
CVID
XLA
group
CCL19
IL-12B
4E-BP1
TNFRSF9
CXCL9
IFN-gamma
CD8A
CDCP1
TNF
IL10
CCL3
CD5
TNFB
ST1A1
CD6
IL18
Flt3L
IL-15RA
PD-L1
ADA
CD40
CCL23
SLAMF1
IL-22 RA1
CSF-1
NT-3
TWEAK
VEGFA
DNER
CCL28
SCF
MCP-2
MCP-4
EN-RAGE
IL7
CXCL5
CXCL10
IL-17A
IL8
TRANCE
IL-18R1
CXCL11
AXIN1
CCL20
SIRT2
CASP-8
IL6
uPA
STAMBP
CCL25
IL-24
LIF-R
FGF-23
IL-10RB
CCL4
FGF-21
CXCL6
TNFSF14
LIF
CCL11
IL-10RA
GDNF
IL33
Beta-NGF
FGF-5
IL-20
NRTN
LAP TGF-beta-1
IL13
TRAIL
IL-1 alpha
TSLP
HGF
IL4
IL2
ARTN
IL-20RA
CD244
IL-2RB
MMP-10
CX3CL1
CXCL1
OPG
MCP-1
OSM
CST5
IL-17C
TGF-alpha
FGF-19
MCP-3
IL5
MMP-1
-1
-0.5
0
0.5
1

