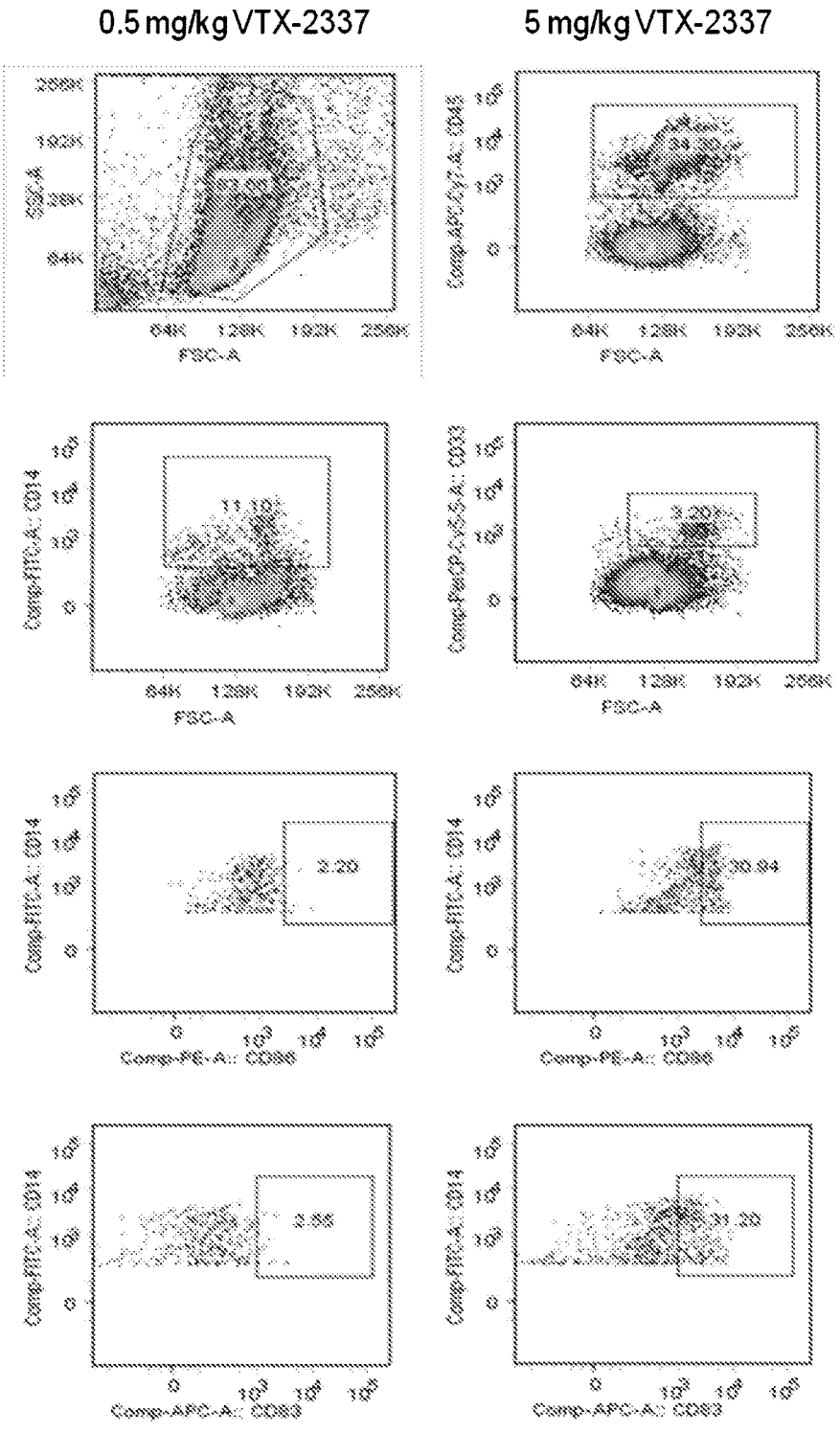

0.5 mg/kg VTX-2337
5 mg/kg VTX-2337
SSC-A
FSC-A
Comp-APC-Cy7-A:: CD45
Comp-FITC-A:: CD14
Comp-PerCP-Cy5-5-A:: CD33
Comp-PE-A:: CD86
Comp-APC-A:: CD83
11.10
3.20
3.20
30.84
2.55
21.20

Figure1A

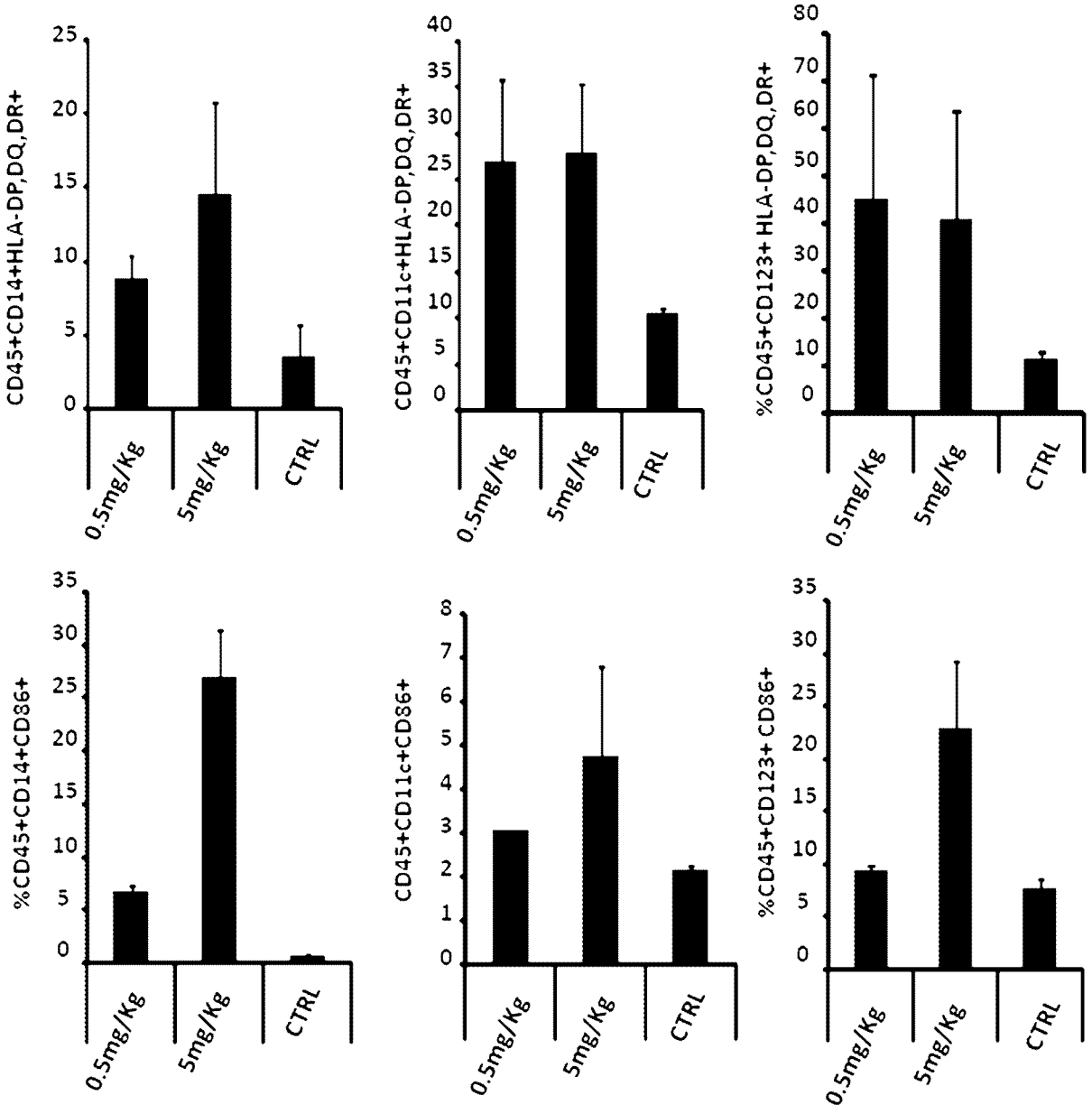

CD45+CD14+HLA-DP,DQ,DR+
CD45+CD11c+HLA-DP,DQ,DR+
%CD45+CD123+ HLA-DP,DQ,DR+
%CD45+CD14+CD86+
CD45+CD11c+CD86+
%CD45+CD123+ CD86+
0.5mg/Kg
5mg/Kg
CTRL

