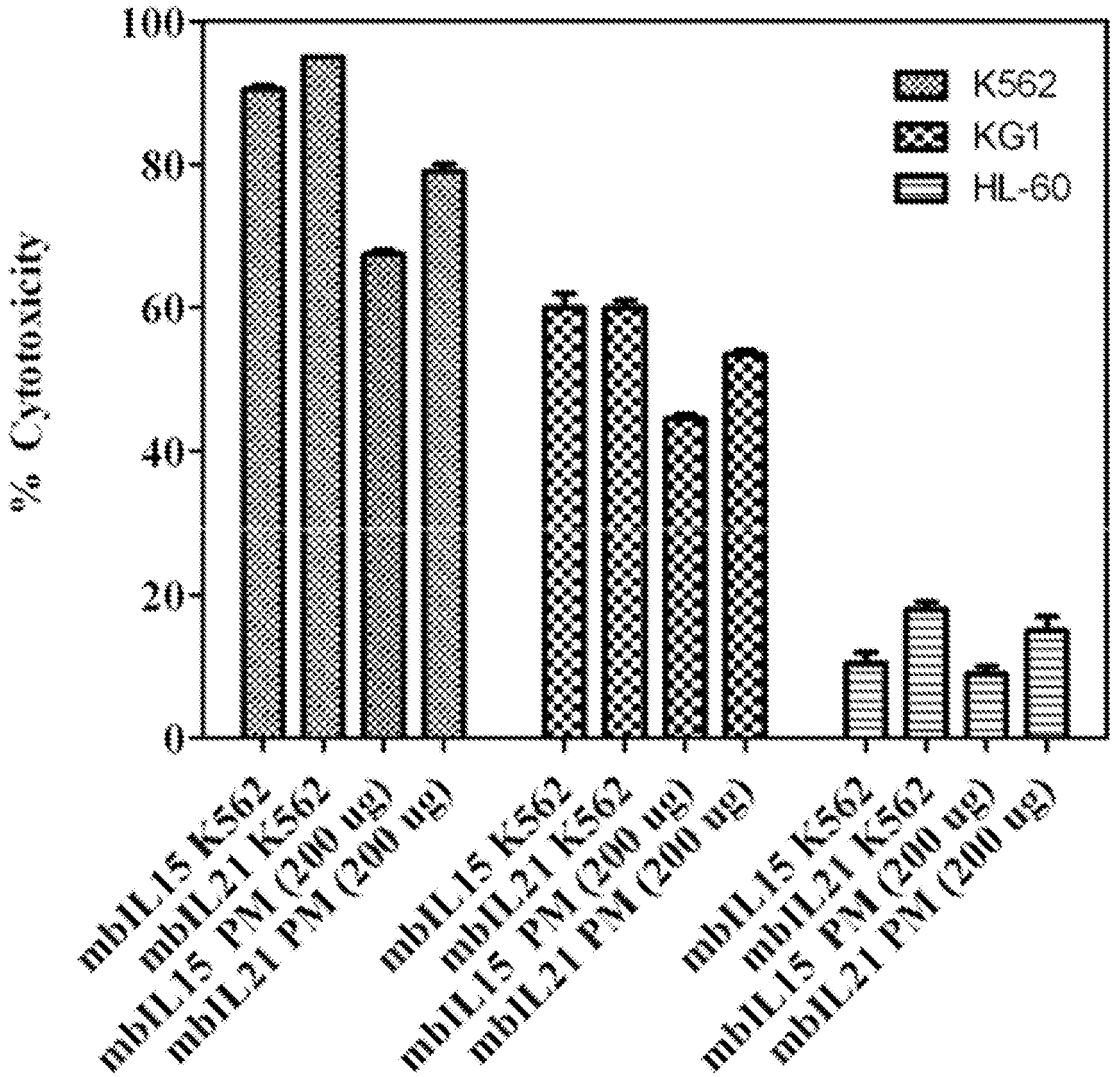
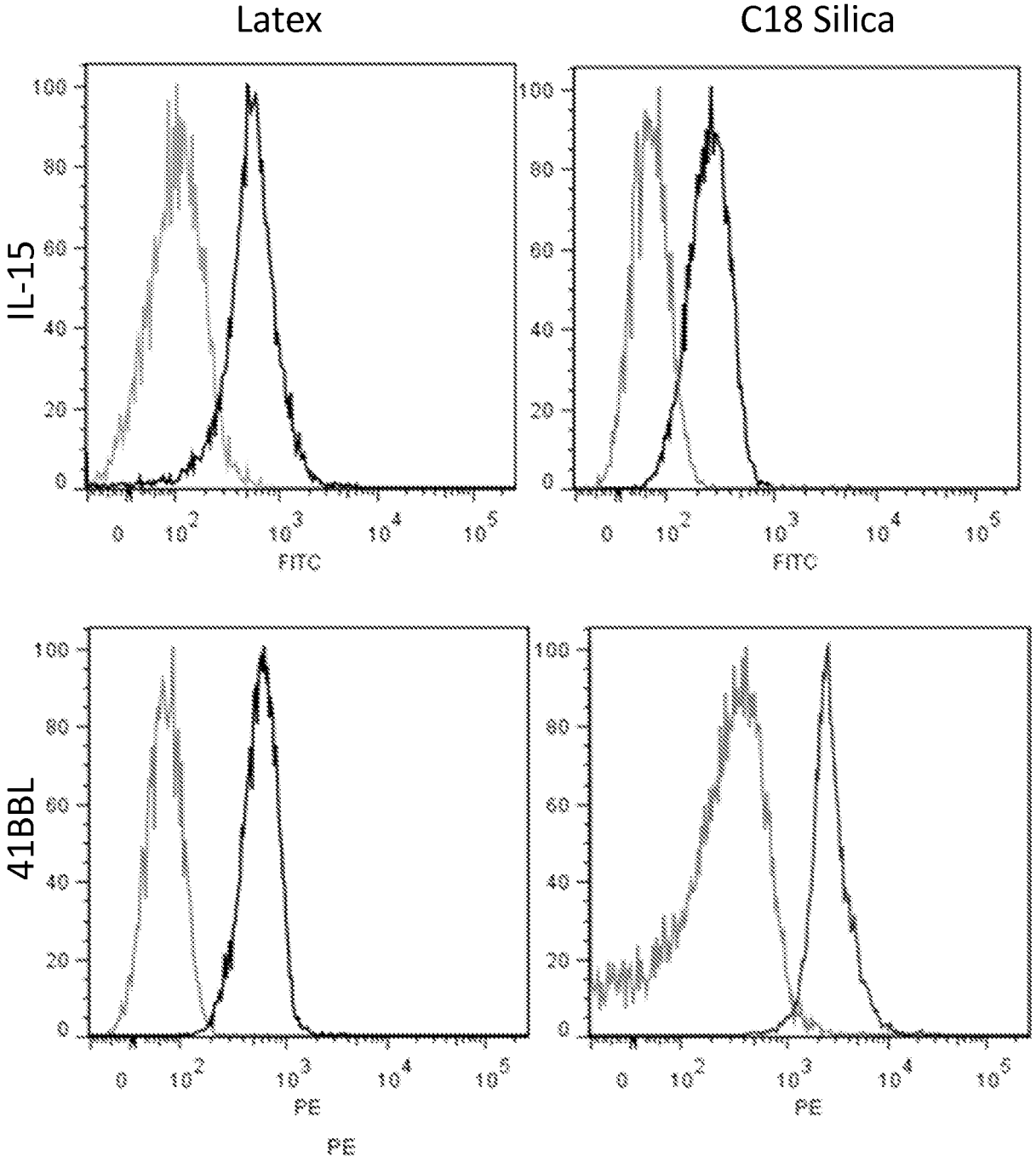
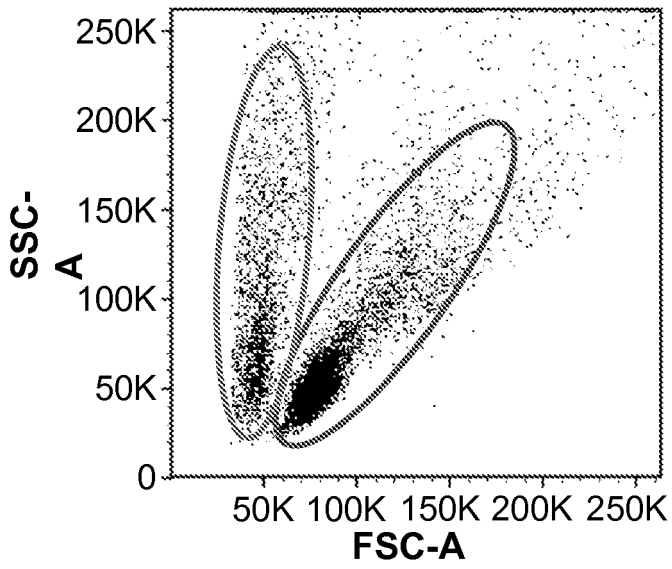