FIG. 1A

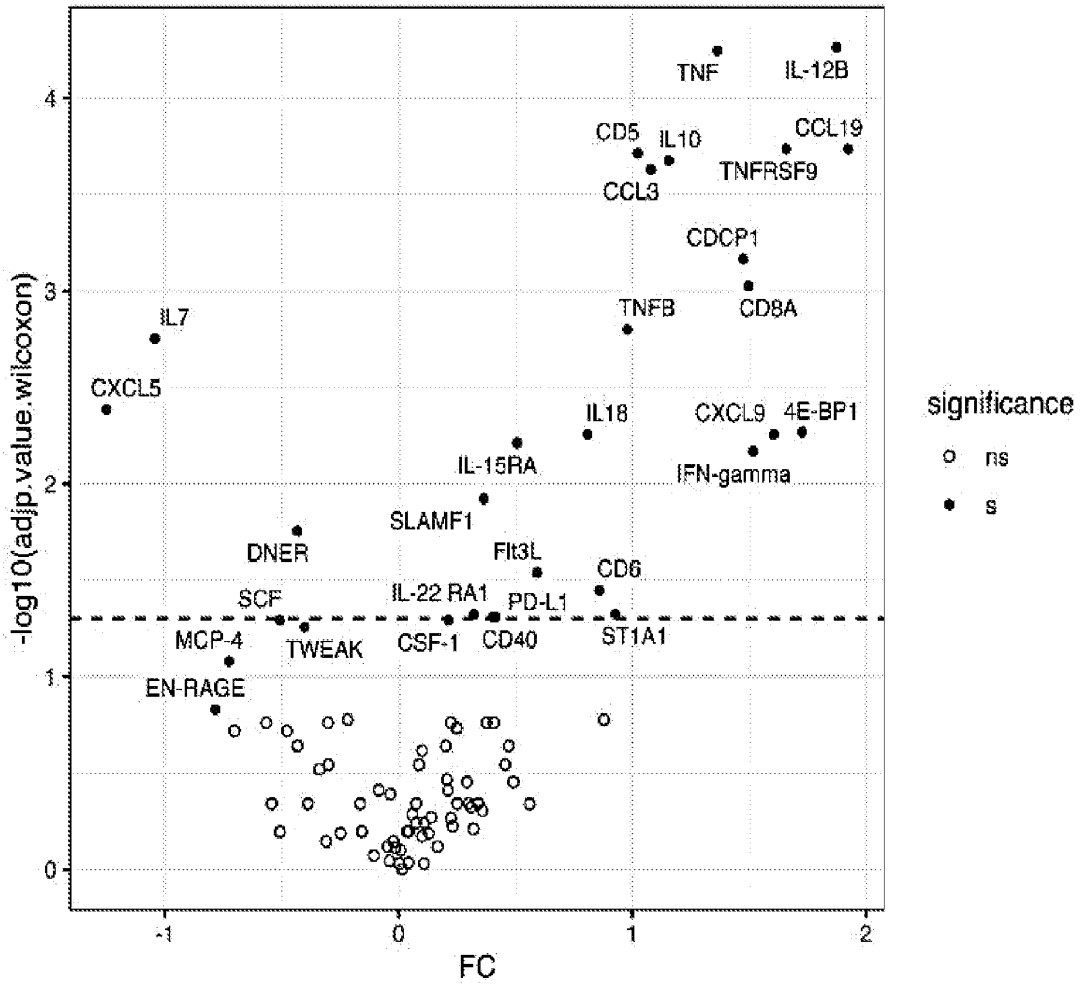

-log10(adjp.value.wilcoxon)
FC
significance
ns
s
TNF
IL-12B
CD5
IL10
CCL19
TNFRSF9
CCL3
CDCP1
CD8A
TNFB
IL7
CXCL5
IL18
CXCL9
4E-BP1
IL-15RA
IFN-gamma
SLAMF1
DNER
Flt3L
CD6
SCF
IL-22 RA1
PD-L1
MCP-4
TWEAK
CSF-1
CD40
ST1A1
EN-RAGE