Figure 1B

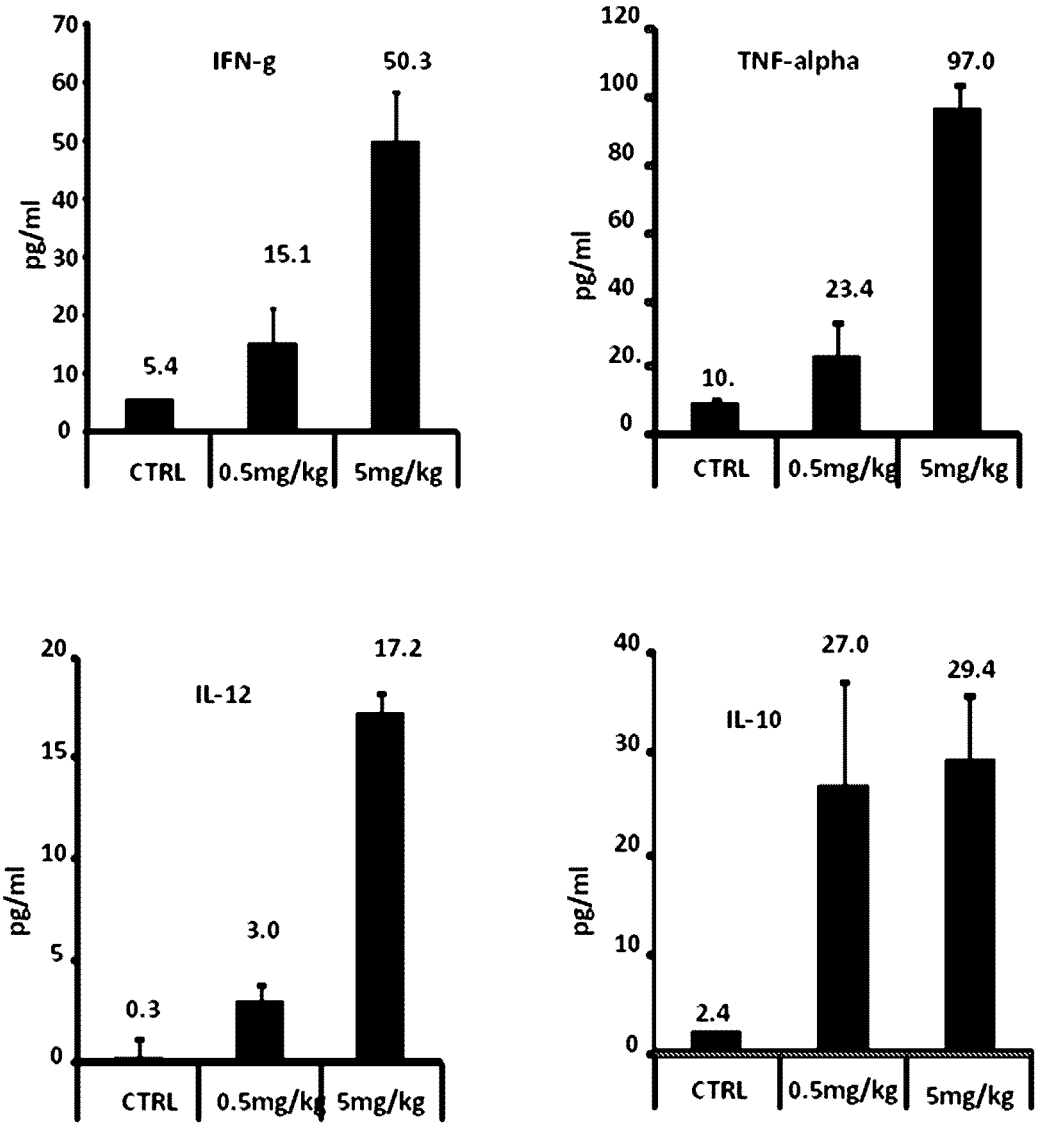

IFN-g
50.3
15.1
5.4
pg/ml
70
60
50
40
30
20
10
0
CTRL
0.5mg/kg
5mg/kg
TNF-alpha
97.0
23.4
10.
120
100
80
60
40
20.
0
IL-12
17.2
3.0
0.3
20
15
10
5
0
IL-10
27.0
29.4
2.4
40
30
20
10

Figure 1C

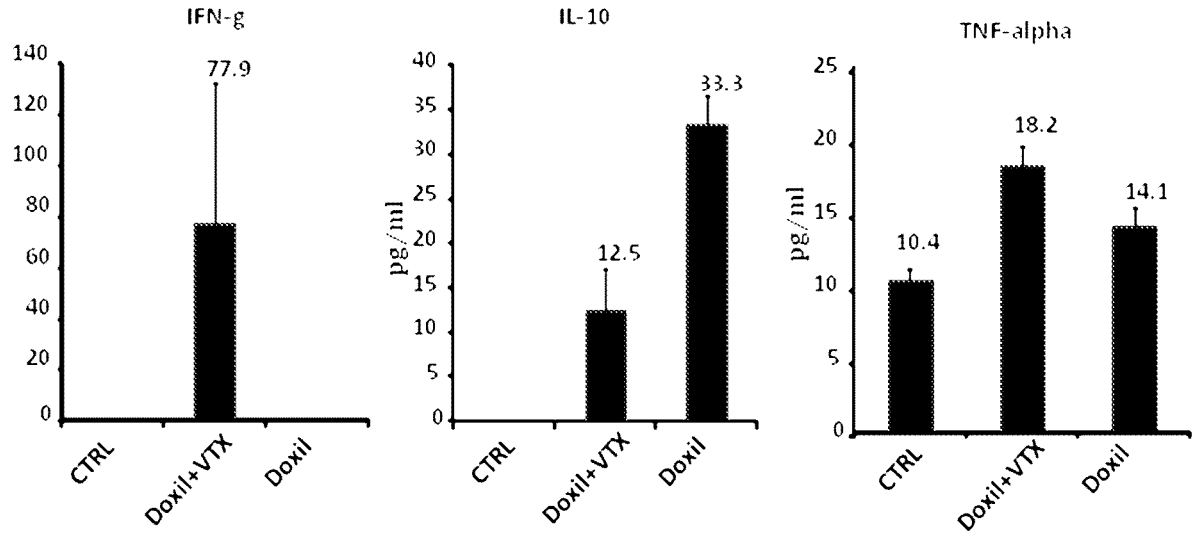


Figure 2

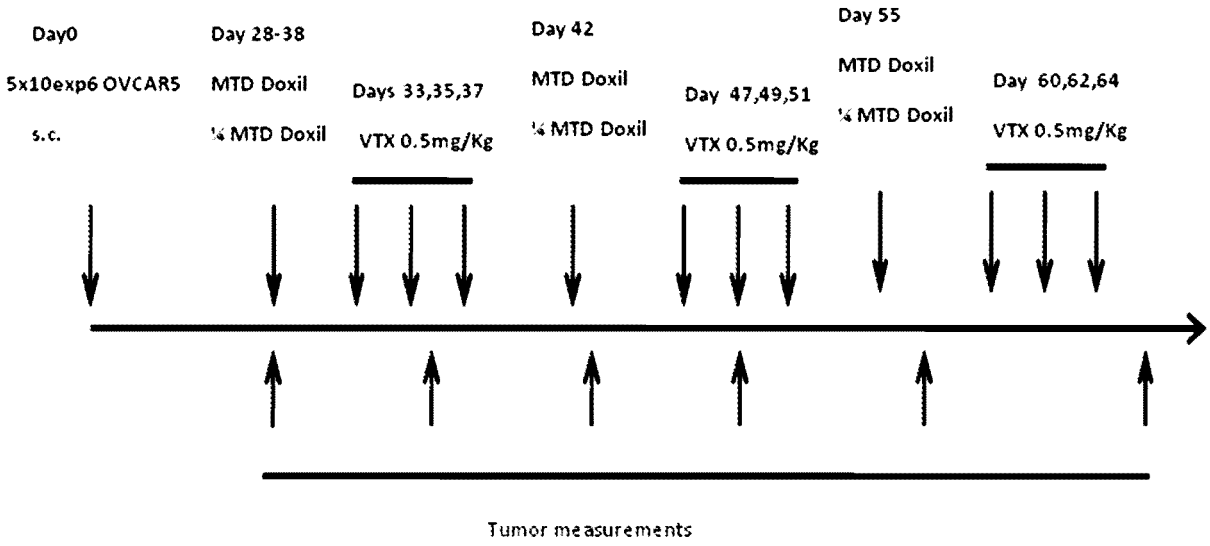


Figure 3A

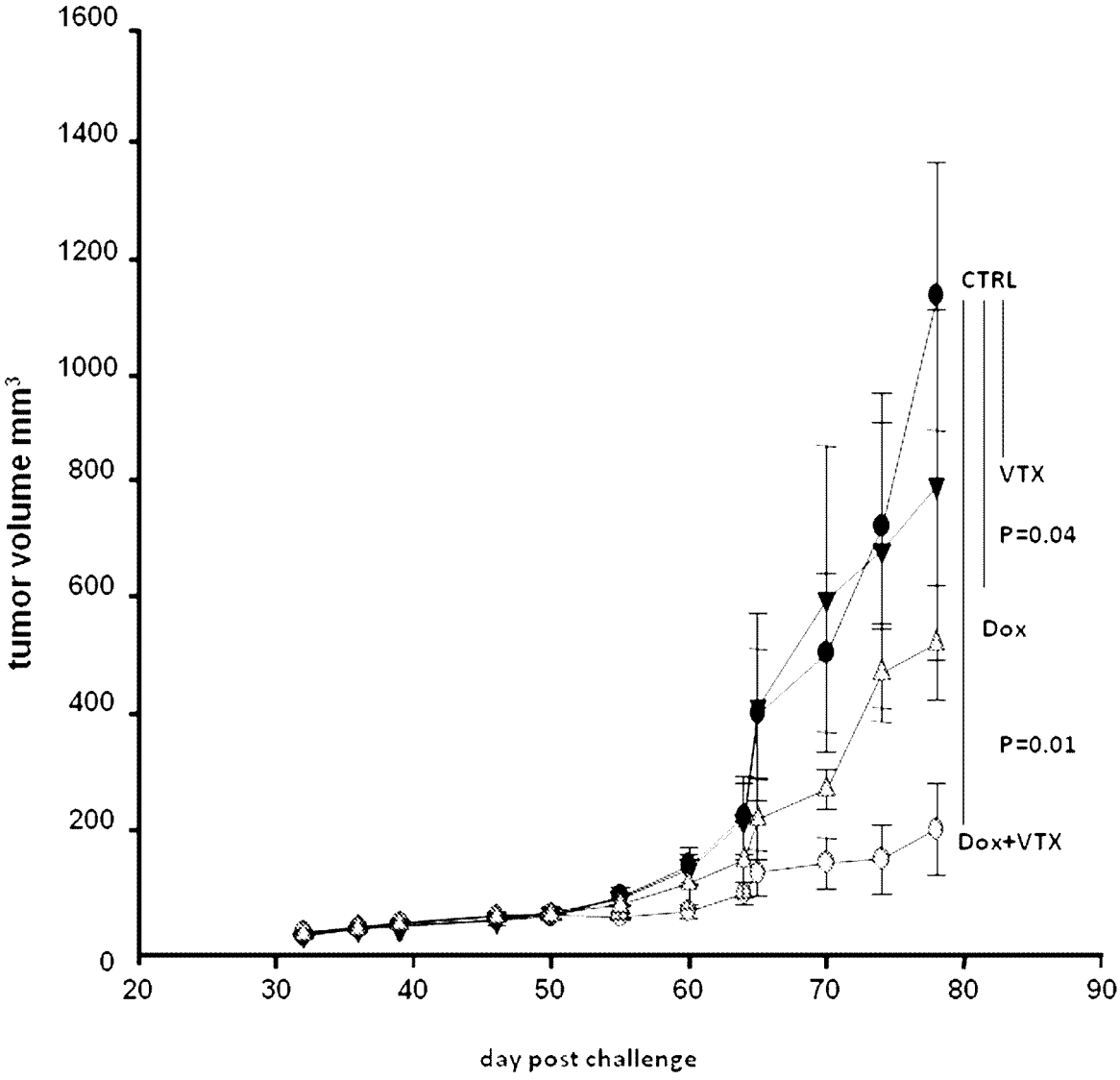

1600
1400
1200
1000
800
600
400
200
0
tumor volume mm3
20
30
40
50
60
70
80
90
day post challenge
CTRL
VTX
P=0.04
Dox
P=0.01
Dox+VTX