% Cytotoxicity
100
80
60
40
20
0
K562
KG1
HL-60
mbIL15 K562
mbIL21 K562
mbIL15 PM (200 ug)
mbIL21 PM (200 ug)
mbIL15 K562
mbIL21 K562
mbIL15 PM (200 ug)
mbIL21 PM (200 ug)
mbIL15 K562
mbIL21 K562
mbIL15 PM (200 ug)
mbIL21 PM (200 ug)

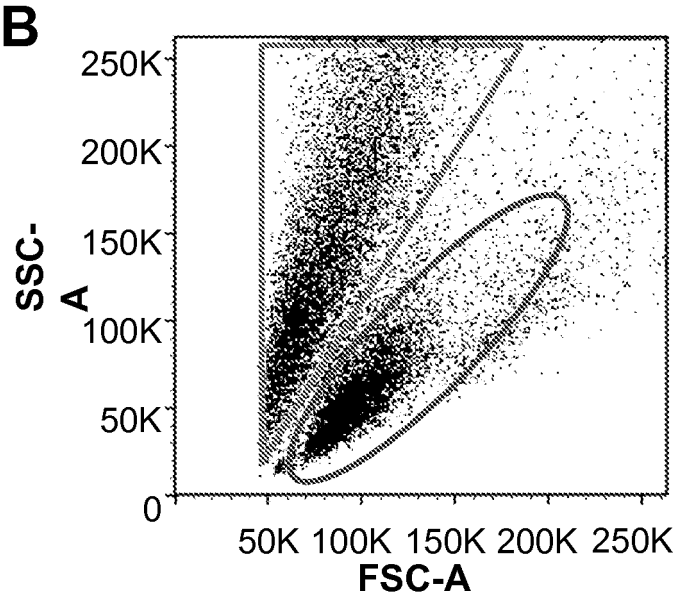
FIG. 6

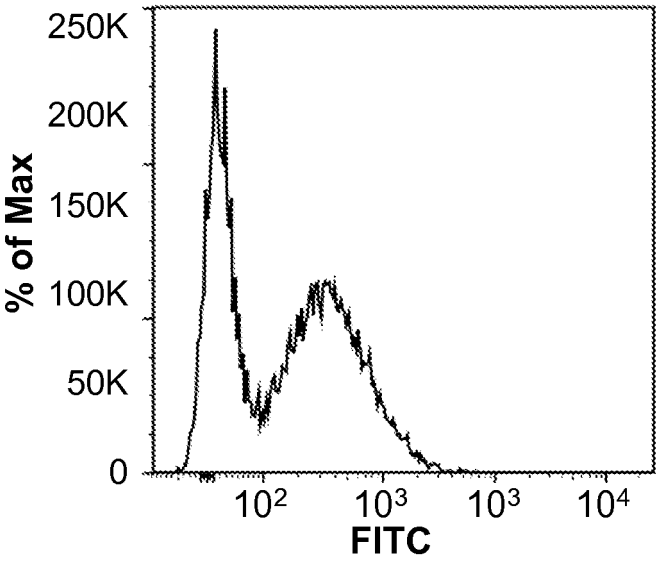

Latex
C18 Silica
IL-15
41BBL
FITC
PE
0
10^2
10^3
10^4
10^5
0
20
40
60
80
100

A



B





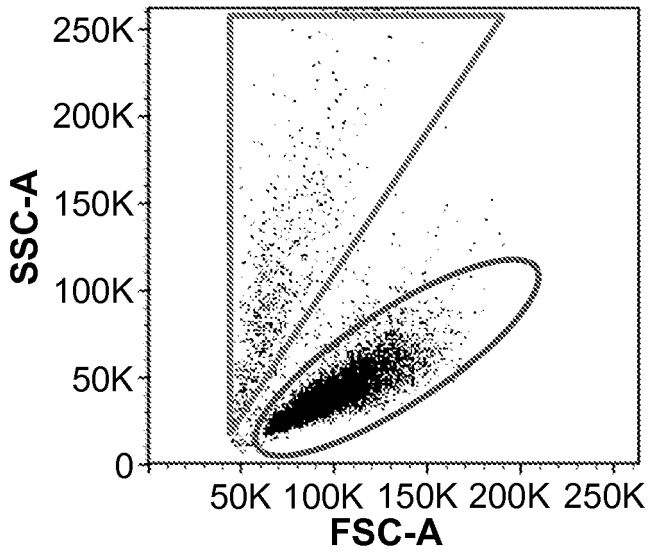