FIG. 1B

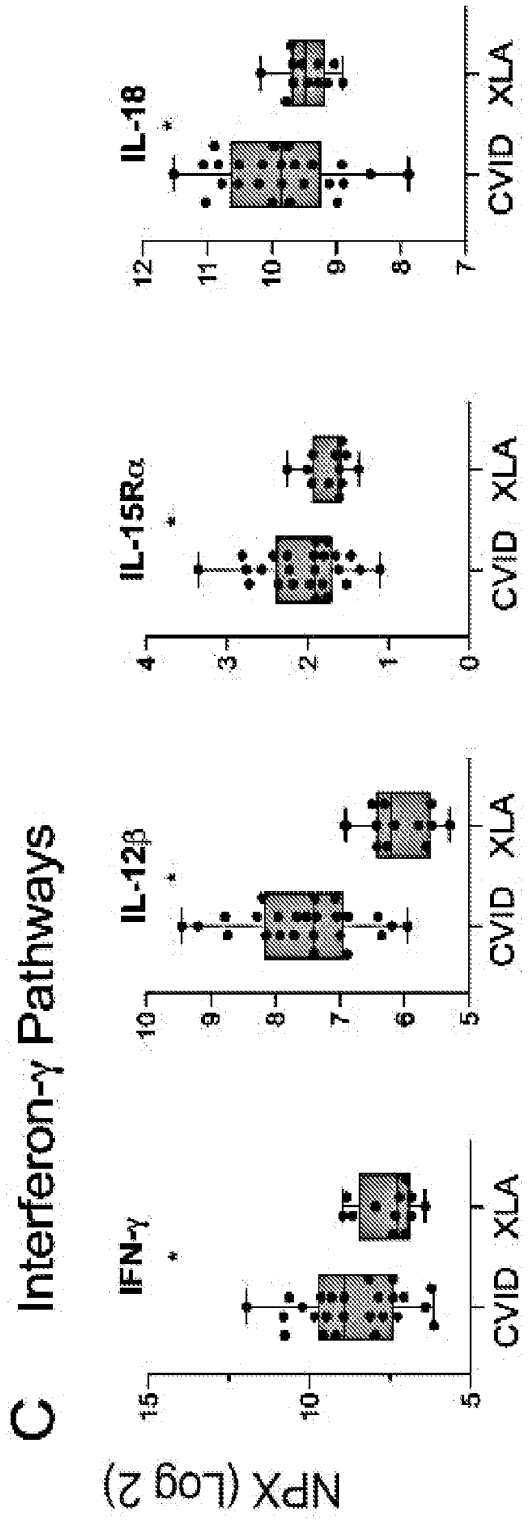

C
Interferon-γ Pathways
NPX (Log 2)
IFN-γ
IL-12β
IL-15Rα
IL-18
CVID
XLA

FIG. 1C

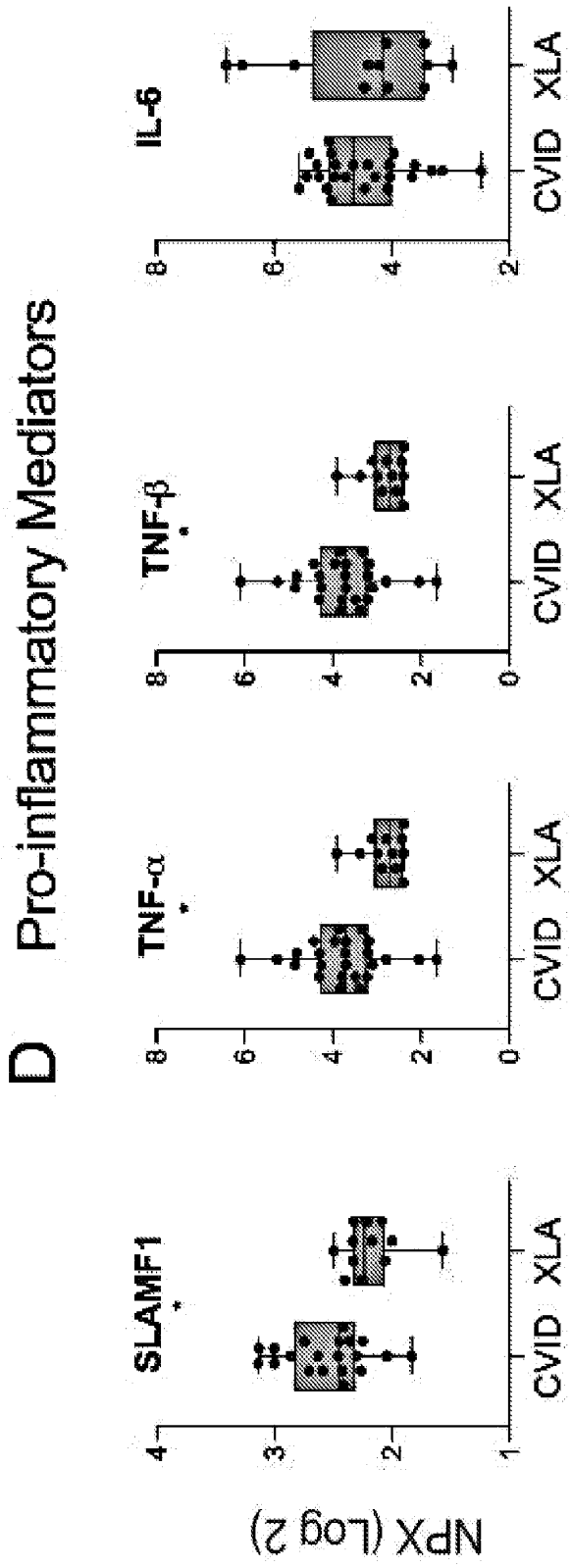

D
Pro-inflammatory Mediators
NPX (Log 2)
SLAMF1
*
TNF-α