Figure 3B

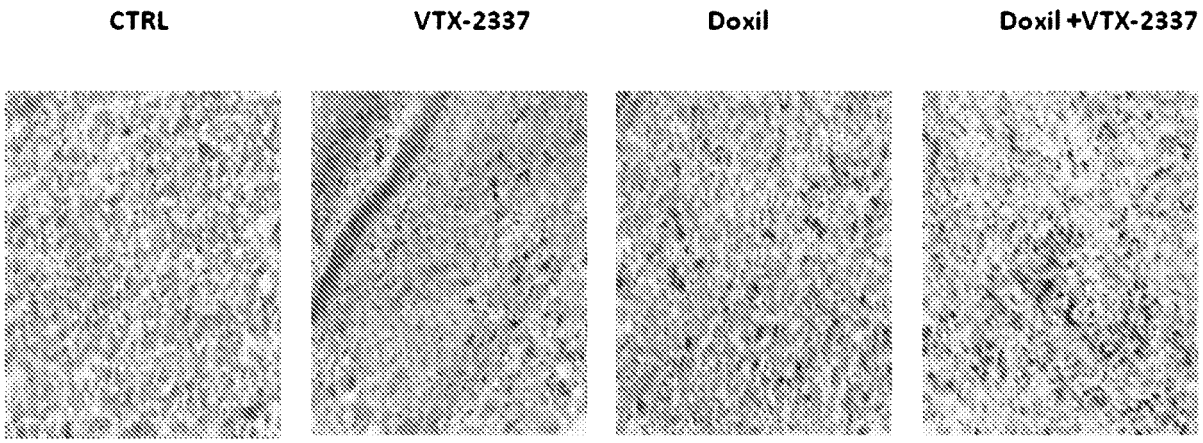


Figure 3C

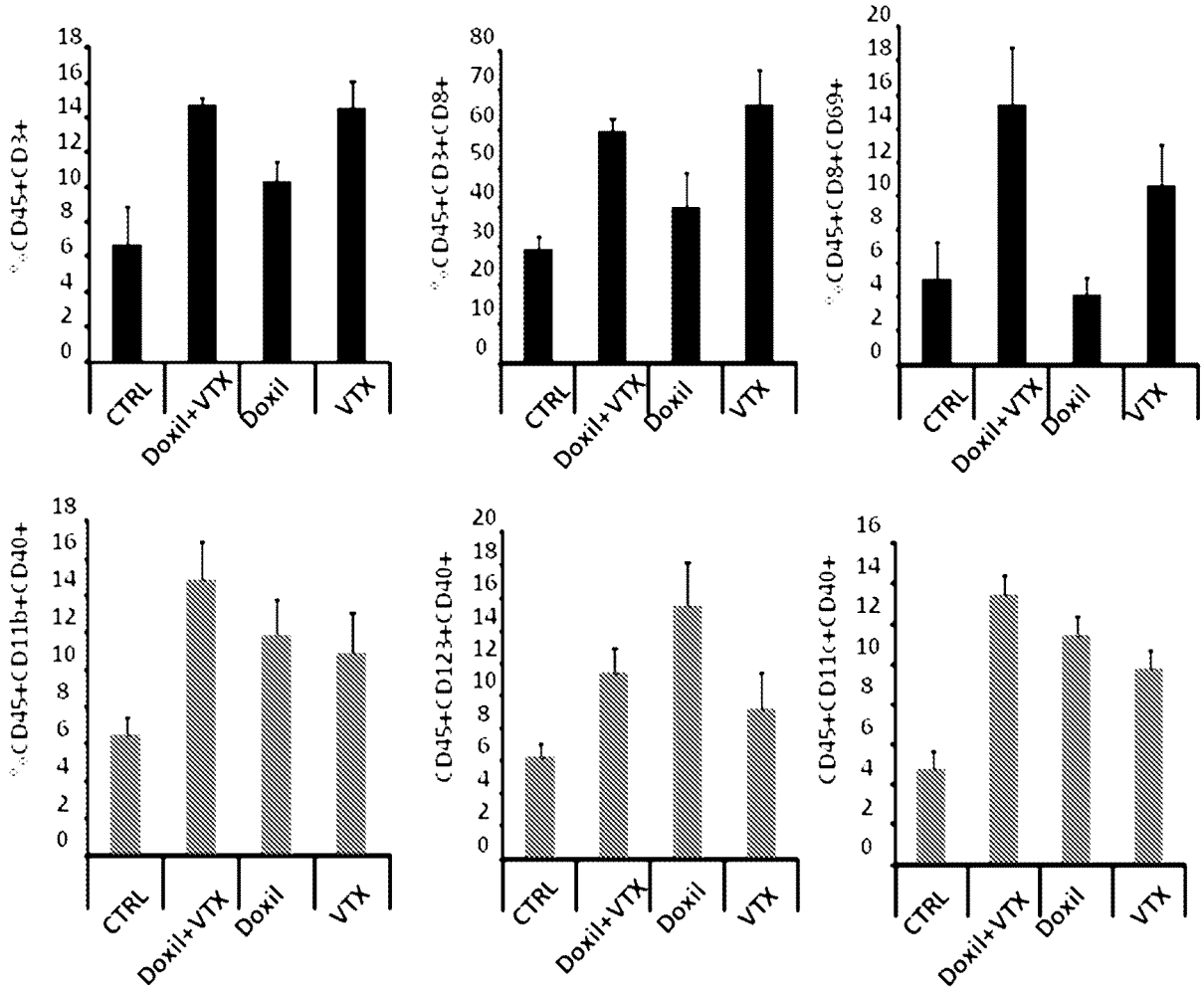

%CD45+CD3+
%CD45+CD3+CD8+
%CD45+CD8+CD69+
%CD45+CD11b+CD40+
CD45+CD123+CD40+
CD45+CD11c+CD40+
CTRL
Doxil+VTX
Doxil
VTX

Figure 3D

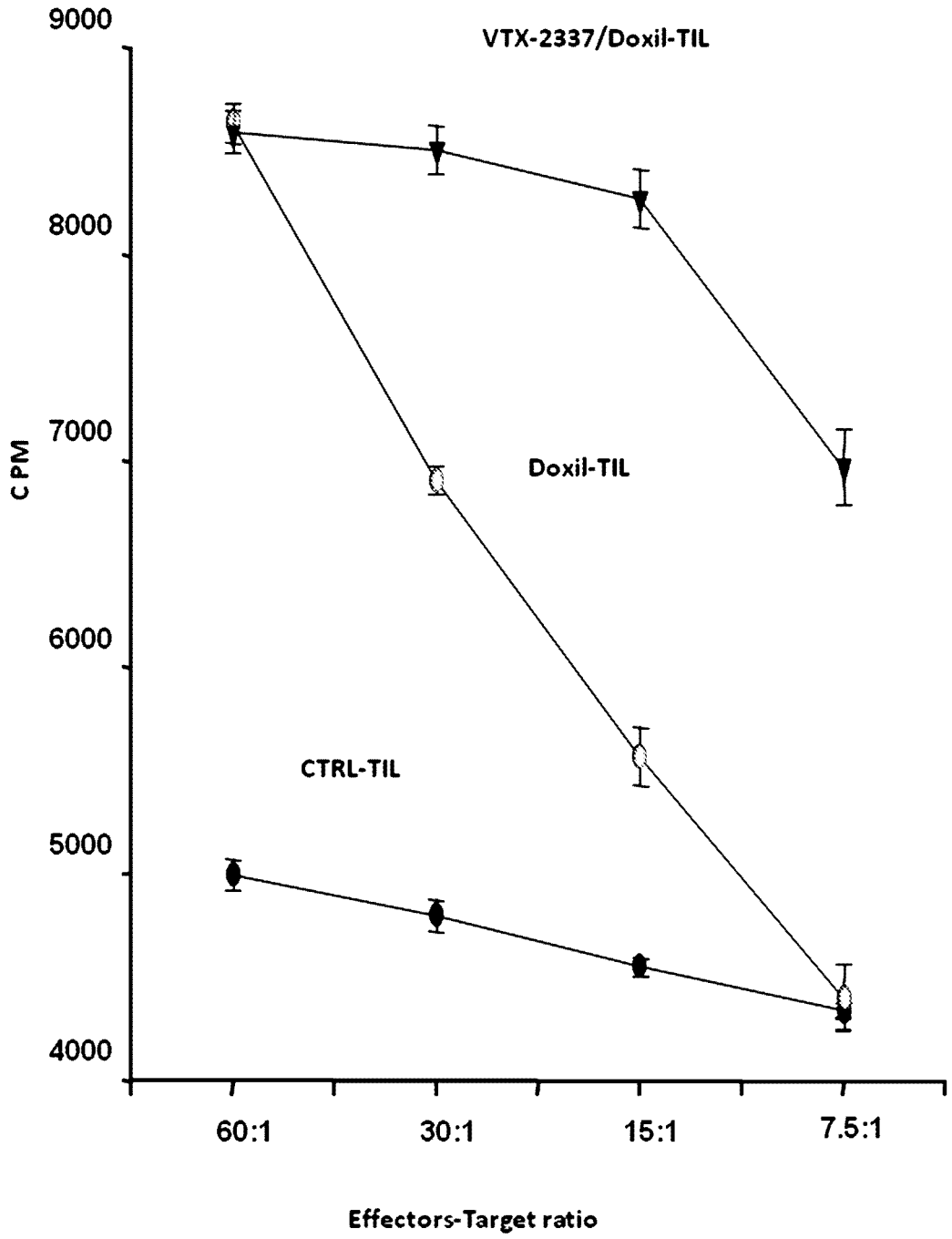

9000
8000
7000
6000
5000
4000
C PM
VTX-2337/Doxil-TIL
Doxil-TIL
CTRL-TIL
60:1
30:1
15:1
7.5:1
Effectors-Target ratio

