Fig. 1

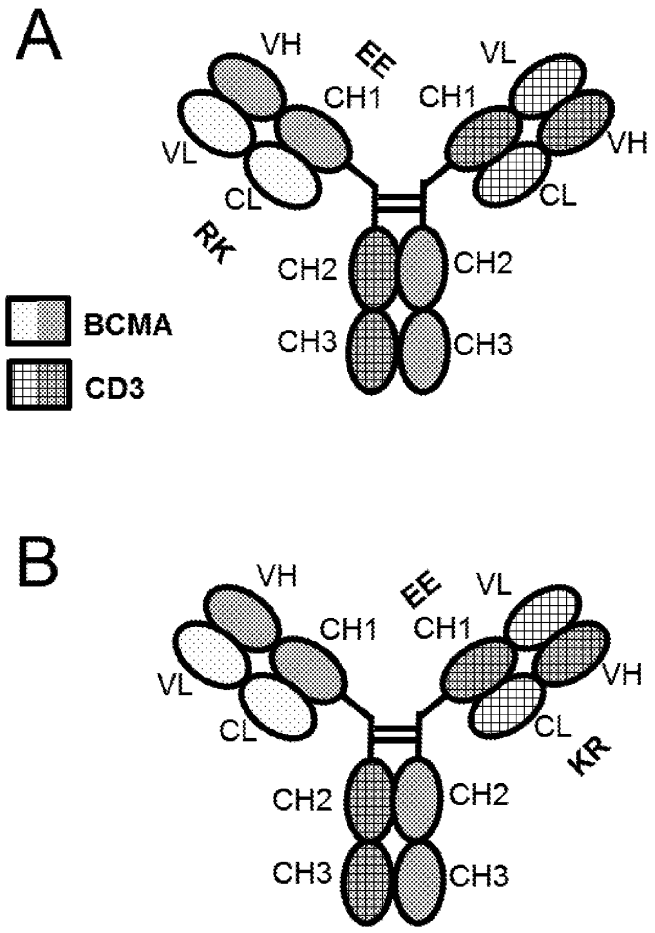

A
VH
EE
VL
CH1
CH1
VH
VL
CL
CL
RK
CH2
CH2
CH3
CH3
BCMA
CD3
B
VH
EE
VL
CH1
CH1
VH
VL
CL
CL
KR
CH2
CH2
CH3
CH3

Fig. 2

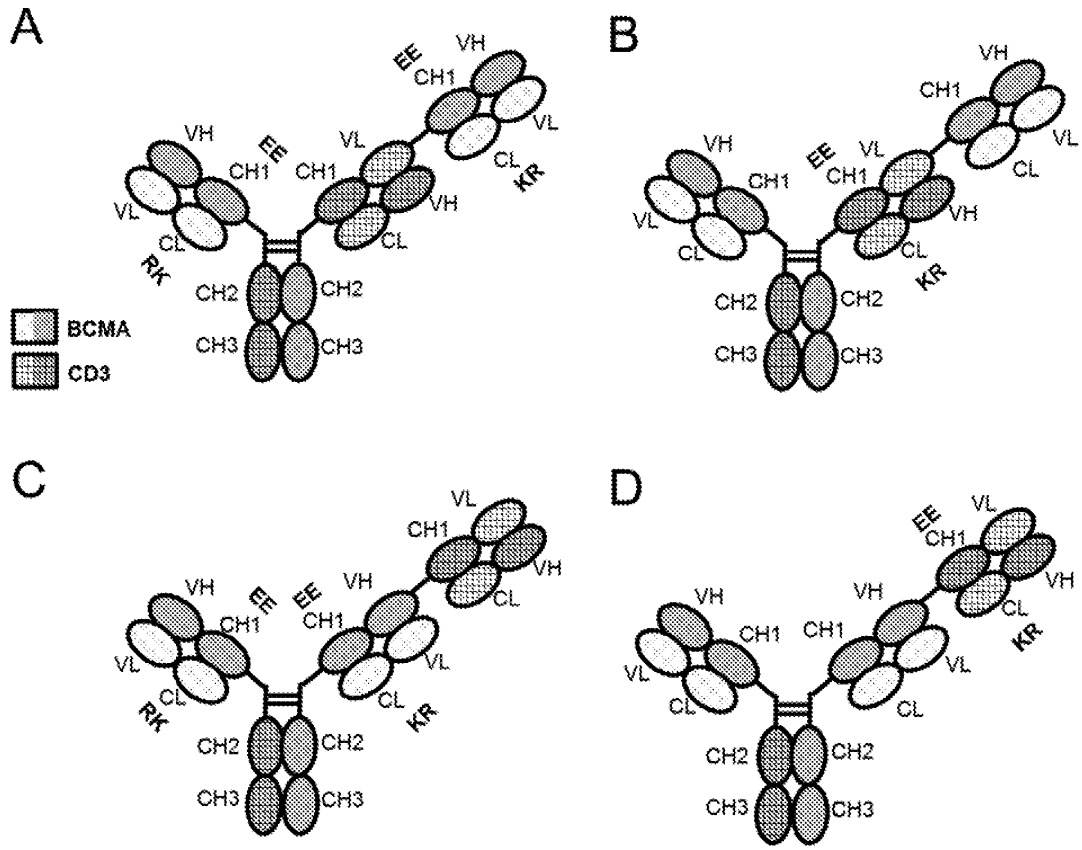


Fig. 3

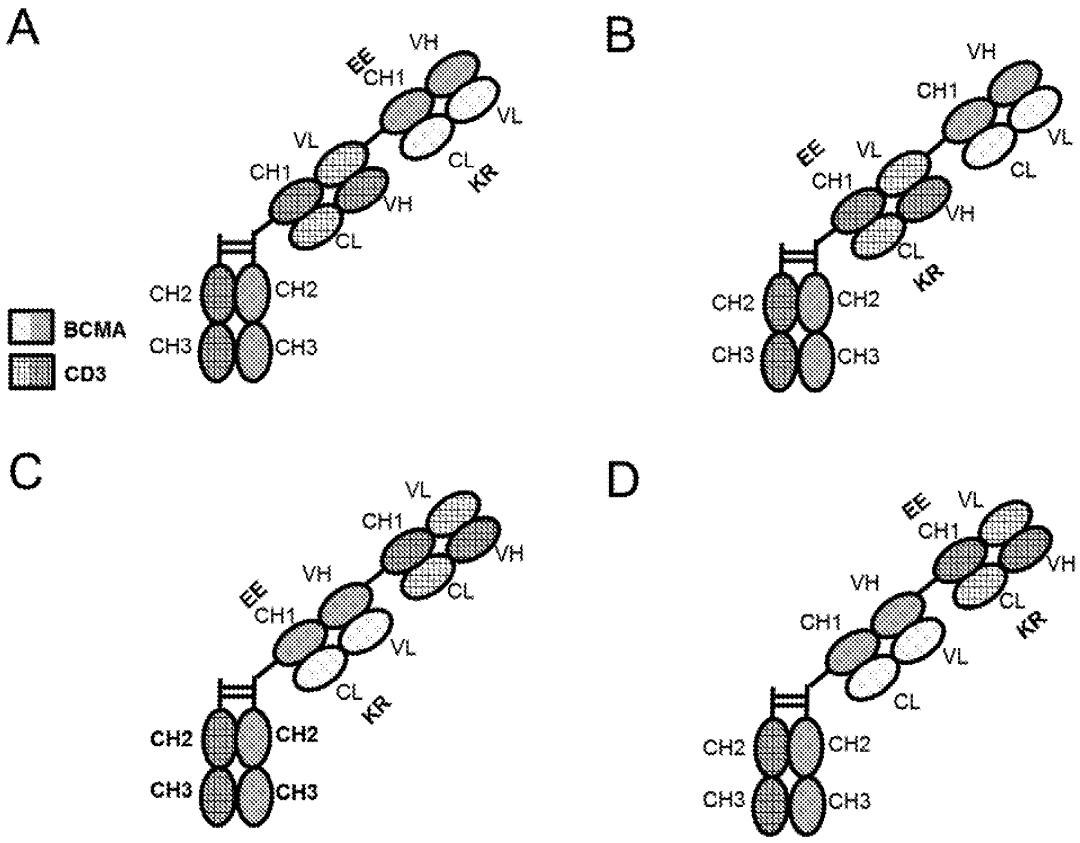


Fig. 4

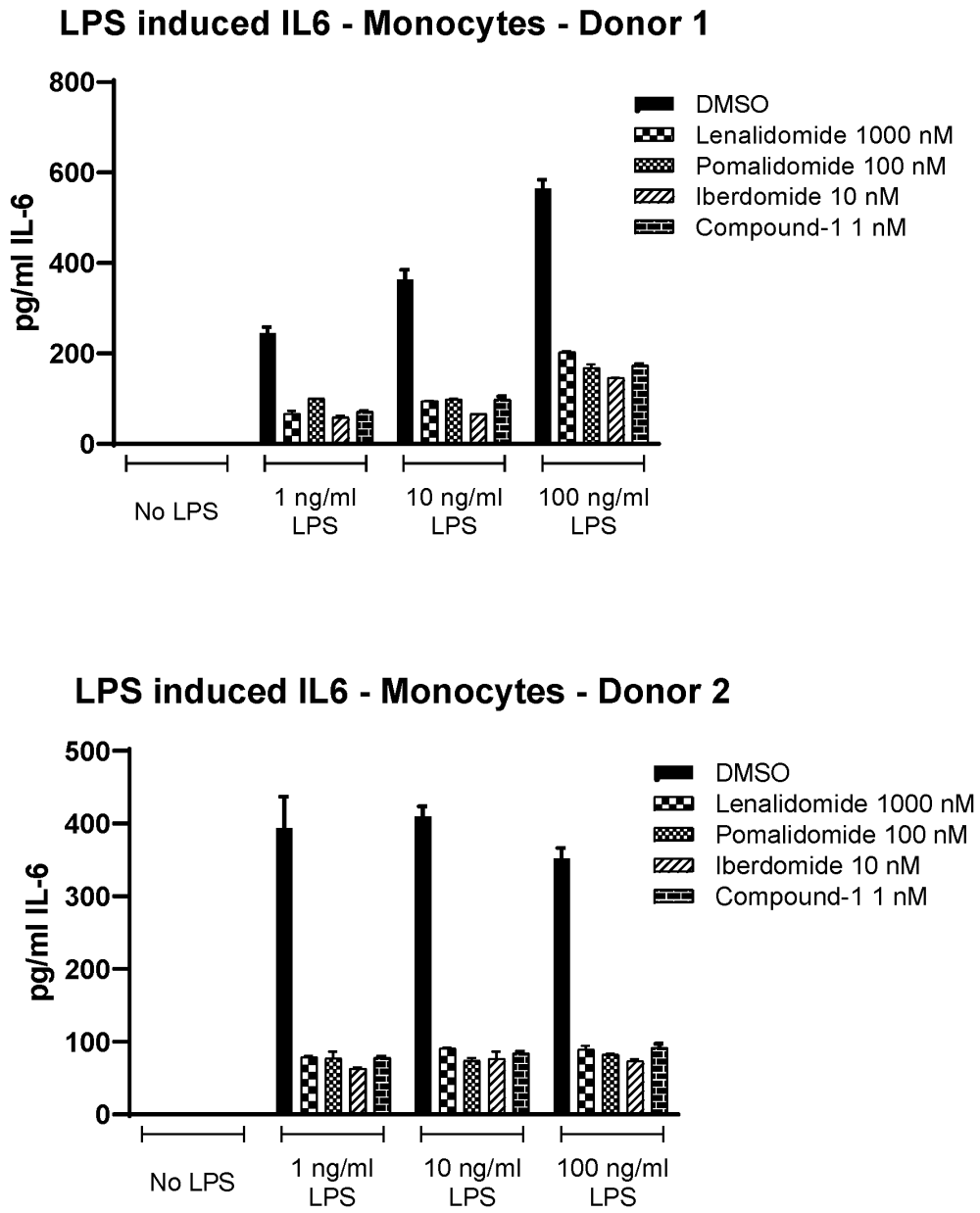
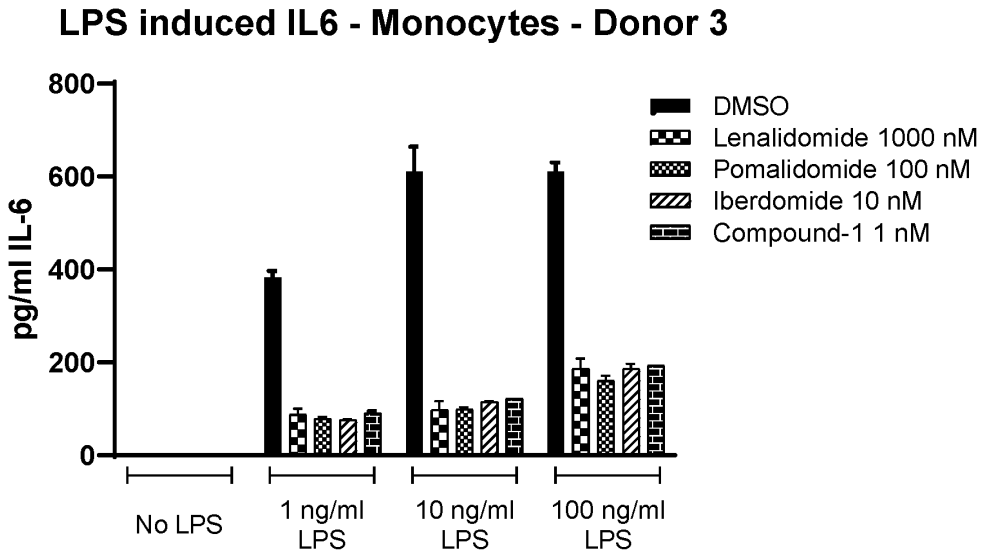

LPS induced IL6 - Monocytes - Donor 1
pg/ml IL-6
800
600
400
200
0
No LPS
1 ng/ml LPS
10 ng/ml LPS
100 ng/ml LPS
DMSO
Lenalidomide 1000 nM
Pomalidomide 100 nM
Iberdomide 10 nM
Compound-1 1 nM
LPS induced IL6 - Monocytes - Donor 2
pg/ml IL-6
500
400
300
200
100
0
No LPS
1 ng/ml LPS
10 ng/ml LPS
100 ng/ml LPS
DMSO
Lenalidomide 1000 nM
Pomalidomide 100 nM
Iberdomide 10 nM
Compound-1 1 nM