*
TNF-β
*
IL-6
CVID
XLA

FIG. 1D

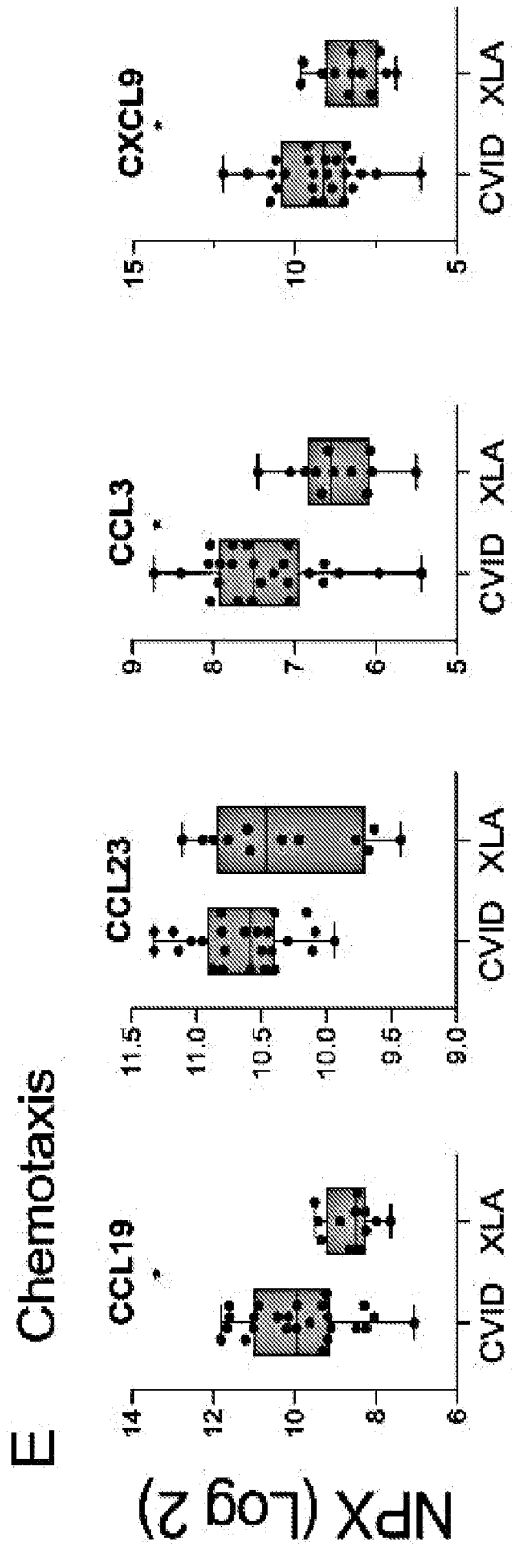


FIG. 1E

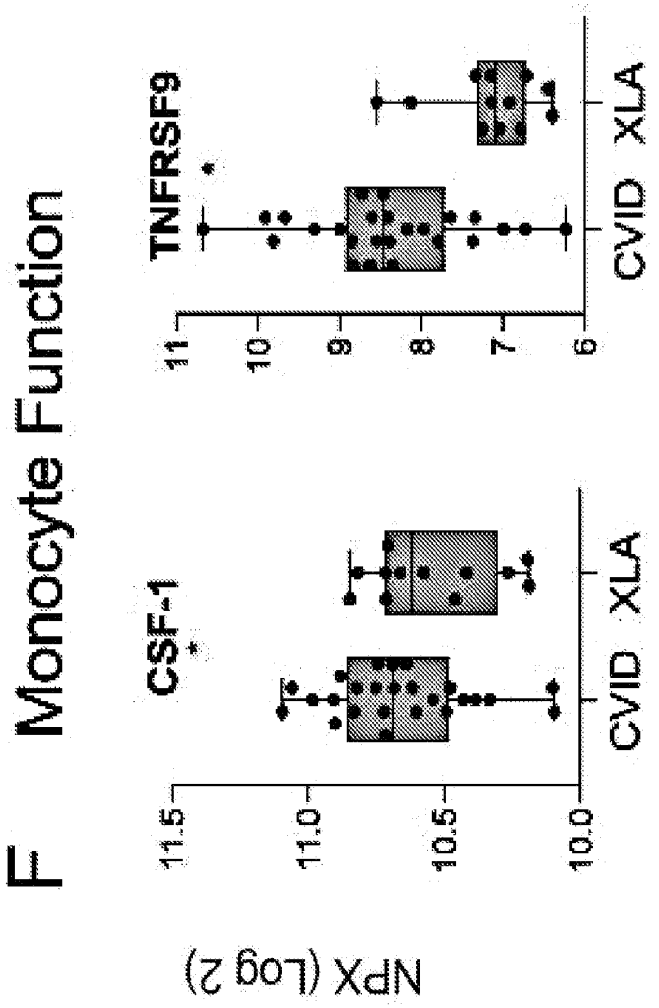

F
Monocyte Function
CSF-1
TNFRSF9
NPX (Log 2)
11.5
11.0
10.5
10.0
11
10
9
8
7
6
CVID
XLA
CVID
XLA