Figure 4A

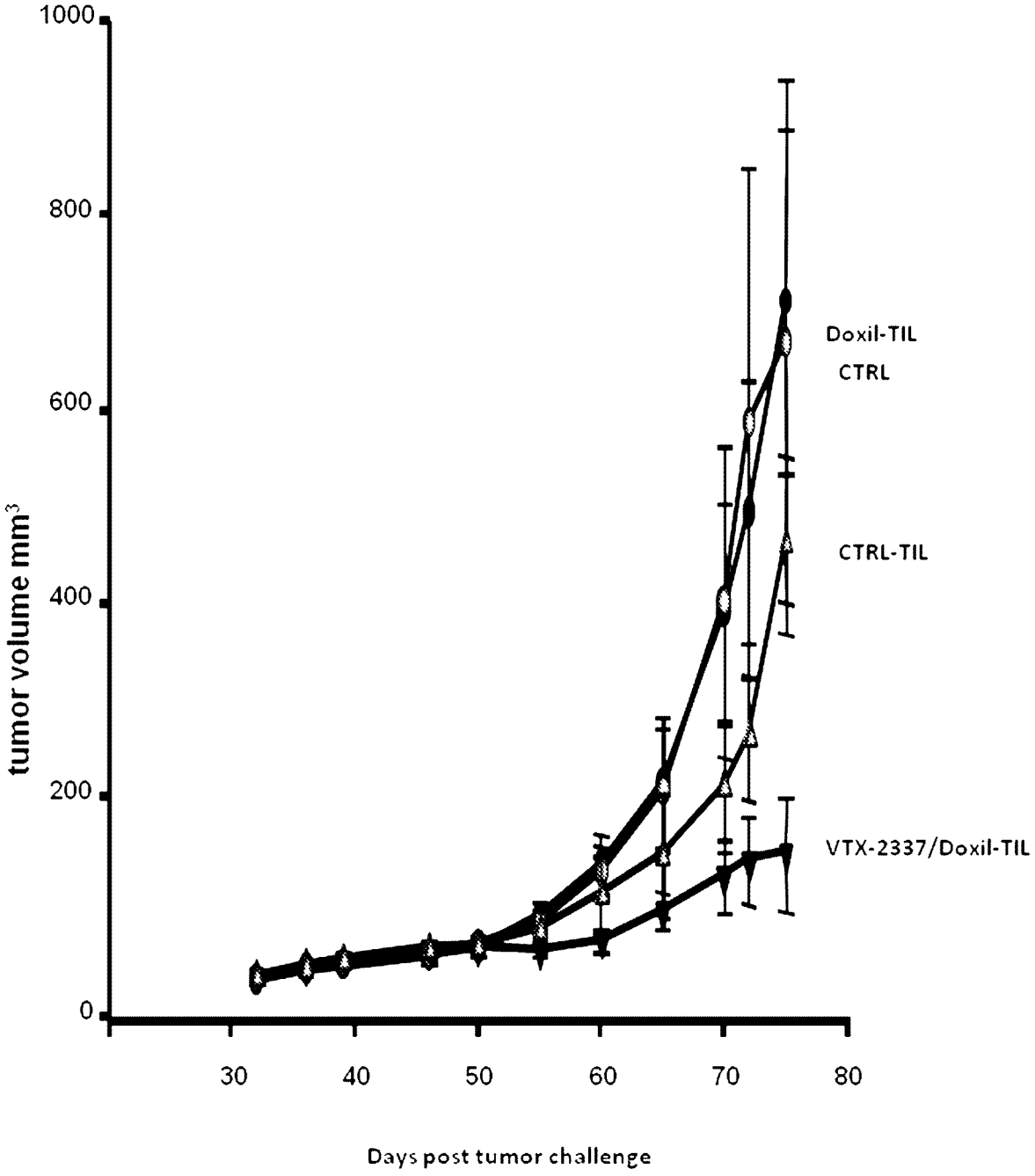

1000
800
600
400
200
0
tumor volume mm3
30
40
50
60
70
80
Days post tumor challenge
Doxil-TIL
CTRL
CTRL-TIL
VTX-2337/Doxil-TIL