Fig. 4 (continued)



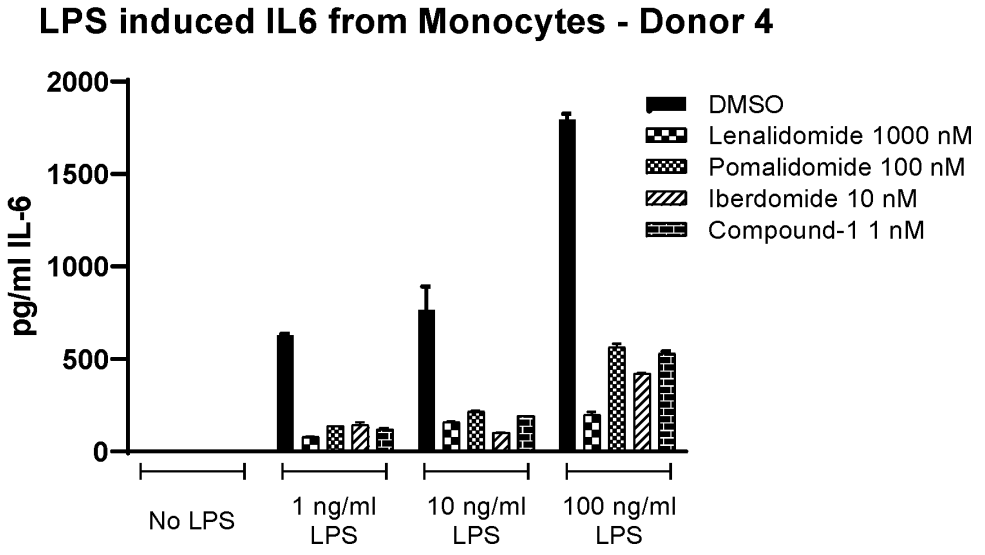
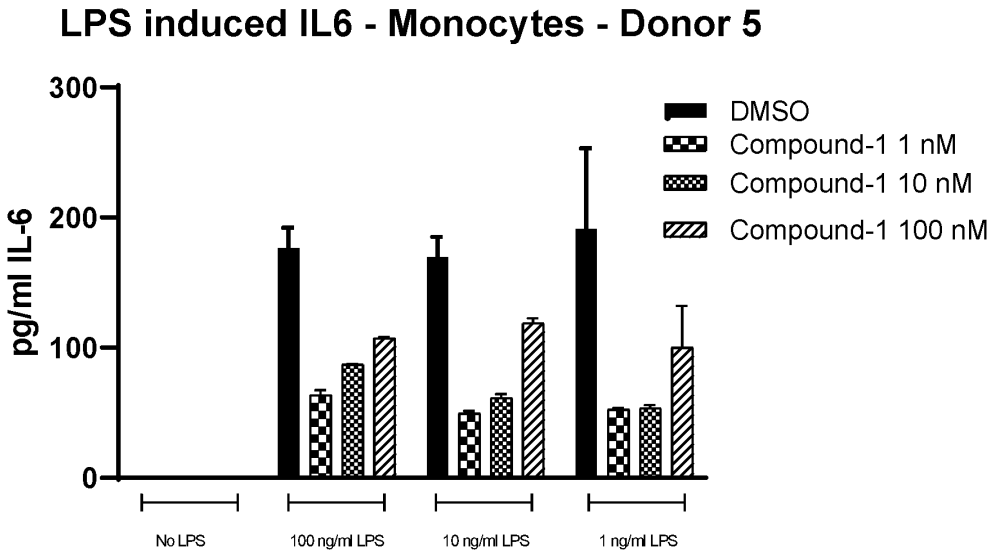


Fig. 5


LPS induced IL6 - Monocytes - Donor 5
pg/ml IL-6
300
200
100
0
DMSO
Compound-1 1 nM
Compound-1 10 nM
Compound-1 100 nM
No LPS
100 ng/ml LPS
10 ng/ml LPS
1 ng/ml LPS

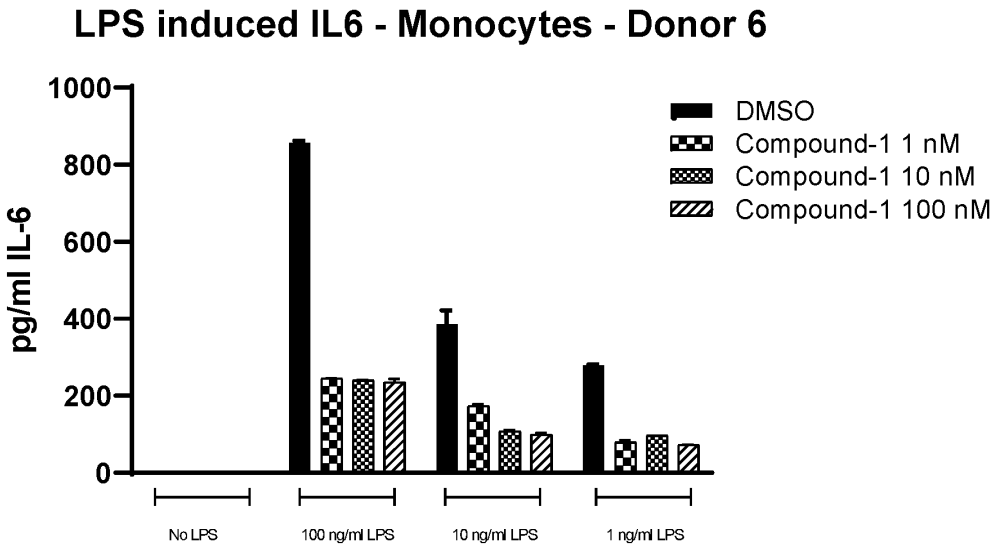
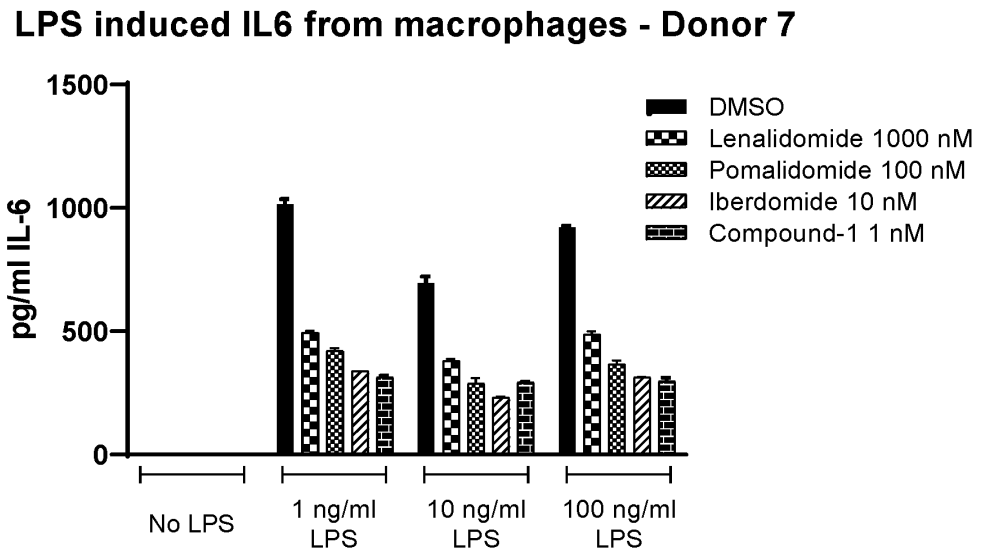