FIG. 8A and FIG. 8B

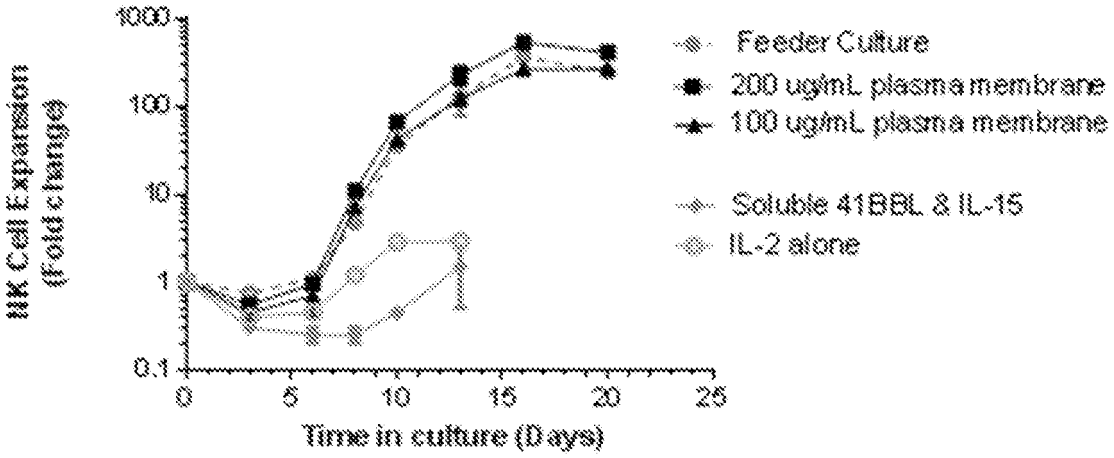

NK Cell Expansion (Fold change)
1000
100
10
1
0.1
0
5
10
15
20
25
Time in culture (Days)
Feeder Culture
200 ug/mL plasma membrane
100 ug/mL plasma membrane
Soluble 41BBL & IL-15
IL-2 alone

FIG. 9

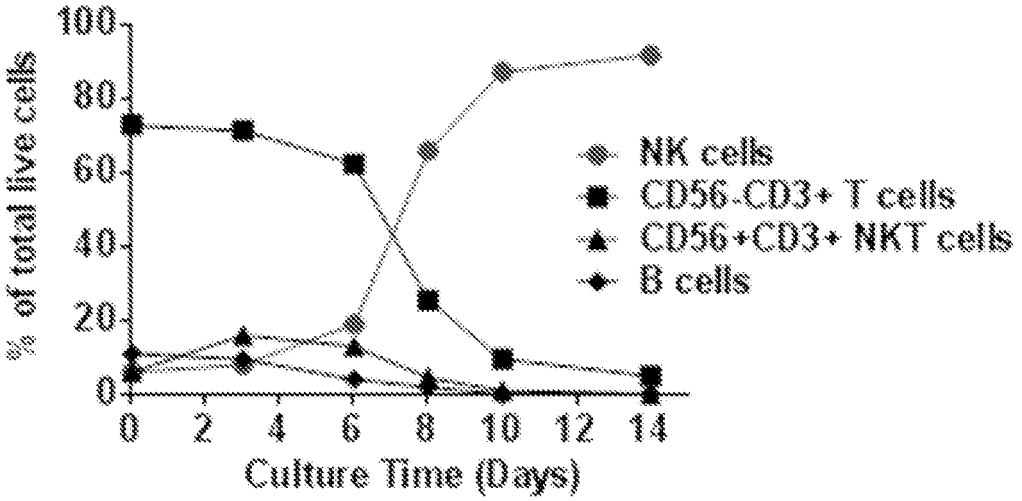

% of total live cells
100
80
60
40
20
0
0
2
4
6
8
10
12
14
Culture Time (Days)
NK cells
CD56-CD3+ T cells
CD56+CD3+ NKT cells
B cells