Figure 4B

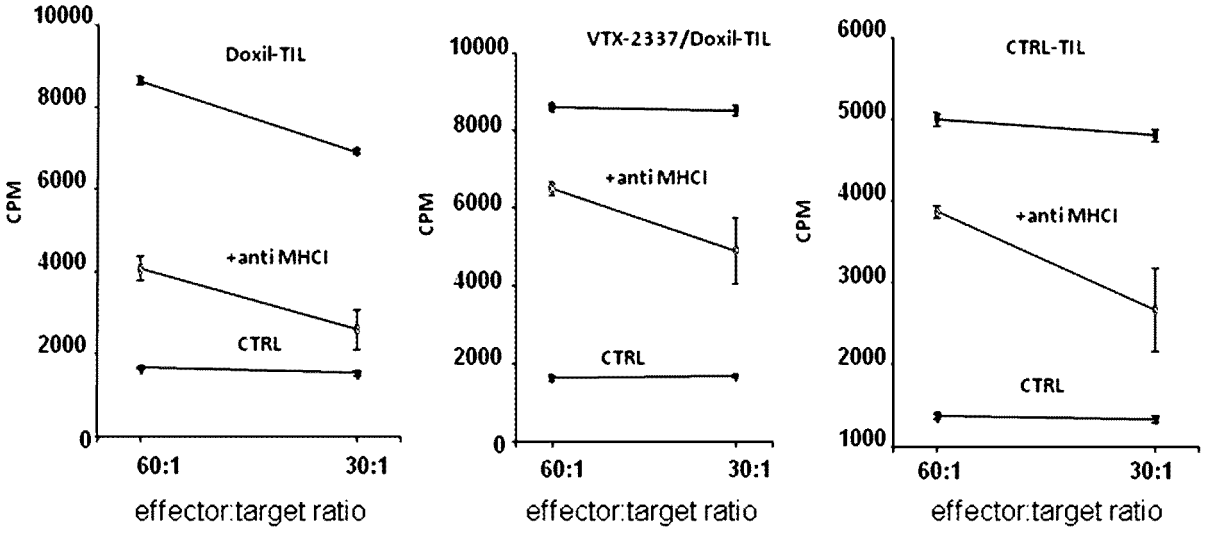


Figure 4C

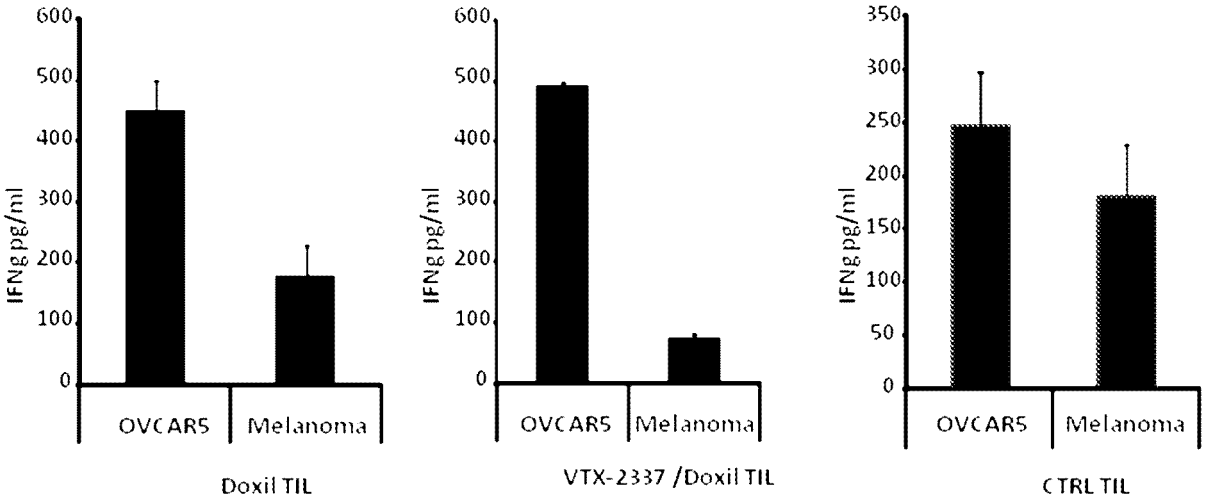


Figure 4D

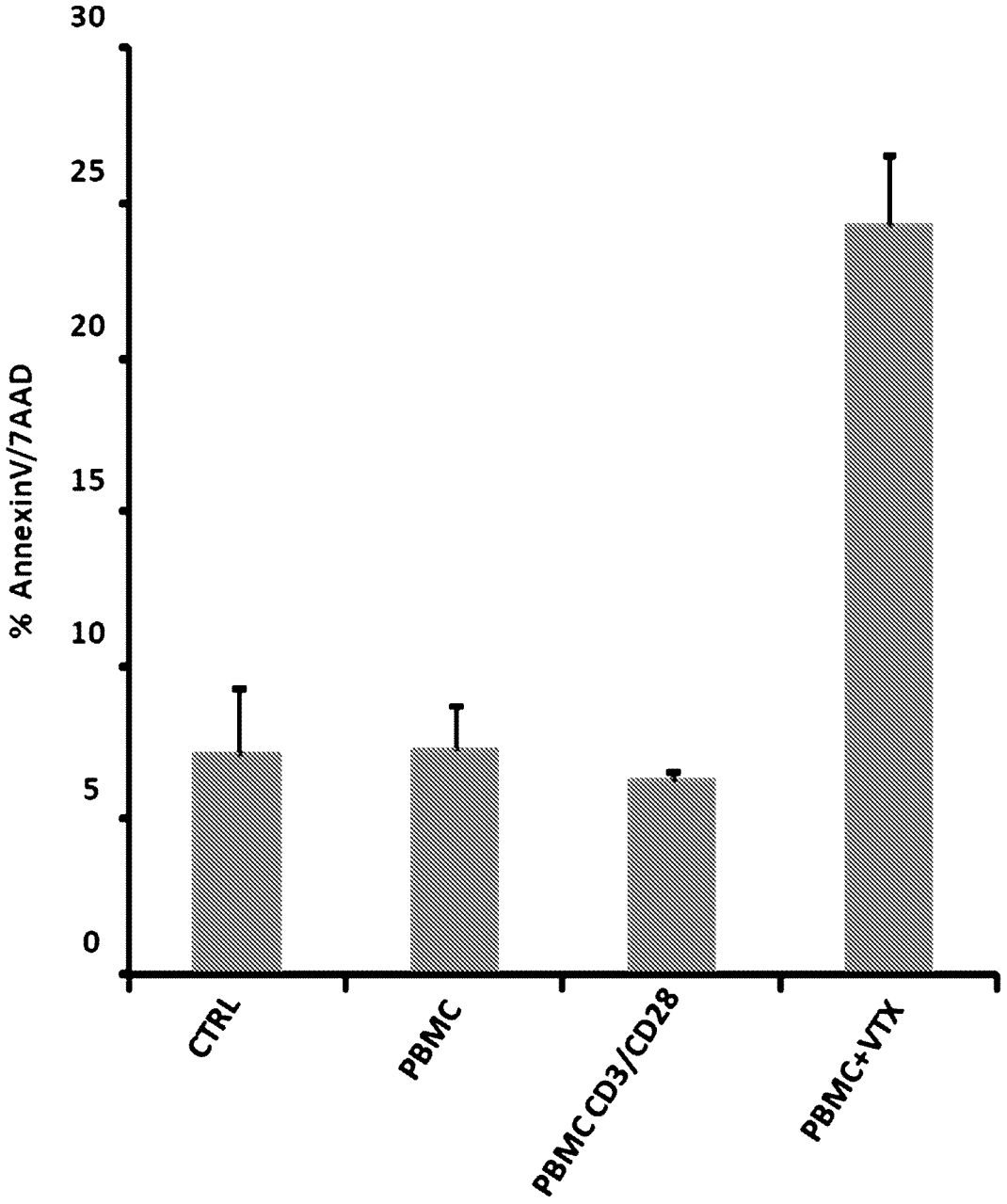

30
25
20
15
10
5
0
% AnnexinV/7AAD
CTRL
PBMC
PBMC CD3/CD28
PBMC+VTX

Figure 5A

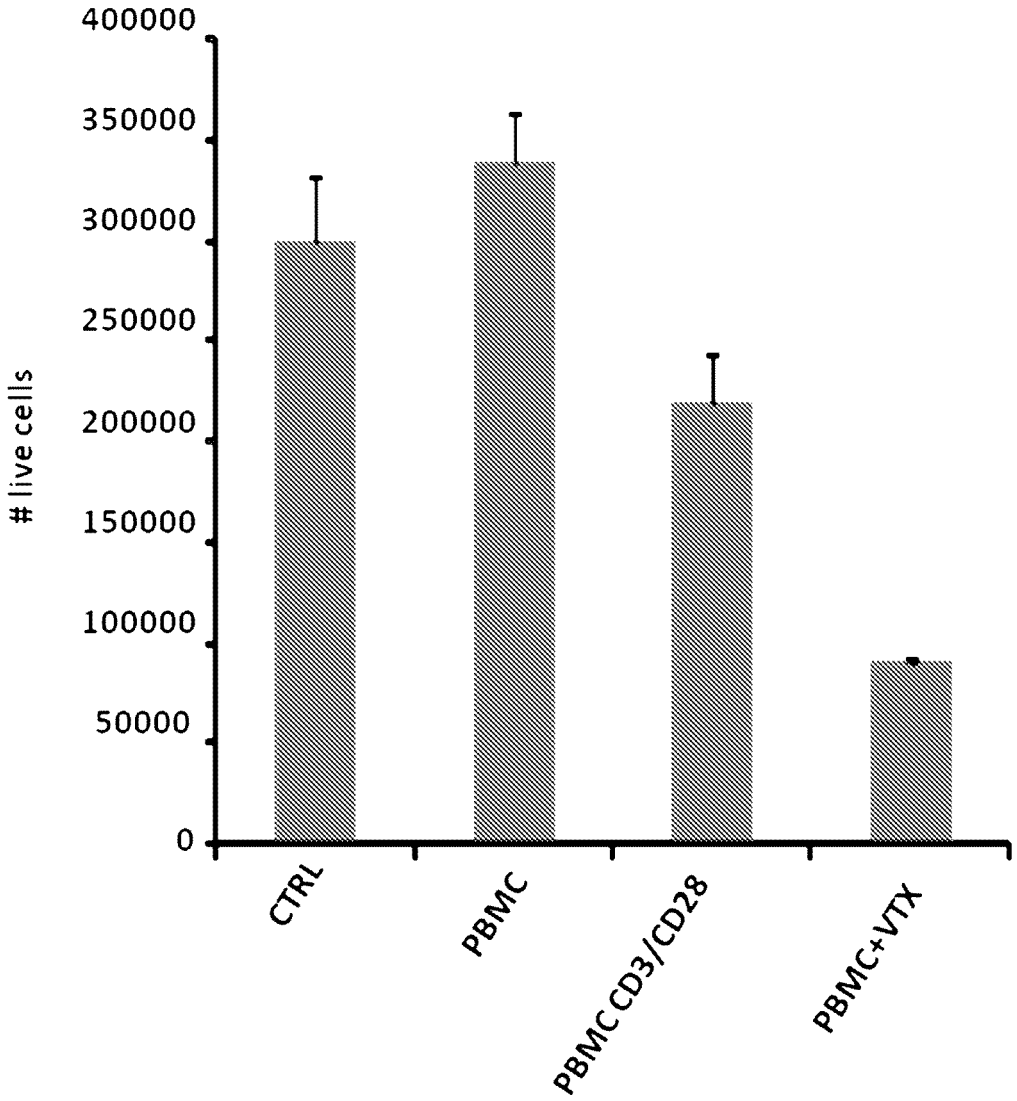

400000
350000
300000
250000
200000
150000
100000
50000
0
live cells
CTRL
PBMC
PBMC CD3/CD28
PBMC+VTX