FIG. 1F

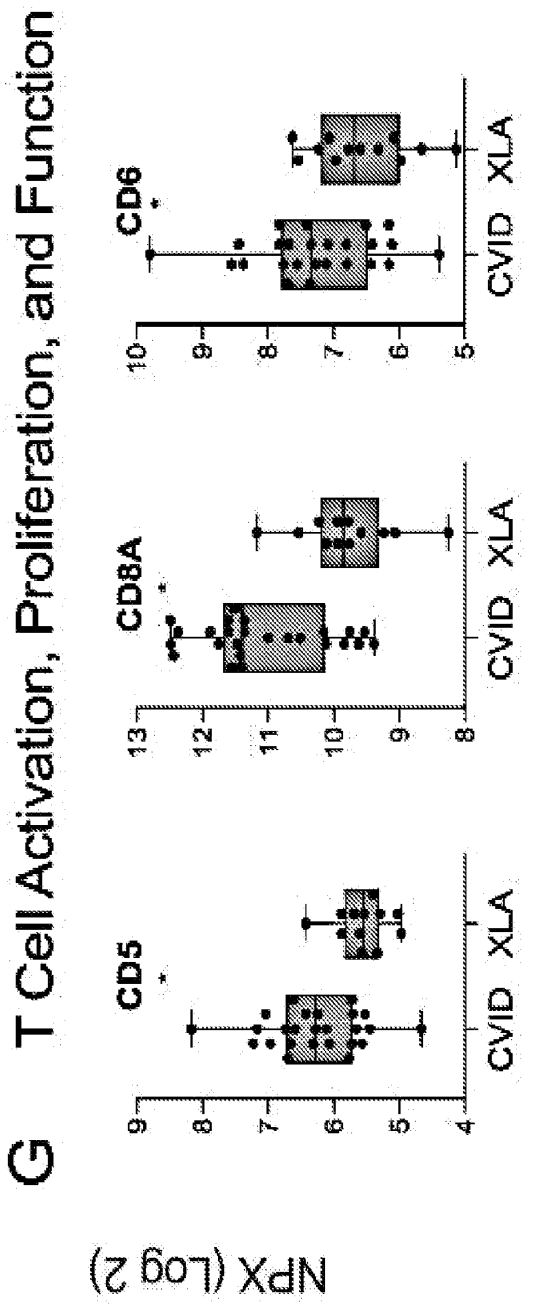

G T Cell Activation, Proliferation, and Function
NPX (Log 2)
CD5
CD8A
CD6
CVID XLA
CVID XLA
CVID XLA

FIG. 1G

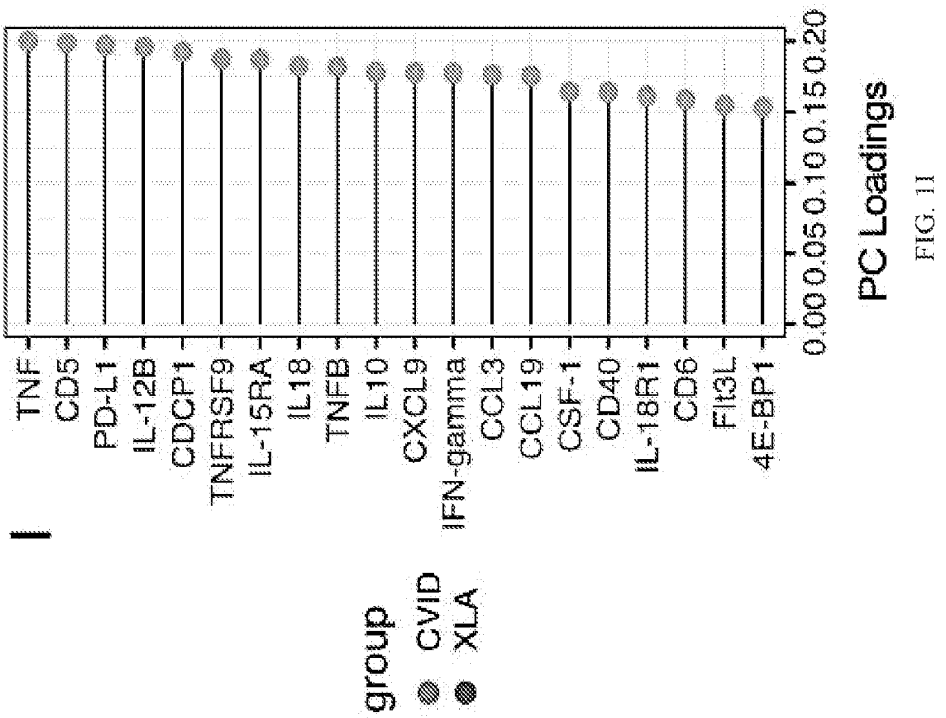

I
TNF
CD5
PD-L1
IL-12B
CDCP1
TNFRSF9
IL-15RA
IL18
TNFB
IL10
CXCL9
IFN-gamma
CCL3
CCL19
CSF-1
CD40
IL-18R1
CD6
Flt3L
4E-BP1
0.00 0.05 0.10 0.15 0.20
PC Loadings
group
CVID
XLA