FIG. 10

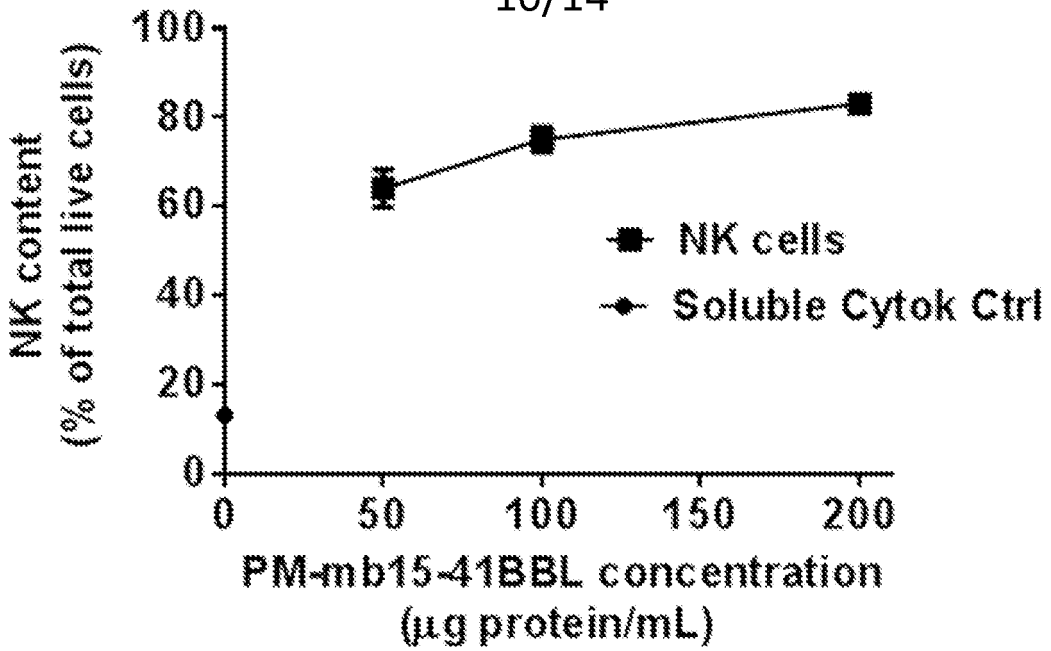

NK content
(% of total live cells)
100
80
60
40
20
0
0
50
100
150
200
PM-mb15-41BBL concentration
(µg protein/mL)
NK cells
Soluble Cytok Ctrl

FIG. 11

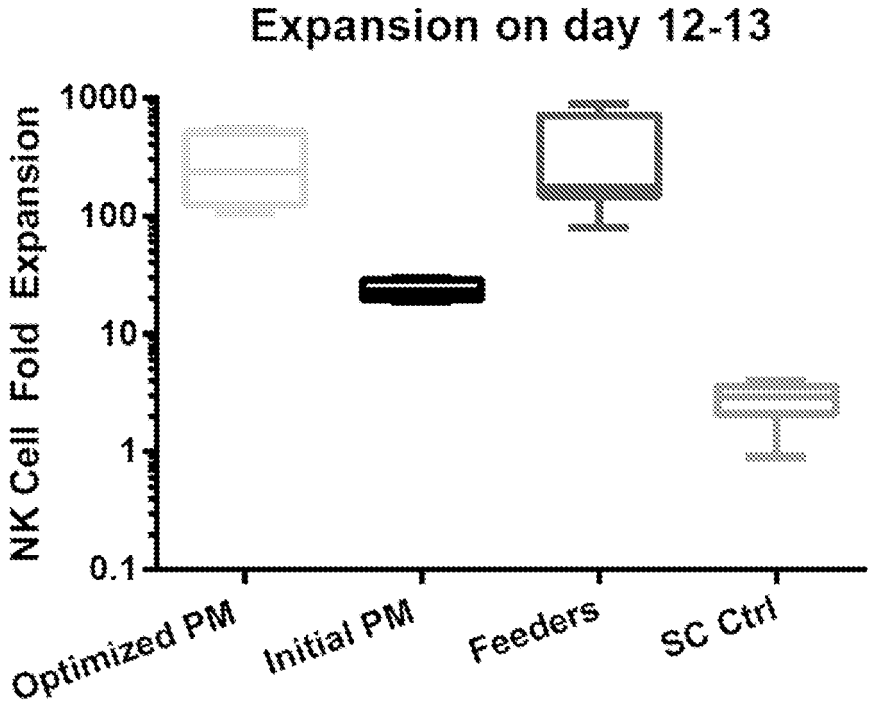

Expansion on day 12-13
NK Cell Fold Expansion
1000
100
10
1
0.1
Optimized PM
Initial PM
Feeders
SC Ctrl