Figure 5B

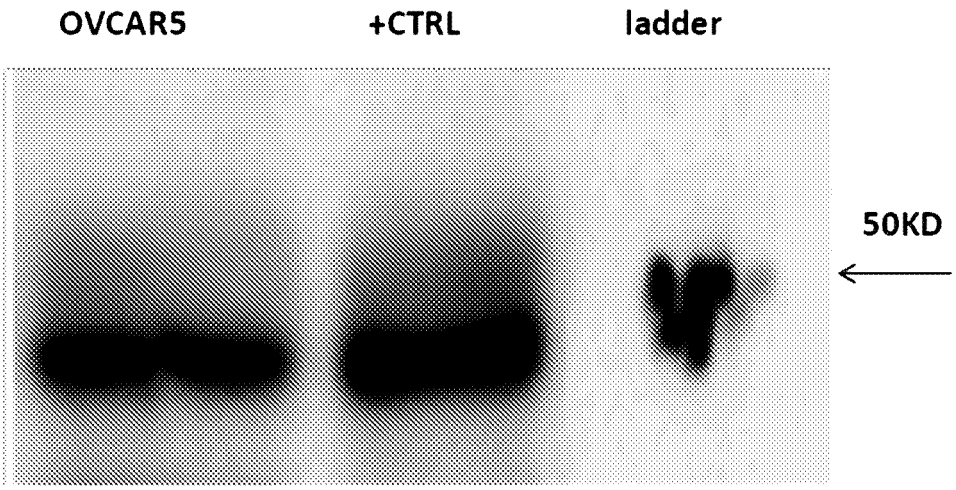


Figure 5C

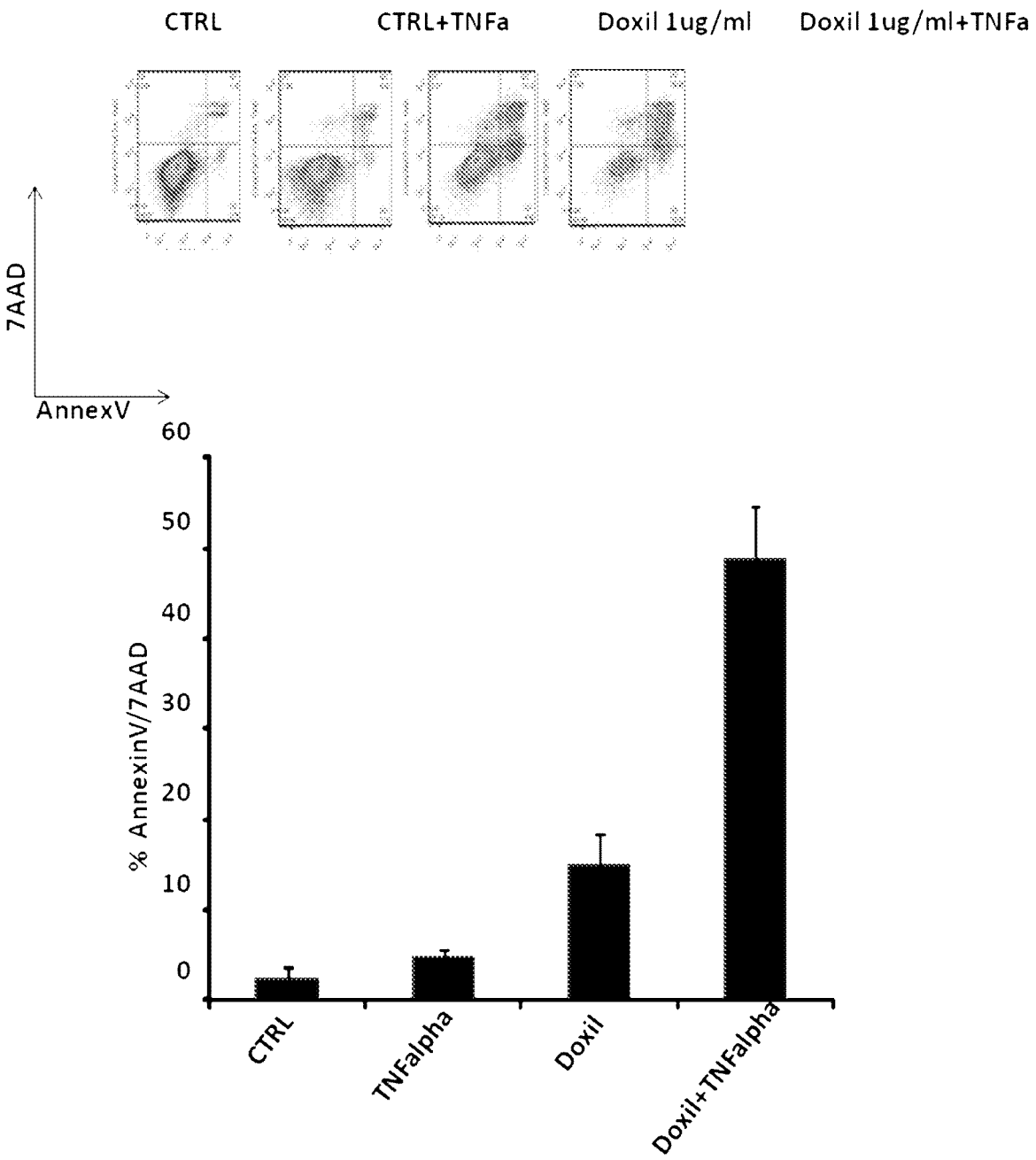

CTRL
CTRL+TNFa
Doxil 1ug/ml
Doxil 1ug/ml+TNFa
7AAD
AnnexV
% AnnexinV/7AAD
60
50
40
30
20
10
0
CTRL
TNFalpha
Doxil
Doxil+TNFalpha

Figure 5D

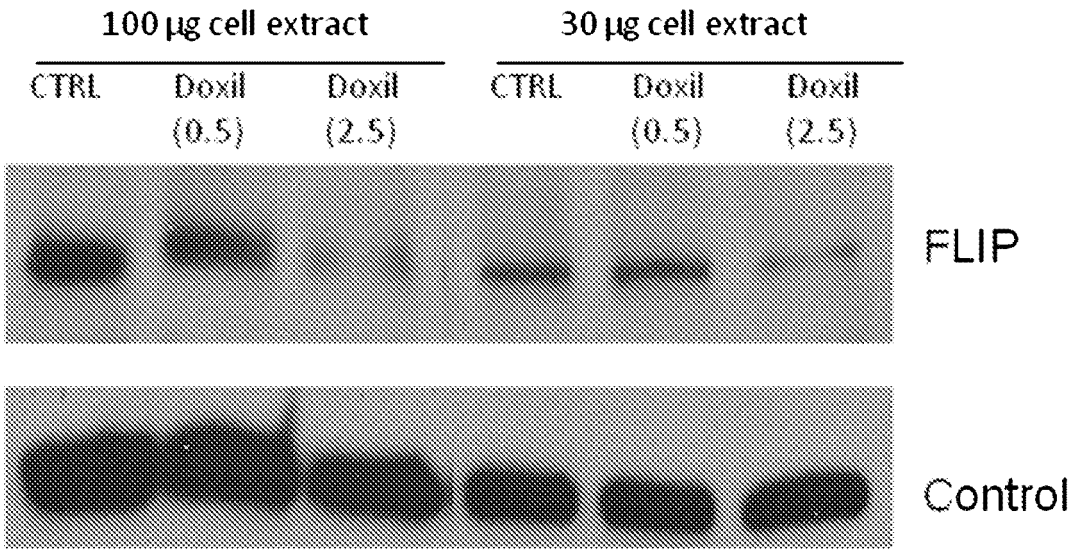

100 µg cell extract
30 µg cell extract
CTRL
Doxil (0.5)
Doxil (2.5)
CTRL
Doxil (0.5)
Doxil (2.5)
FLIP
Control

Figure 5E

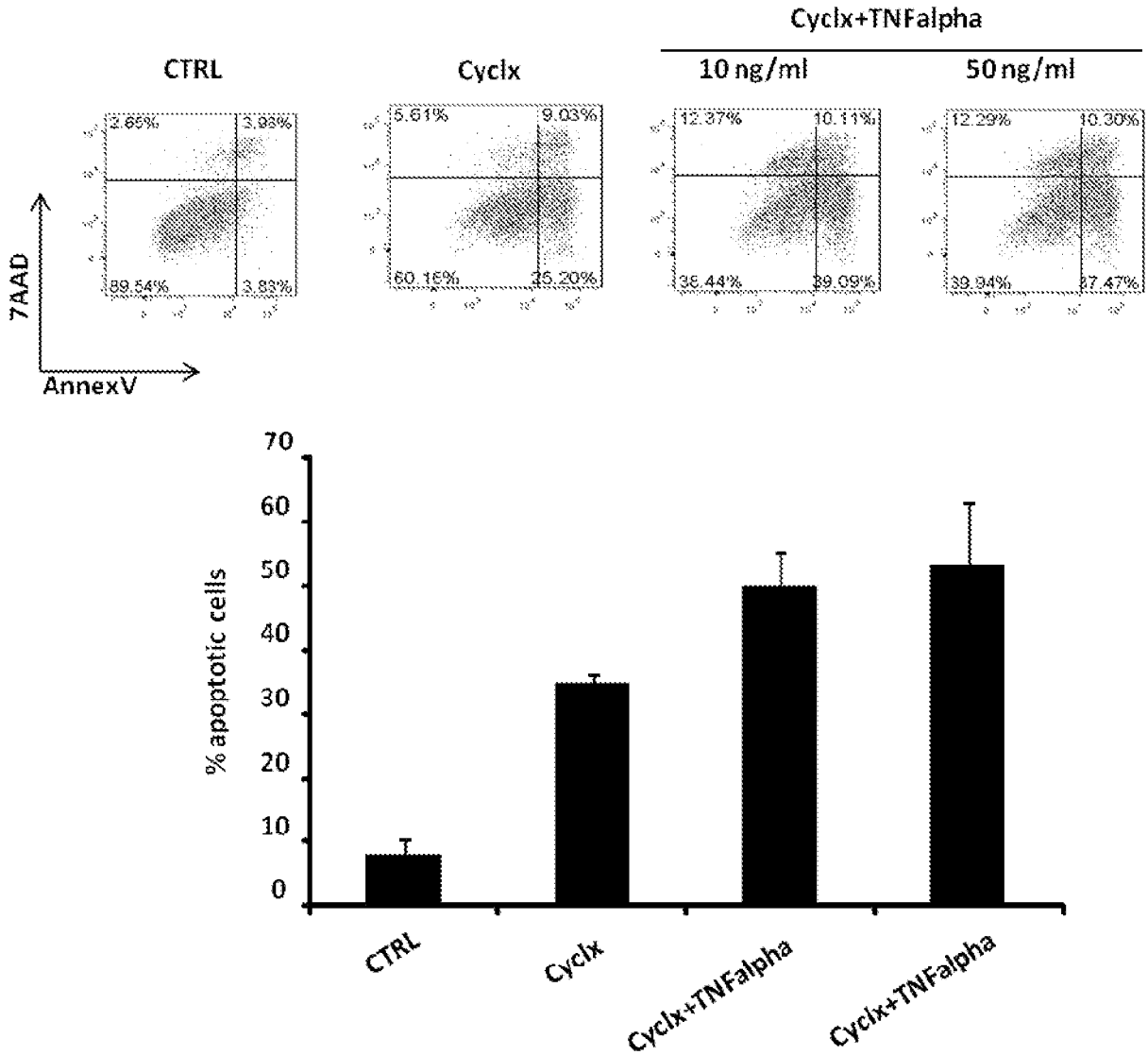

Cyclx+TNFalpha
CTRL
Cyclx
10 ng/ml
50 ng/ml
2.66%
3.83%
89.54%
3.83%
5.61%
9.03%
60.16%
25.20%
12.37%
10.11%
38.44%
39.09%
12.29%
10.30%
39.94%
37.47%
7AAD
AnnexV
% apoptotic cells
70
60
50
40
30
20
10
0
CTRL
Cyclx
Cyclx+TNFalpha
Cyclx+TNFalpha

Figure 5F

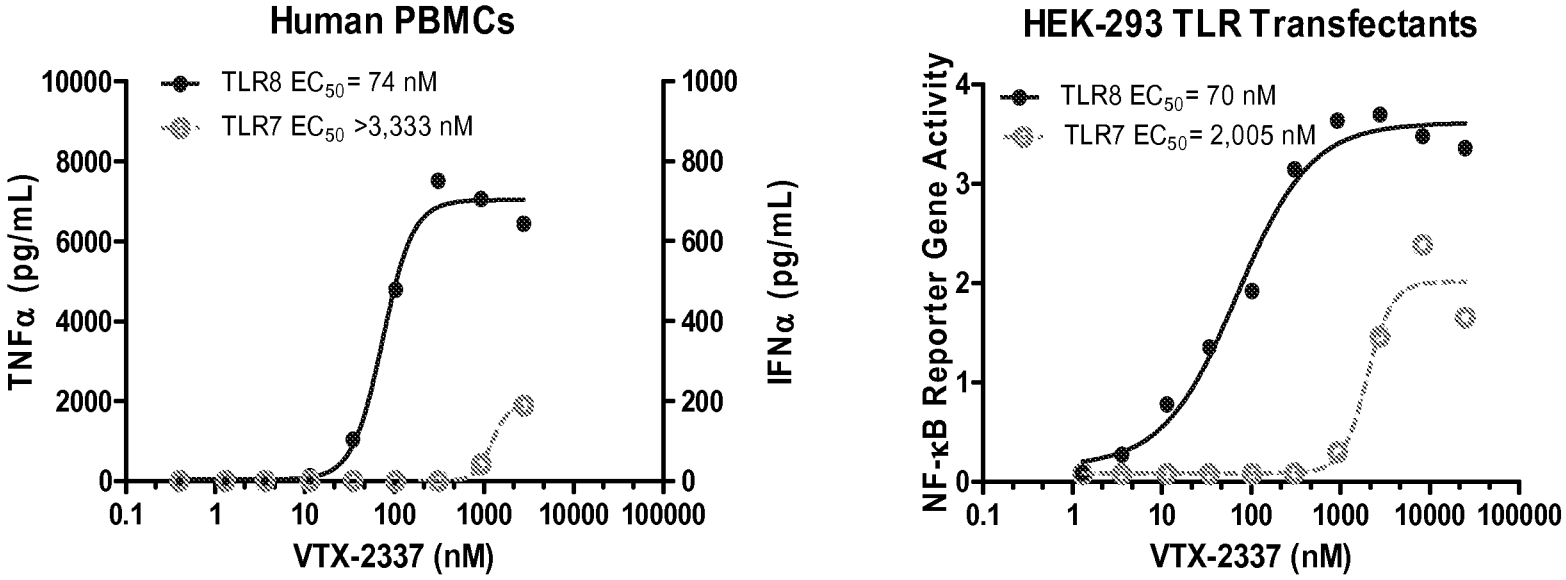

Human PBMCs
TLR8 EC50= 74 nM
TLR7 EC50 >3,333 nM
TNFα (pg/mL)
IFNα (pg/mL)
VTX-2337 (nM)
HEK-293 TLR Transfectants
TLR8 EC50= 70 nM
TLR7 EC50= 2,005 nM
NF-κB Reporter Gene Activity
VTX-2337 (nM)