FIG. 1I

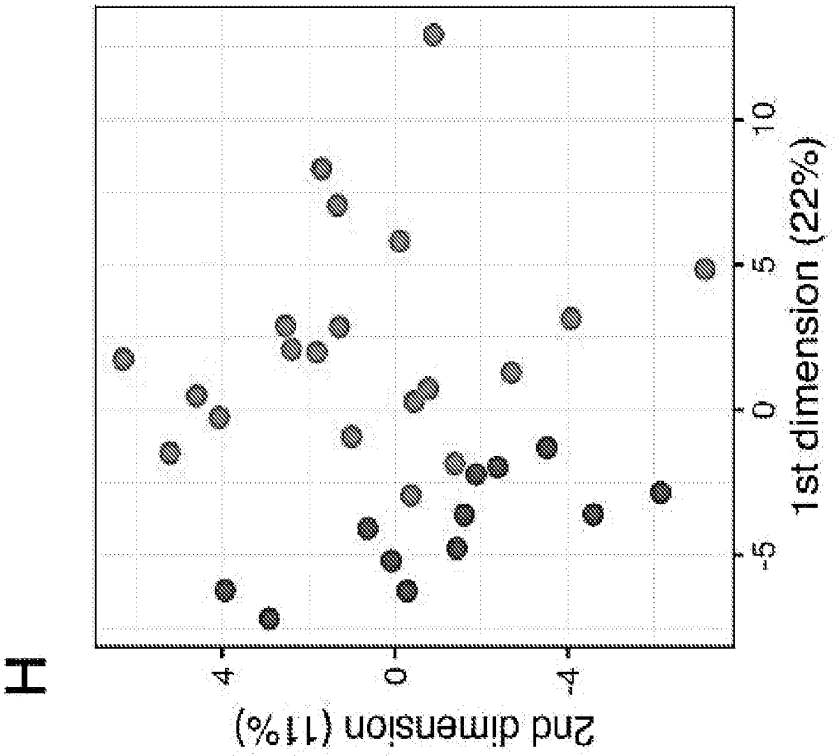

H
2nd dimension (11%)
4
0
-4
-5
0
5
10
1st dimension (22%)