LPS induced IL6 - Monocytes - Donor 6
pg/ml IL-6
1000
800
600
400
200
0
DMSO
Compound-1 1 nM
Compound-1 10 nM
Compound-1 100 nM
No LPS
100 ng/ml LPS
10 ng/ml LPS
1 ng/ml LPS

Fig. 6


LPS induced IL6 from macrophages - Donor 7
pg/ml IL-6
1500
1000
500
0
No LPS
1 ng/ml LPS
10 ng/ml LPS
100 ng/ml LPS
DMSO
Lenalidomide 1000 nM
Pomalidomide 100 nM
Iberdomide 10 nM
Compound-1 1 nM

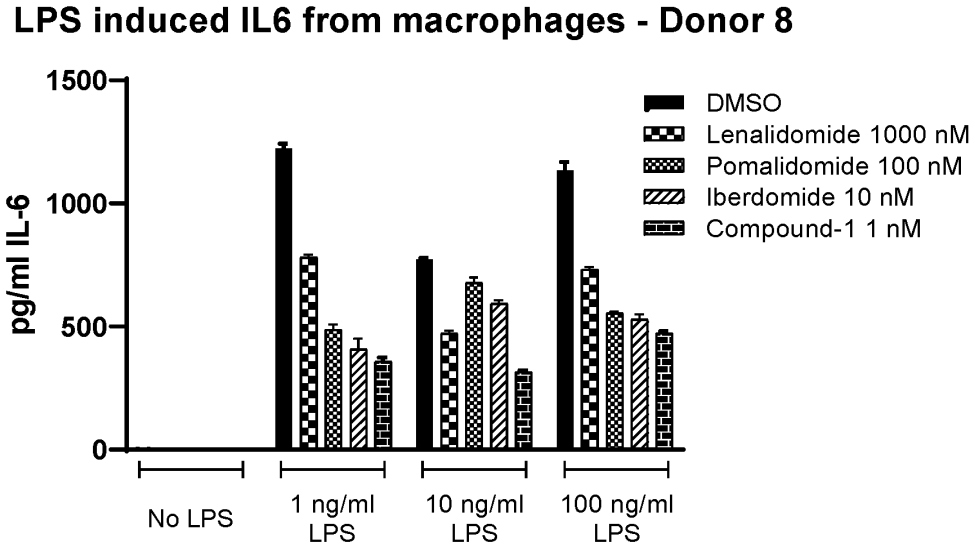

LPS induced IL6 from macrophages - Donor 8
pg/ml IL-6
1500
1000
500
0
No LPS
1 ng/ml LPS
10 ng/ml LPS
100 ng/ml LPS
DMSO
Lenalidomide 1000 nM
Pomalidomide 100 nM
Iberdomide 10 nM
Compound-1 1 nM

Fig. 7

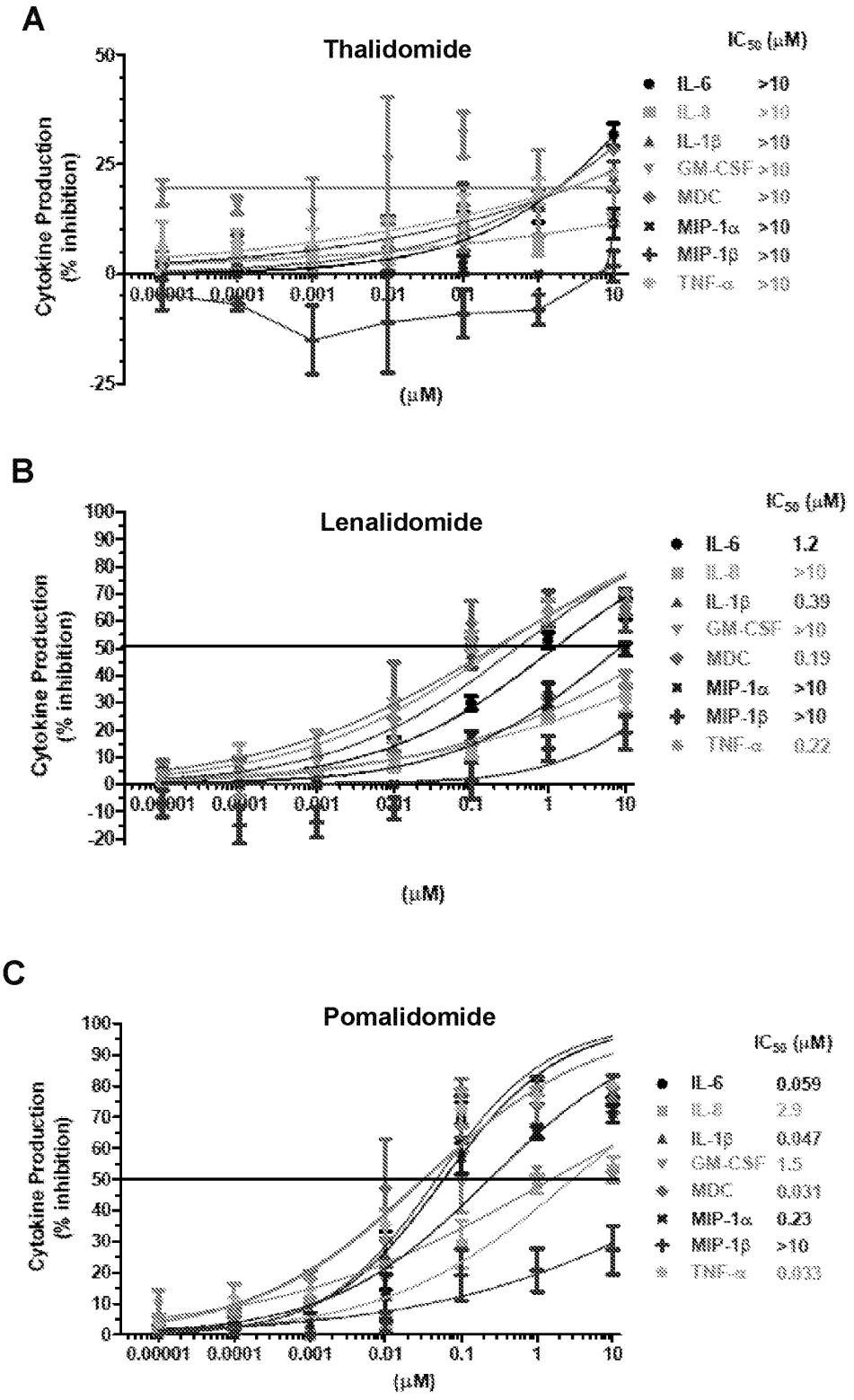

A
Thalidomide
IC50 (μM)
IL-6 >10
IL-8 >10
IL-1β >10
GM-CSF >10
MDC >10
MIP-1α >10
MIP-1β >10
TNF-α >10
Cytokine Production (% inhibition)
50
25
0
-25
0.00001 0.0001 0.001 0.01 0.1 1 10
(μM)
B
Lenalidomide
IC50 (μM)
IL-6 1.2
IL-8 >10
IL-1β 0.39
GM-CSF >10
MDC 0.19
MIP-1α >10
MIP-1β >10
TNF-α 0.22
Cytokine Production (% inhibition)
100 90 80 70 60 50 40 30 20 10 0 -10 -20
0.00001 0.0001 0.001 0.01 0.1 1 10
(μM)
C
Pomalidomide
IC50 (μM)
IL-6 0.059
IL-8 2.9
IL-1β 0.047
GM-CSF 1.5
MDC 0.031
MIP-1α 0.23
MIP-1β >10
TNF-α 0.033
Cytokine Production (% inhibition)
100 90 80 70 60 50 40 30 20 10 0
0.00001 0.0001 0.001 0.01 0.1 1 10
(μM)