Figure 6

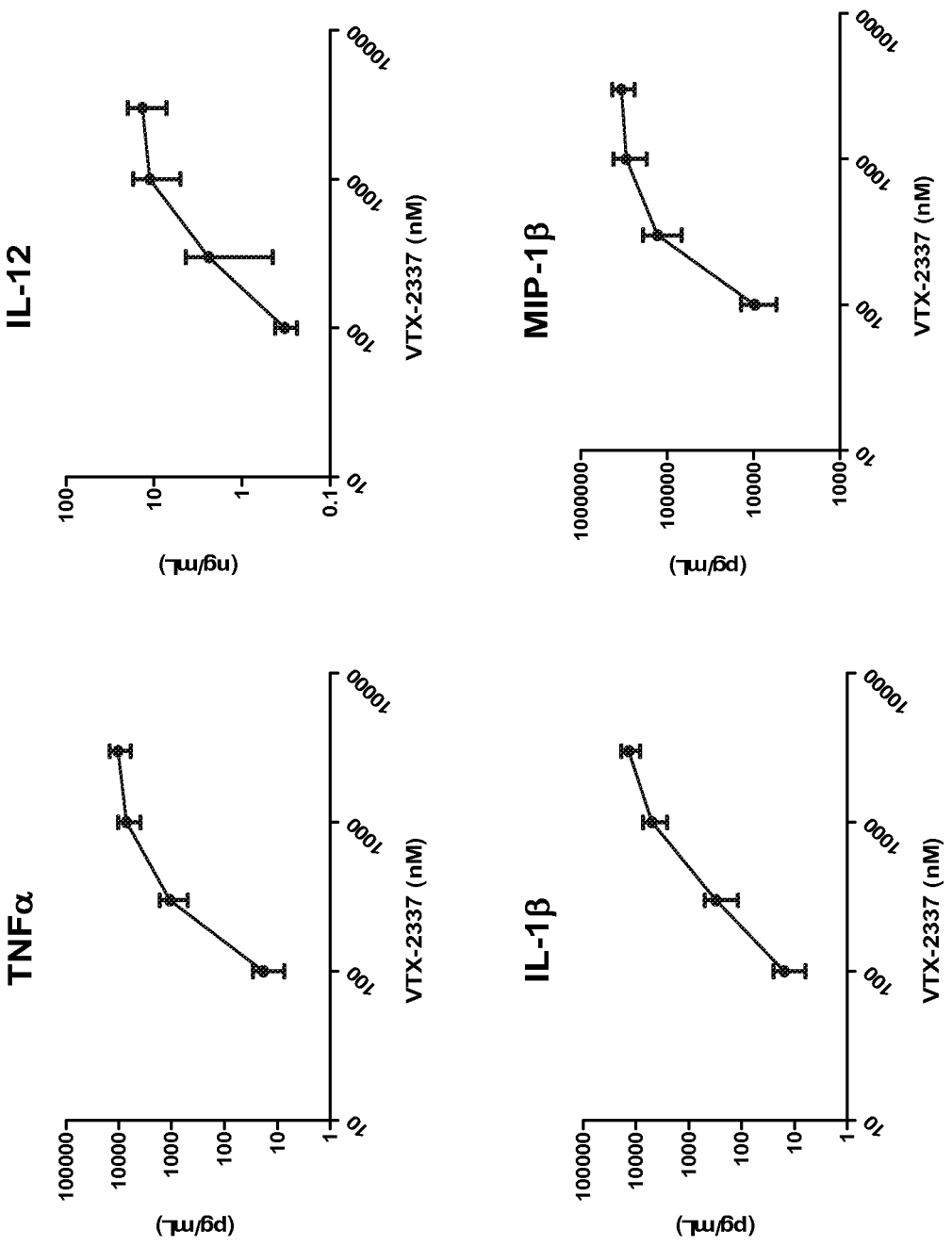

IL-12
(ng/mL)
100
10
1
0.1
10
100
1000
10000
VTX-2337 (nM)
MIP-1β
(pg/mL)
1000000
100000
10000
1000
10
100
1000
10000
VTX-2337 (nM)
TNFα
(pg/mL)
100000
10000
1000
100
10
1
10
100
1000
10000
VTX-2337 (nM)
IL-1β
(pg/mL)
100000
10000
1000
100
10
1
10
100
1000
10000
VTX-2337 (nM)

Figure 7

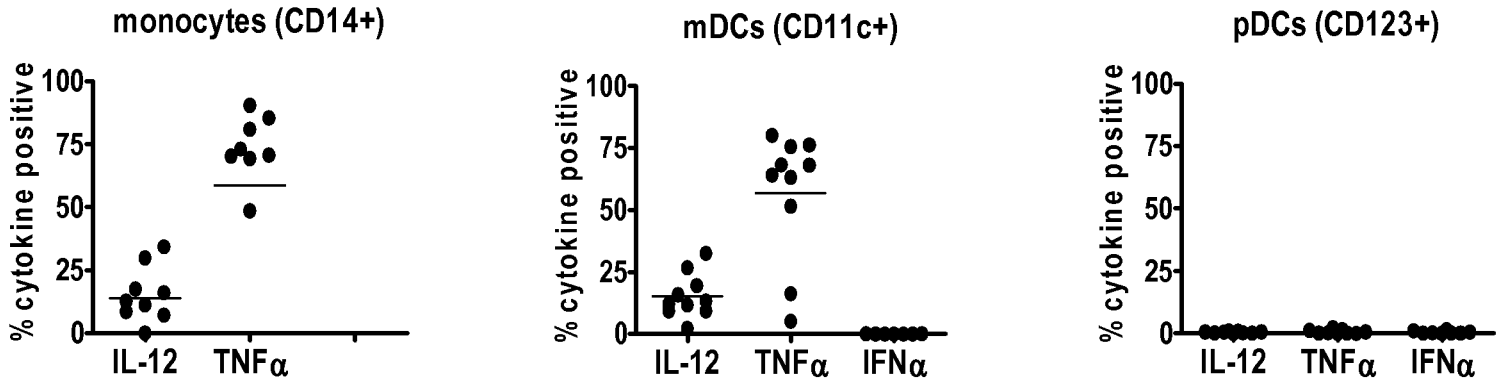

monocytes (CD14+)
% cytokine positive
100
75
50
25
0
IL-12
TNFα
mDCs (CD11c+)
% cytokine positive
100
75
50
25
0
IL-12
TNFα
IFNα
pDCs (CD123+)
% cytokine positive
100
75
50
25
0
IL-12
TNFα
IFNα