FIG. 1H

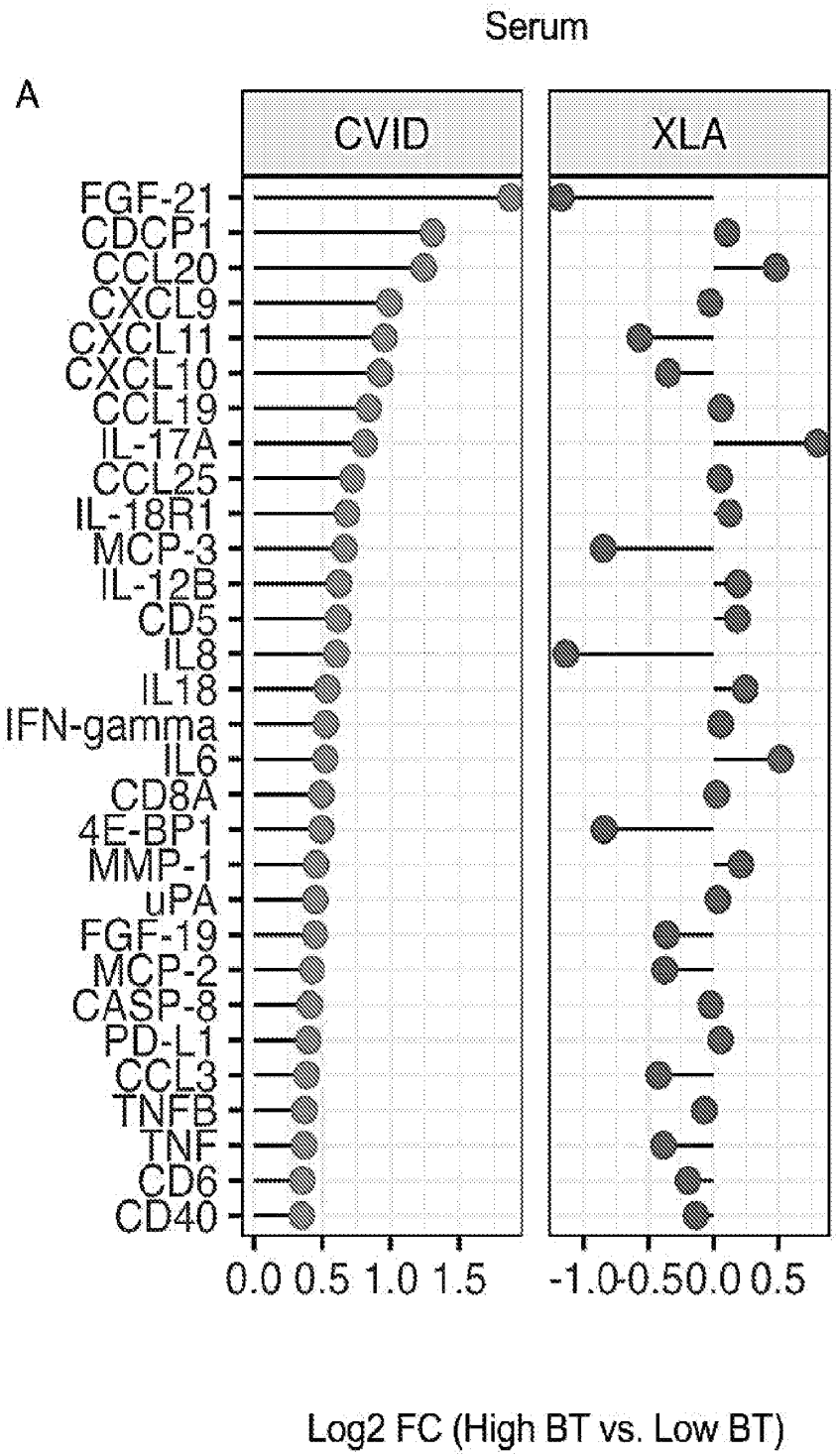

Serum
A
CVID
XLA
FGF-21
CDCP1
CCL20
CXCL9
CXCL11
CXCL10
CCL19
IL-17A
CCL25
IL-18R1
MCP-3
IL-12B
CD5
IL8
IL18
IFN-gamma
IL6
CD8A
4E-BP1
MMP-1
uPA
FGF-19
MCP-2
CASP-8
PD-L1
CCL3
TNFB
TNF
CD6
CD40
0.0 0.5 1.0 1.5
-1.0-0.50.0 0.5
Log2 FC (High BT vs. Low BT)

FIG. 2A

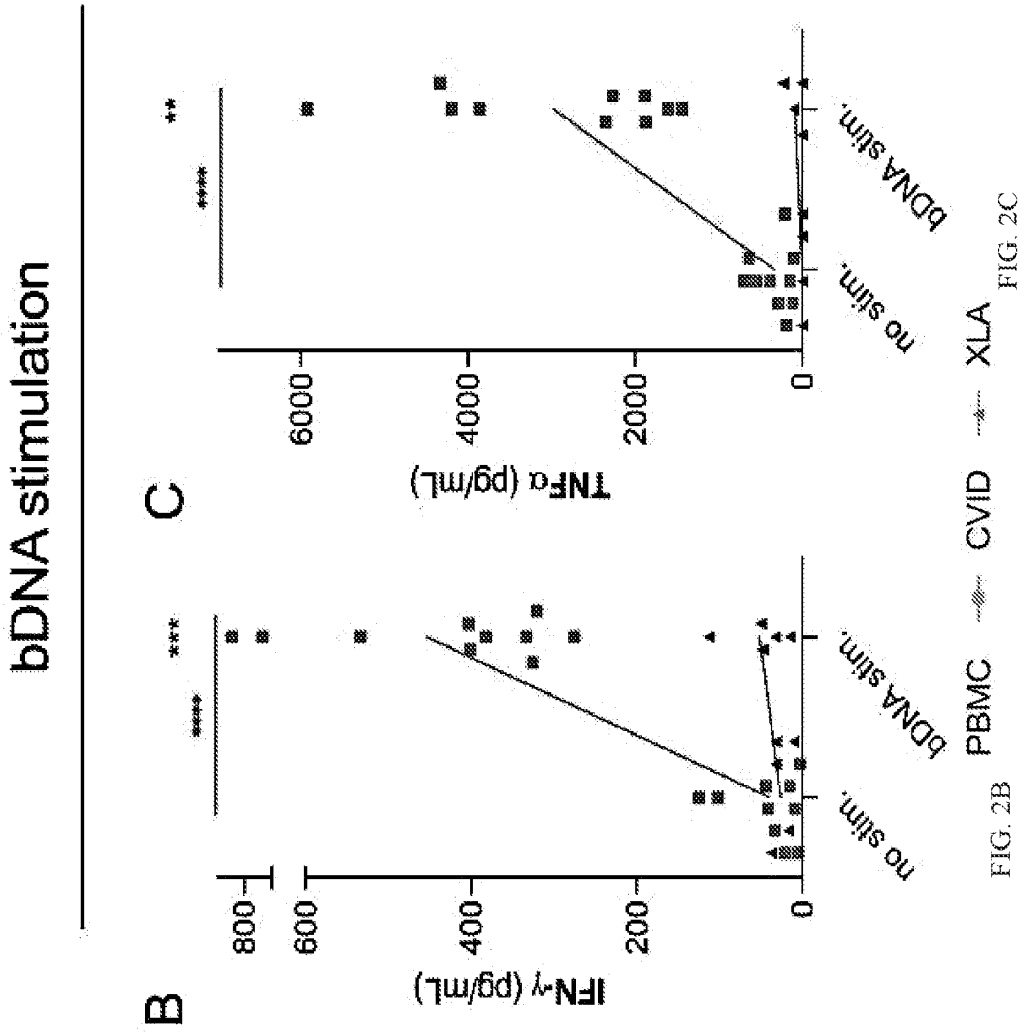

bDNA stimulation
B
IFN-γ (pg/mL)
800
600
400
200
0
****
***
no stim.
bDNA stim.
C
TNFα (pg/mL)
6000
4000
2000
0
****
**
no stim.
bDNA stim.
PBMC
CVID
XLA