FIG. 12

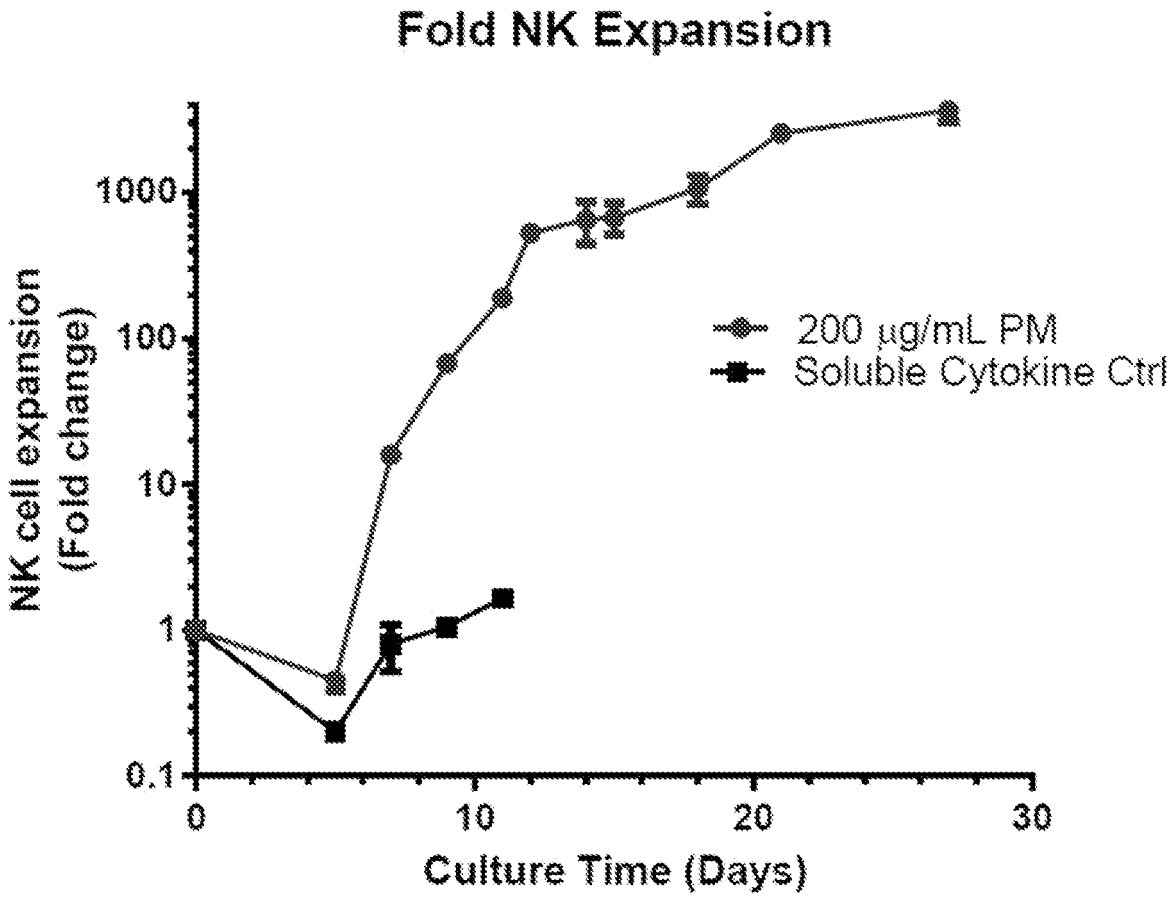

Fold NK Expansion
NK cell expansion (Fold change)
1000
100
10
1
0.1
0
10
20
30
Culture Time (Days)
200 μg/mL PM
Soluble Cytokine Ctrl