Fig. 8

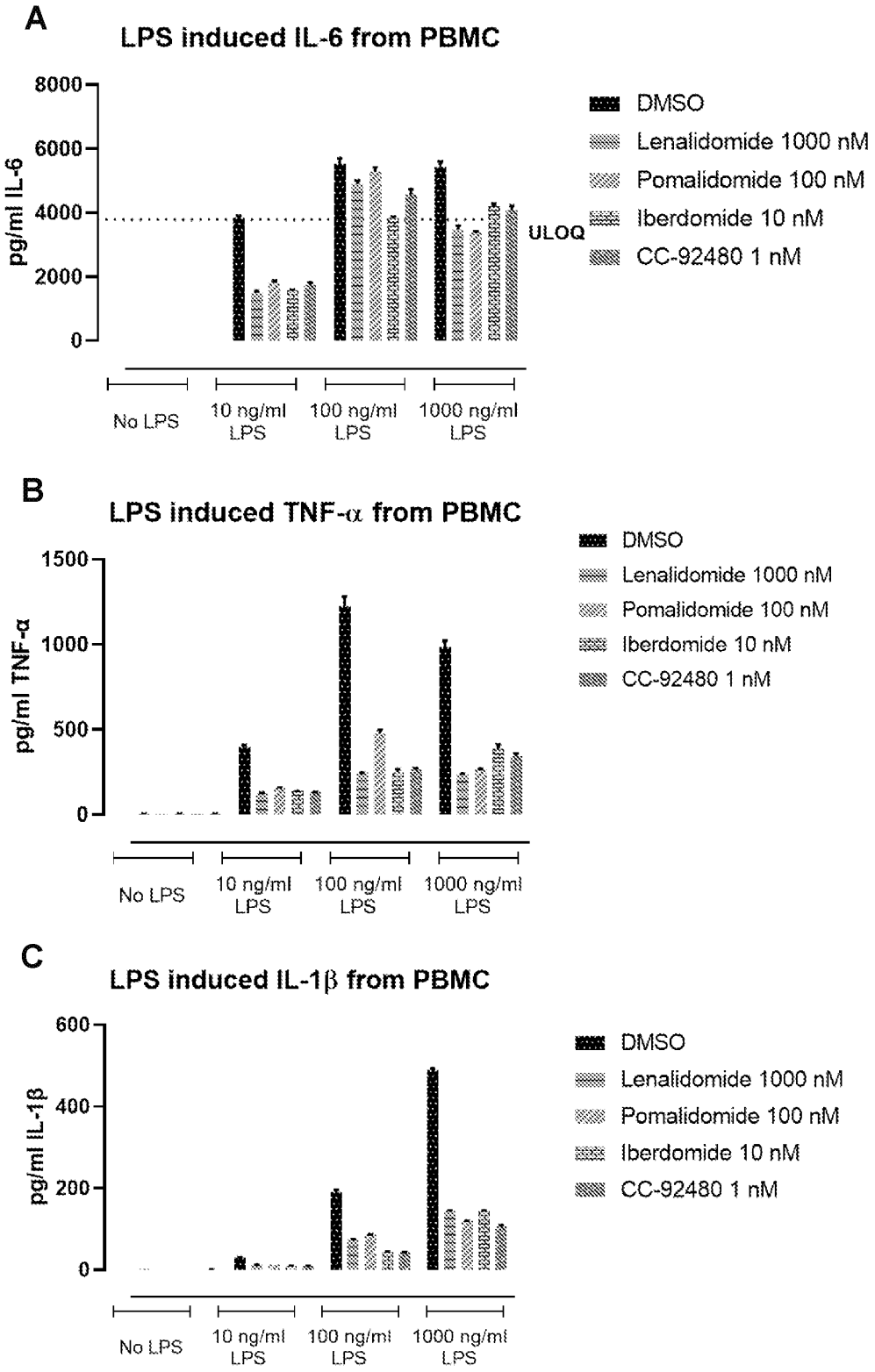
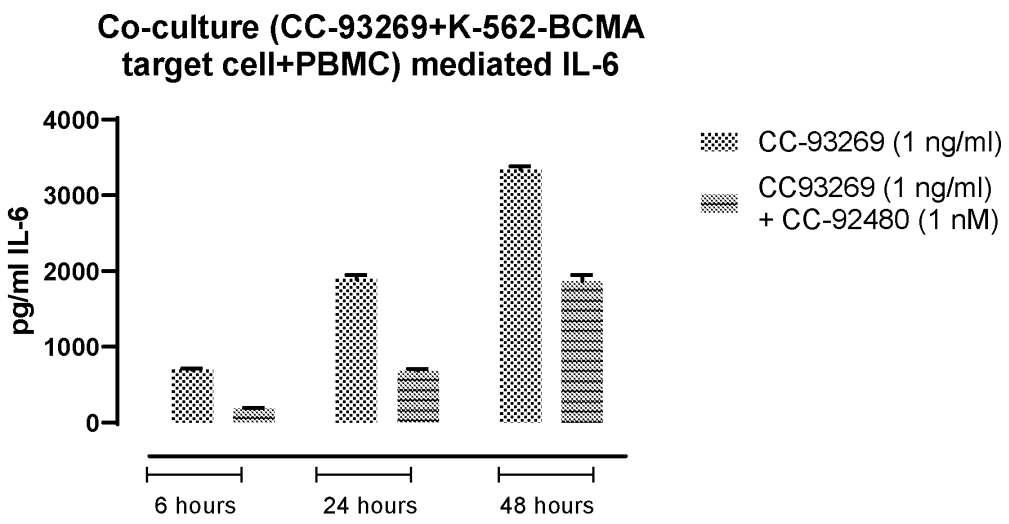

A
LPS induced IL-6 from PBMC
pg/ml IL-6
8000
6000
4000
2000
0
ULOQ
No LPS
10 ng/ml LPS
100 ng/ml LPS
1000 ng/ml LPS
DMSO
Lenalidomide 1000 nM
Pomalidomide 100 nM
Iberdomide 10 nM
CC-92480 1 nM
B
LPS induced TNF-α from PBMC
pg/ml TNF-α
1500
1000
500
0
No LPS
10 ng/ml LPS
100 ng/ml LPS
1000 ng/ml LPS
DMSO
Lenalidomide 1000 nM
Pomalidomide 100 nM
Iberdomide 10 nM
CC-92480 1 nM
C
LPS induced IL-1β from PBMC
pg/ml IL-1β
600
400
200
0
No LPS
10 ng/ml LPS
100 ng/ml LPS
1000 ng/ml LPS
DMSO
Lenalidomide 1000 nM
Pomalidomide 100 nM
Iberdomide 10 nM
CC-92480 1 nM