Figure 8

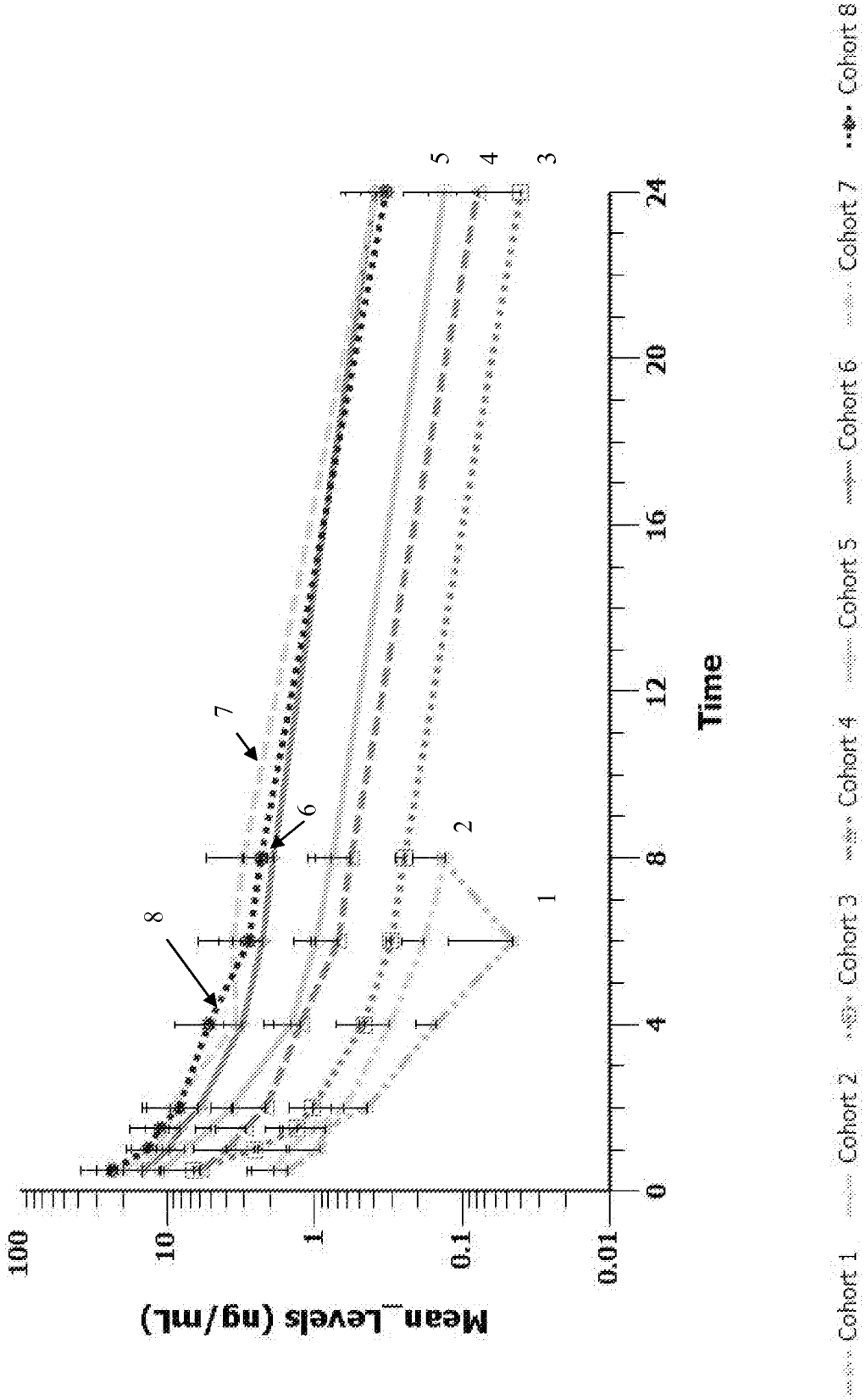

Mean_Levels (ng/mL)
100
10
1
0.1
0.01
0
4
8
12
16
20
24
Time
1
2
3
4
5
6
7
8
Cohort 1
Cohort 2
Cohort 3
Cohort 4
Cohort 5
Cohort 6
Cohort 7
Cohort 8

Figure 9

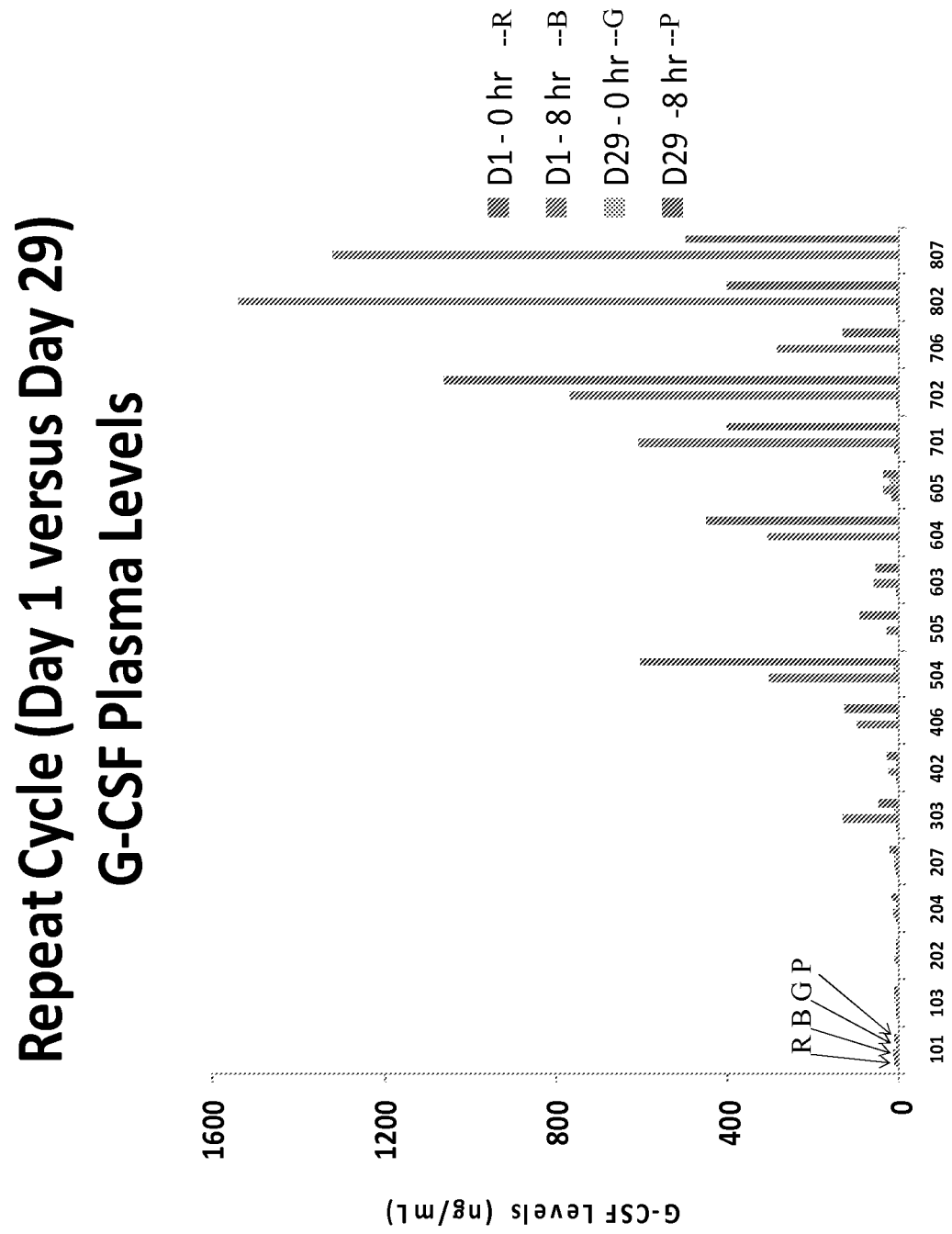

Repeat Cycle (Day 1 versus Day 29)
G-CSF Plasma Levels
D1 - 0 hr --R
D1 - 8 hr --B
D29 - 0 hr --G
D29 -8 hr --P
G-CSF Levels (ng/mL)
1600
1200
800
400
0
R B G P
101 103 202 204 207 303 402 406 504 505 603 604 605 701 702 706 802 807

Figure 10A

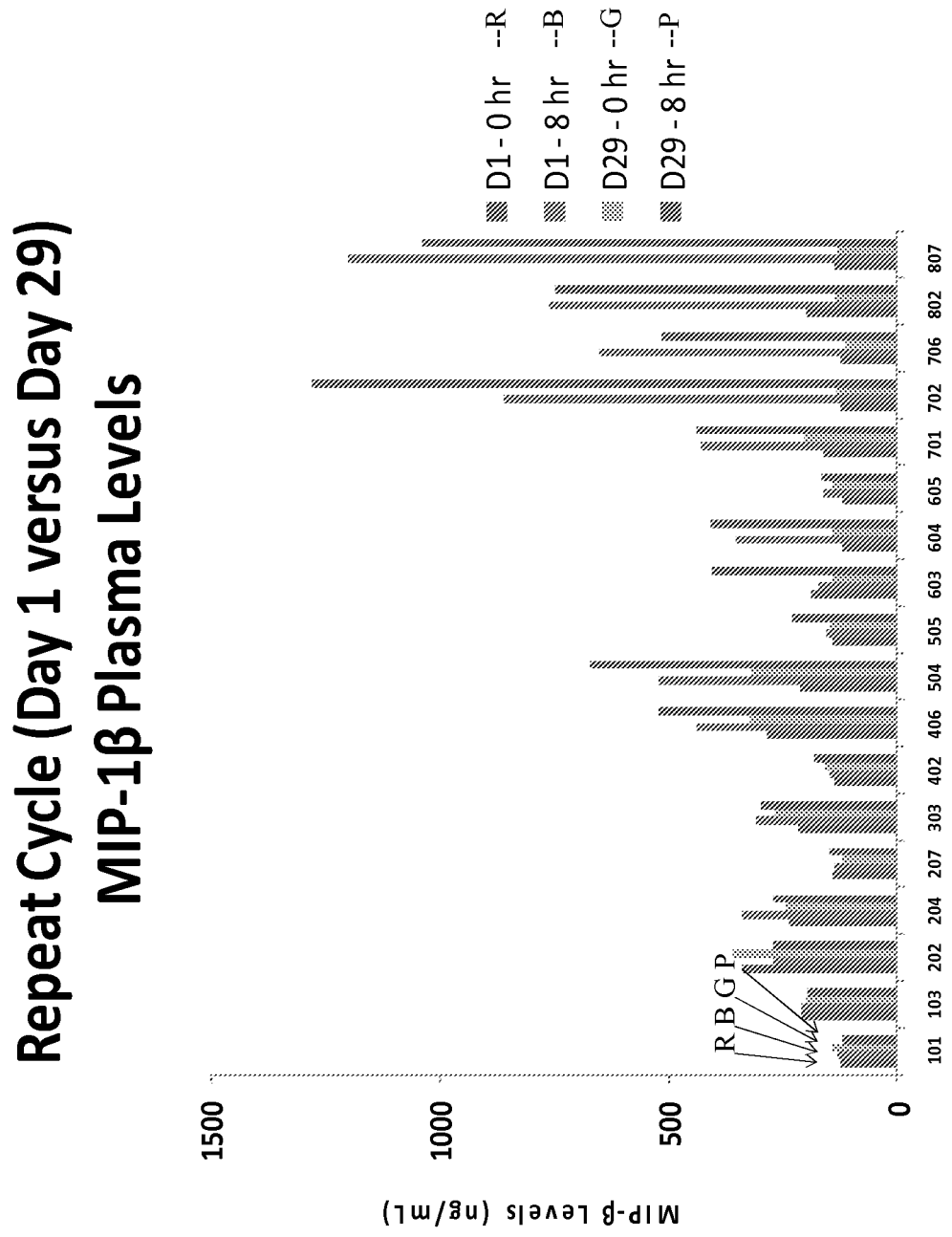

Repeat Cycle (Day 1 versus Day 29)
MIP-1β Plasma Levels
D1 - 0 hr --R
D1 - 8 hr --B
D29 - 0 hr --G
D29 - 8 hr --P
MIP-β Levels (ng/mL)
1500
1000
500
0
R B G P
101 103 202 204 207 303 402 406 504 505 603 604 605 701 702 706 802 807

Figure 10B