FIG. 13

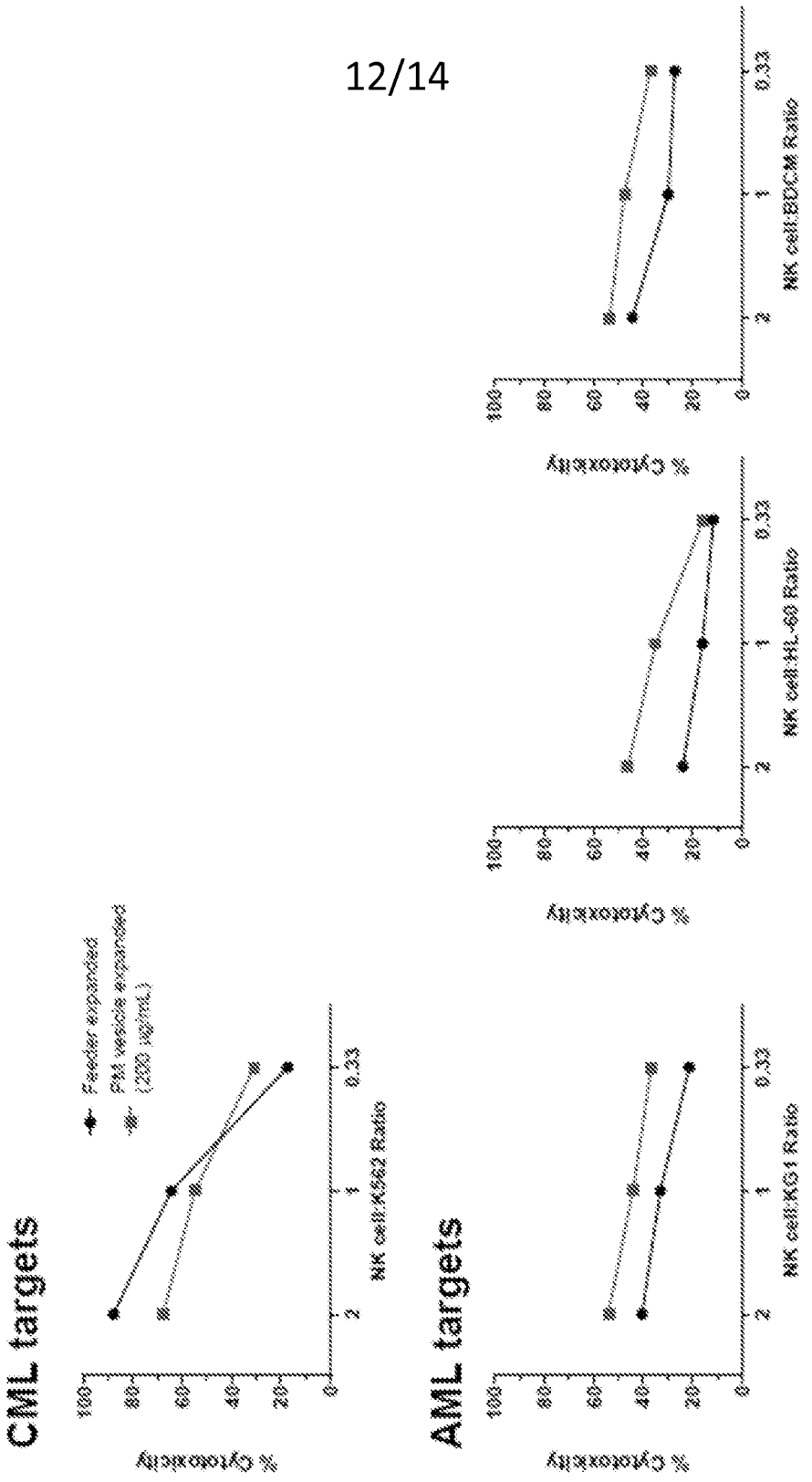
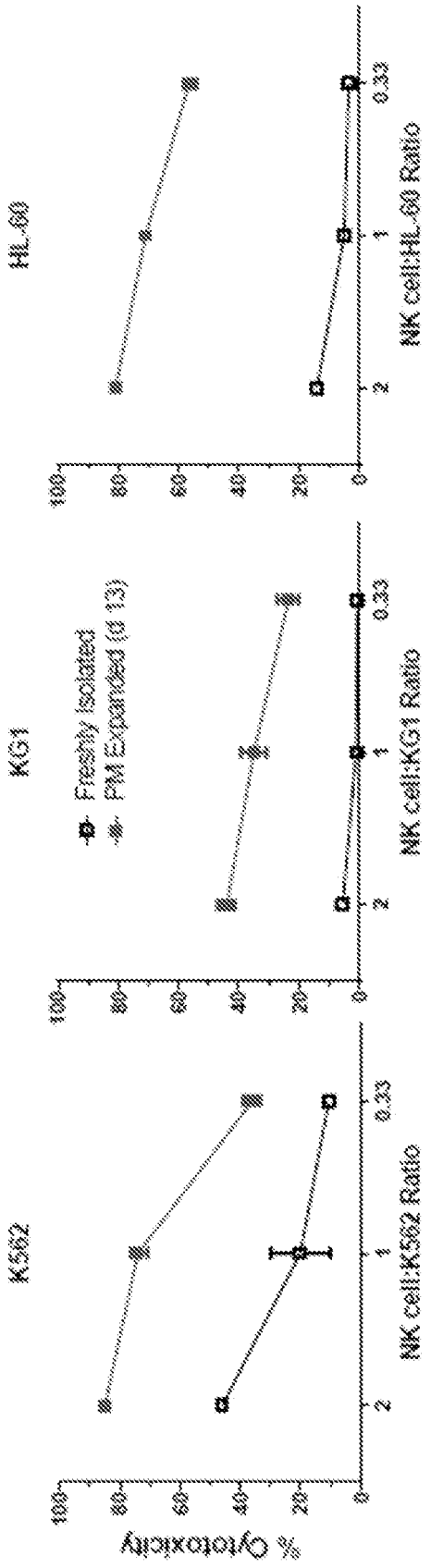

CML targets
AML targets
Feeder expanded
EM vesicle expanded
(200 ng/mL)
% Cytotoxicity
NK cell:K562 Ratio
NK cell:KG1 Ratio
NK cell:HL-60 Ratio
NK cell:BDCM Ratio
0
20
40
60
80
100
2
1
0.33