Fig. 9

A


Co-culture (CC-93269+K-562-BCMA target cell+PBMC) mediated IL-6
pg/ml IL-6
4000
3000
2000
1000
0
6 hours
24 hours
48 hours
CC-93269 (1 ng/ml)
CC93269 (1 ng/ml) + CC-92480 (1 nM)

B

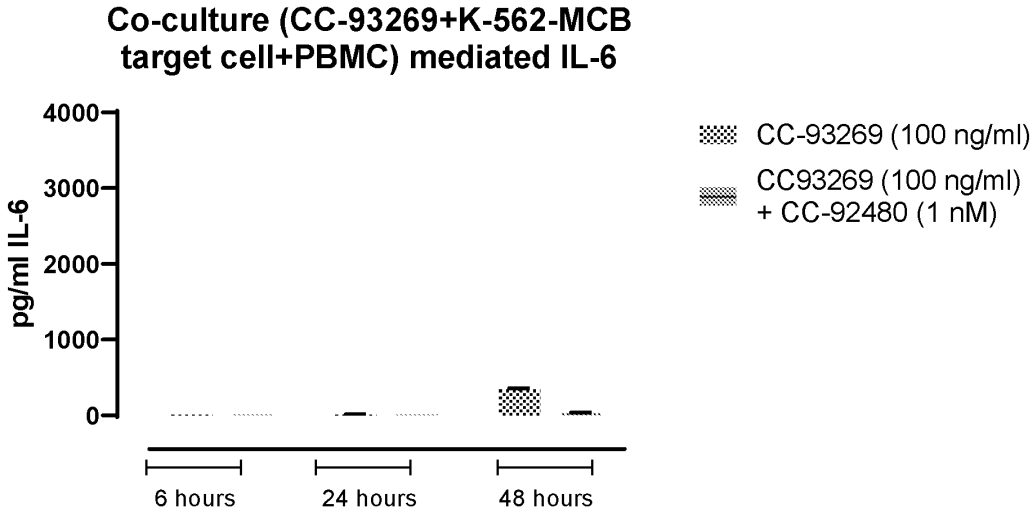
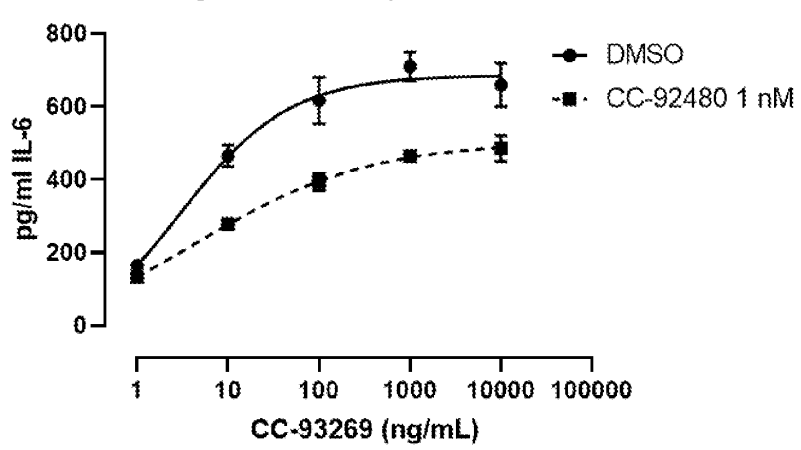

Co-culture (CC-93269+K-562-MCB target cell+PBMC) mediated IL-6
pg/ml IL-6
4000
3000
2000
1000
0
6 hours
24 hours
48 hours
CC-93269 (100 ng/ml)
CC93269 (100 ng/ml) + CC-92480 (1 nM)

Fig. 10

A


Co-culture (CC-93269+K-562-BCMA target cell+PBMC) mediated IL-6
pg/ml IL-6
800
600
400
200
0
DMSO
CC-92480 1 nM
1
10
100
1000
10000
100000
CC-93269 (ng/mL)

B

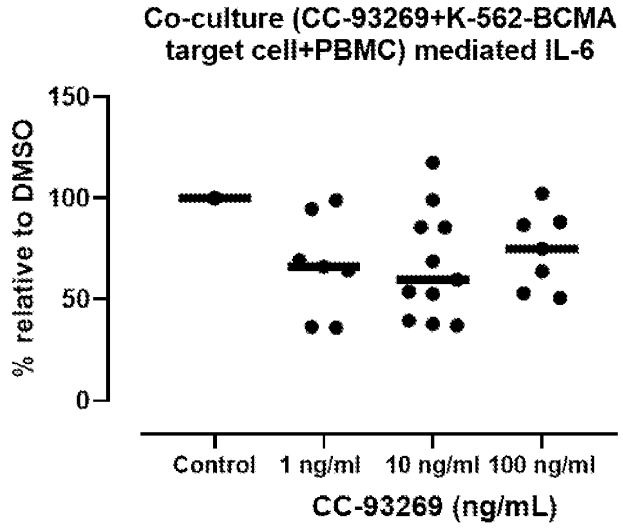

Co-culture (CC-93269+K-562-BCMA target cell+PBMC) mediated IL-6
% relative to DMSO
150
100
50
0
Control
1 ng/ml
10 ng/ml
100 ng/ml
CC-93269 (ng/mL)

Fig. 11

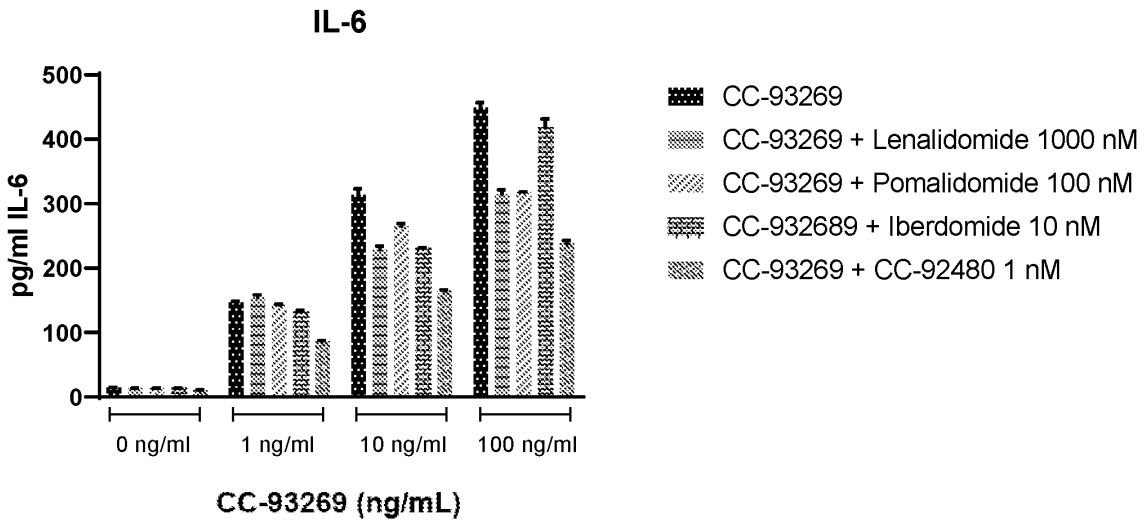
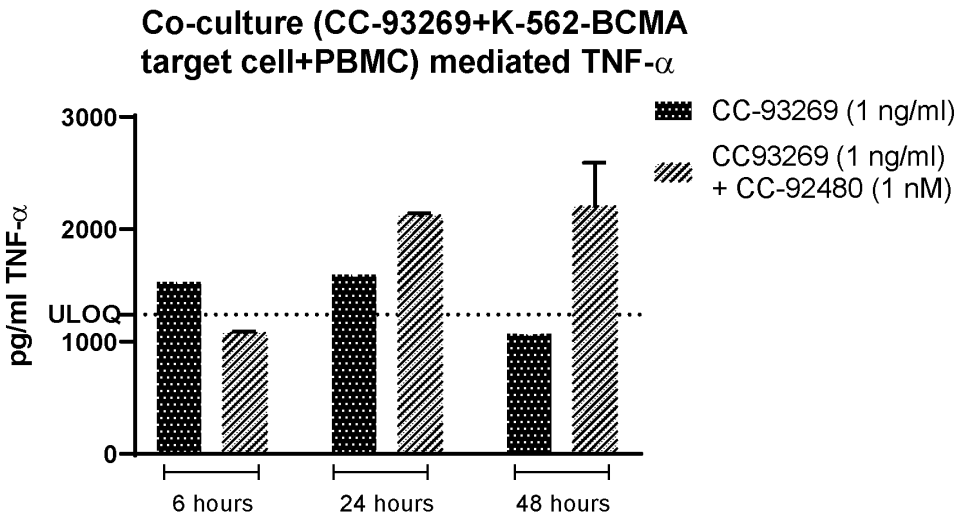

IL-6
500
400
300
200
100
0
pg/ml IL-6
0 ng/ml
1 ng/ml
10 ng/ml
100 ng/ml
CC-93269 (ng/mL)
CC-93269
CC-93269 + Lenalidomide 1000 nM
CC-93269 + Pomalidomide 100 nM
CC-932689 + Iberdomide 10 nM
CC-93269 + CC-92480 1 nM

Fig. 12

A


Co-culture (CC-93269+K-562-BCMA target cell+PBMC) mediated TNF-α
pg/ml TNF-α
3000
2000
ULOQ
1000
0
6 hours
24 hours
48 hours
CC-93269 (1 ng/ml)
CC93269 (1 ng/ml) + CC-92480 (1 nM)

B

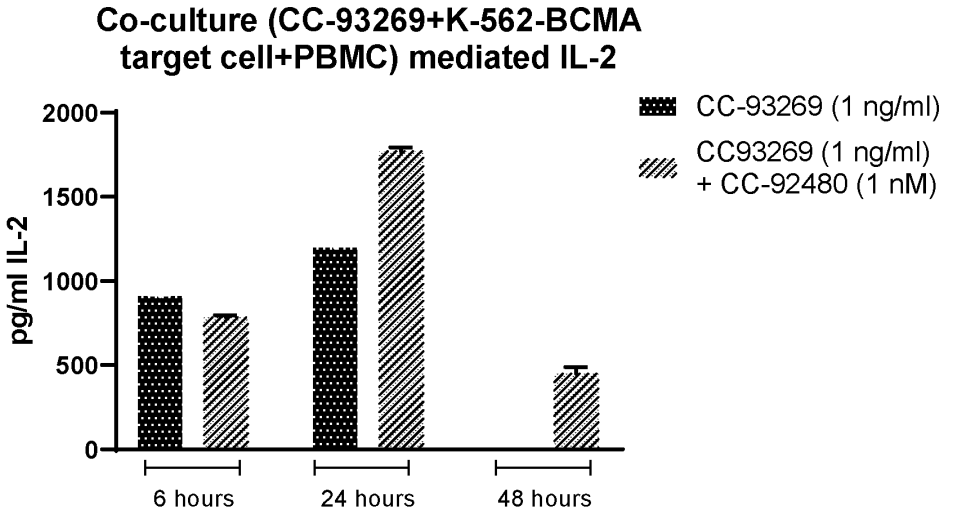
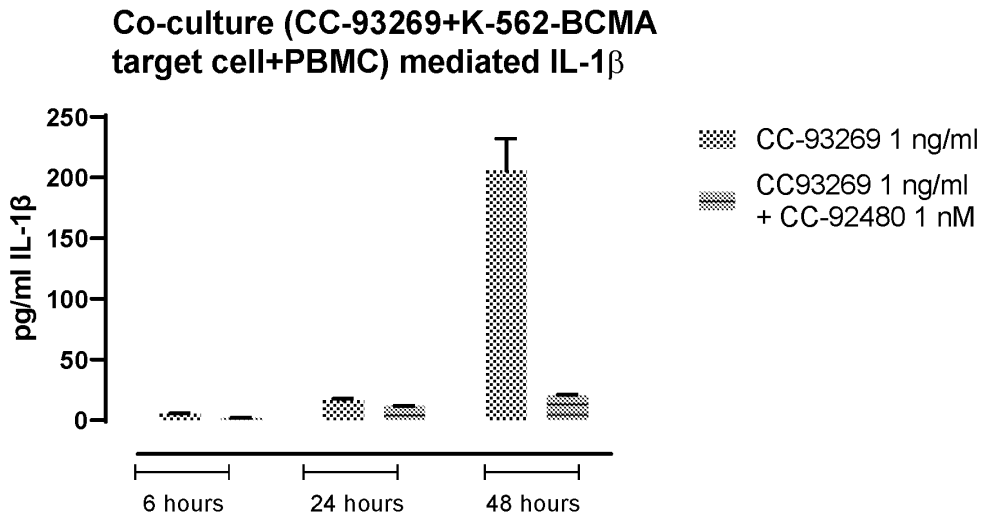

Co-culture (CC-93269+K-562-BCMA target cell+PBMC) mediated IL-2
pg/ml IL-2
2000
1500
1000
500
0
6 hours
24 hours
48 hours
CC-93269 (1 ng/ml)
CC93269 (1 ng/ml) + CC-92480 (1 nM)

Fig. 13

A


Co-culture (CC-93269+K-562-BCMA target cell+PBMC) mediated IL-1β
pg/ml IL-1β
250
200
150
100
50
0
6 hours
24 hours
48 hours
CC-93269 1 ng/ml
CC93269 1 ng/ml + CC-92480 1 nM