FIG. 14


% Cytotoxicity
K562
KG1
HL-60
Freshly Isolated
PM Expanded (d 13)
NK cell:K562 Ratio
NK cell:KG1 Ratio
NK cell:HL-60 Ratio
100
80
60
40
20
0
2
1
0.33

13/14

FIG. 15

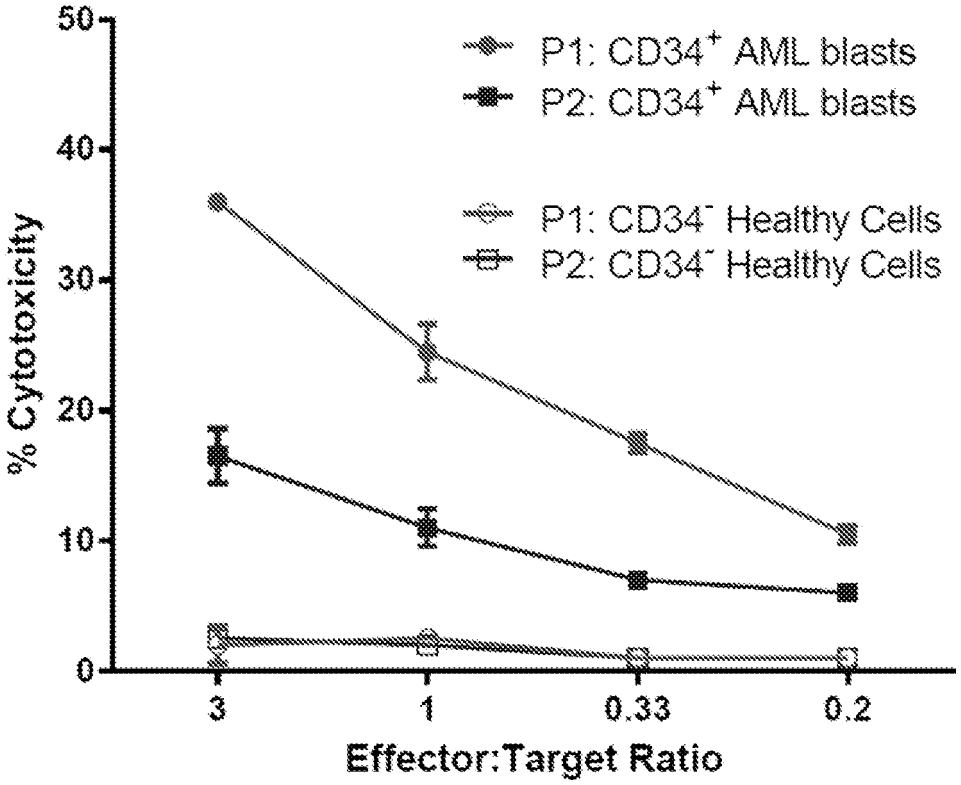

50
40
30
20
10
0
% Cytotoxicity
P1: CD34+ AML blasts
P2: CD34+ AML blasts
P1: CD34- Healthy Cells
P2: CD34- Healthy Cells
3
1
0.33
0.2
Effector:Target Ratio

FIG. 16

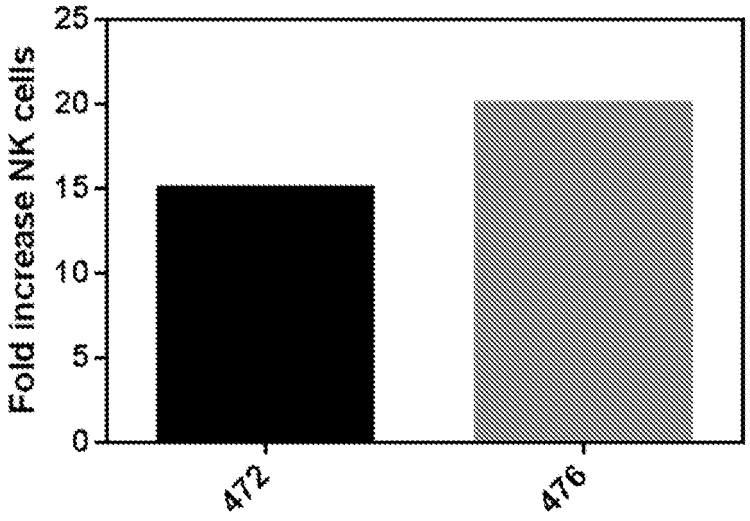

25
20
15
10
5
0
Fold increase NK cells
472
476

FIG. 17