B

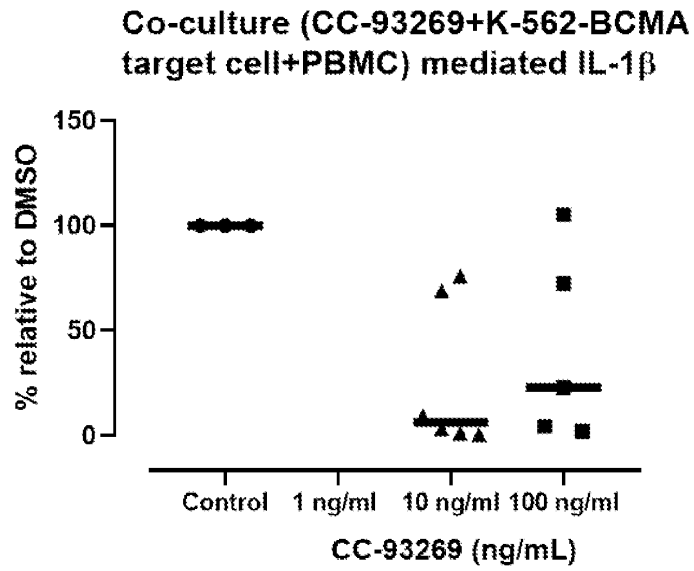
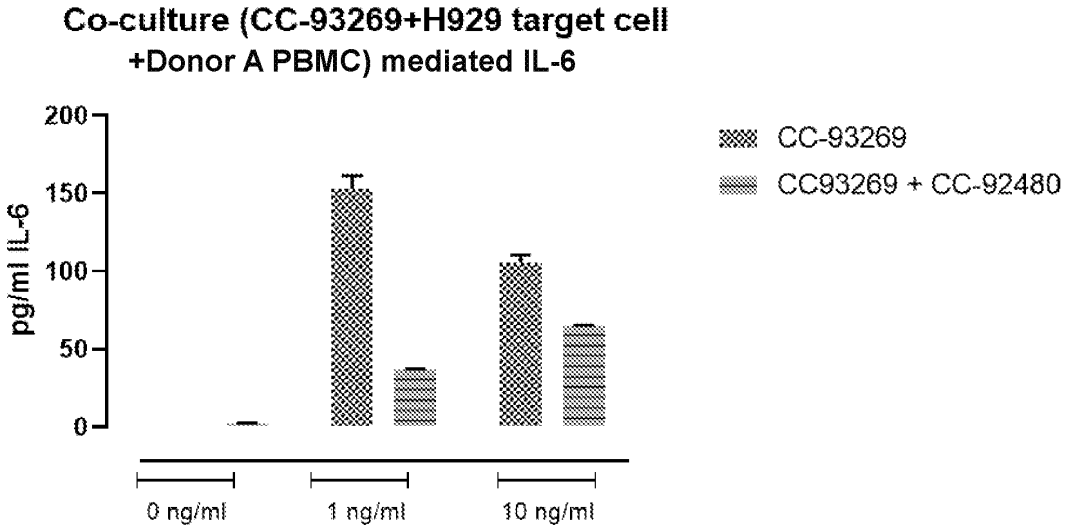

Co-culture (CC-93269+K-562-BCMA target cell+PBMC) mediated IL-1β
% relative to DMSO
150
100
50
0
Control
1 ng/ml
10 ng/ml
100 ng/ml
CC-93269 (ng/mL)

Fig. 14

A


Co-culture (CC-93269+H929 target cell
+Donor A PBMC) mediated IL-6
pg/ml IL-6
200
150
100
50
0
0 ng/ml
1 ng/ml
10 ng/ml
CC-93269
CC93269 + CC-92480

B

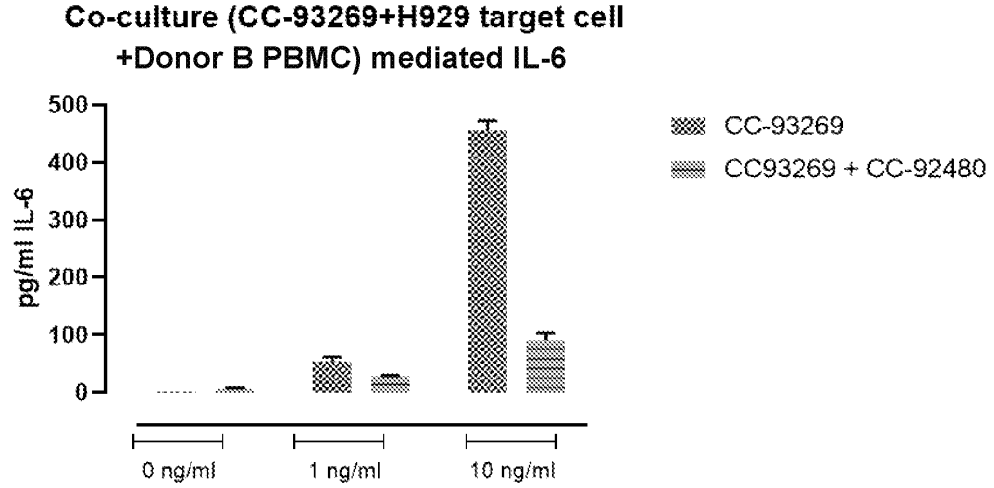
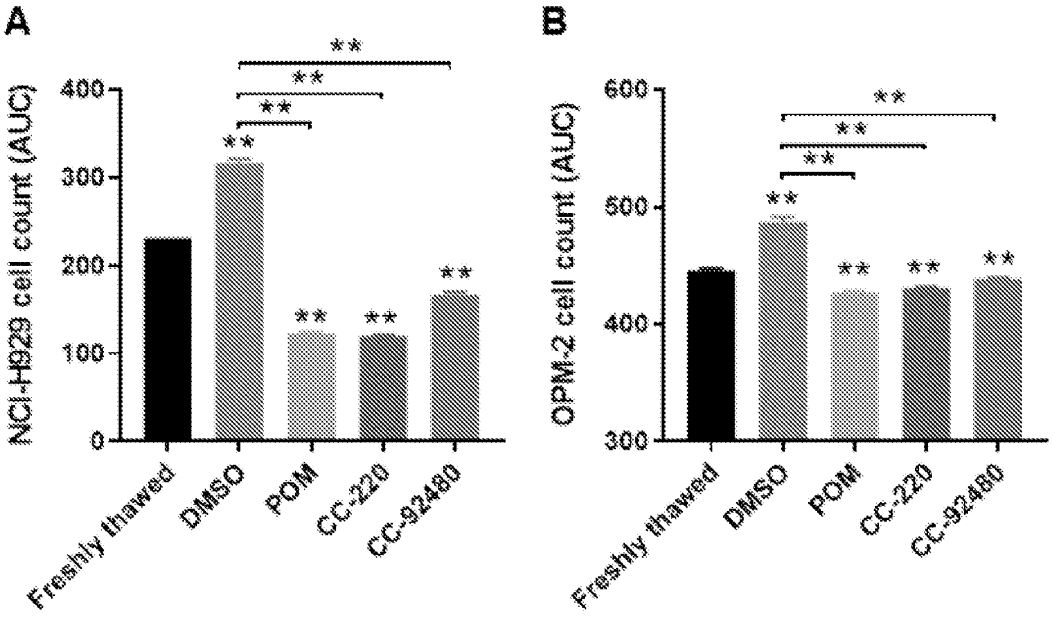

Co-culture (CC-93269+H929 target cell
+Donor B PBMC) mediated IL-6
pg/ml IL-6
500
400
300
200
100
0
0 ng/ml
1 ng/ml
10 ng/ml
CC-93269
CC93269 + CC-92480

Fig. 15


A
NCI-H929 cell count (AUC)
400
300
200
100
0
**
Freshly thawed
DMSO
POM
CC-220
CC-92480
B
OPM-2 cell count (AUC)
600
500
400
300