FIG. 2B

FIG. 2C

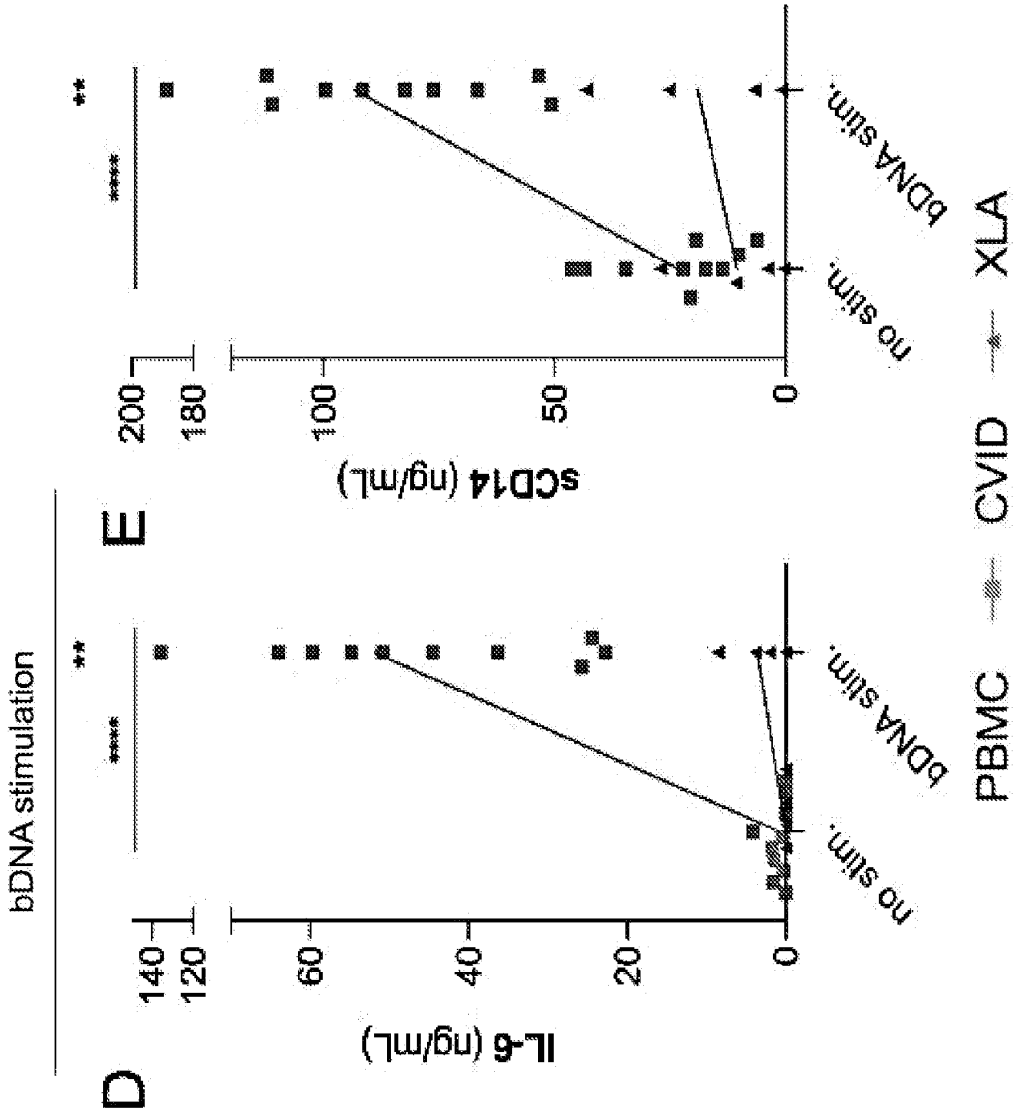

bDNA stimulation
D
IL-6 (ng/mL)
140
120
60
40
20
0
****
**
no stim.
bDNA stim.
PBMC
CVID
XLA

FIG. 2D

E
sCD14 (ng/mL)
200
180
100
50
0
****
**
no stim.
bDNA stim.
PBMC
CVID
XLA

FIG. 2E

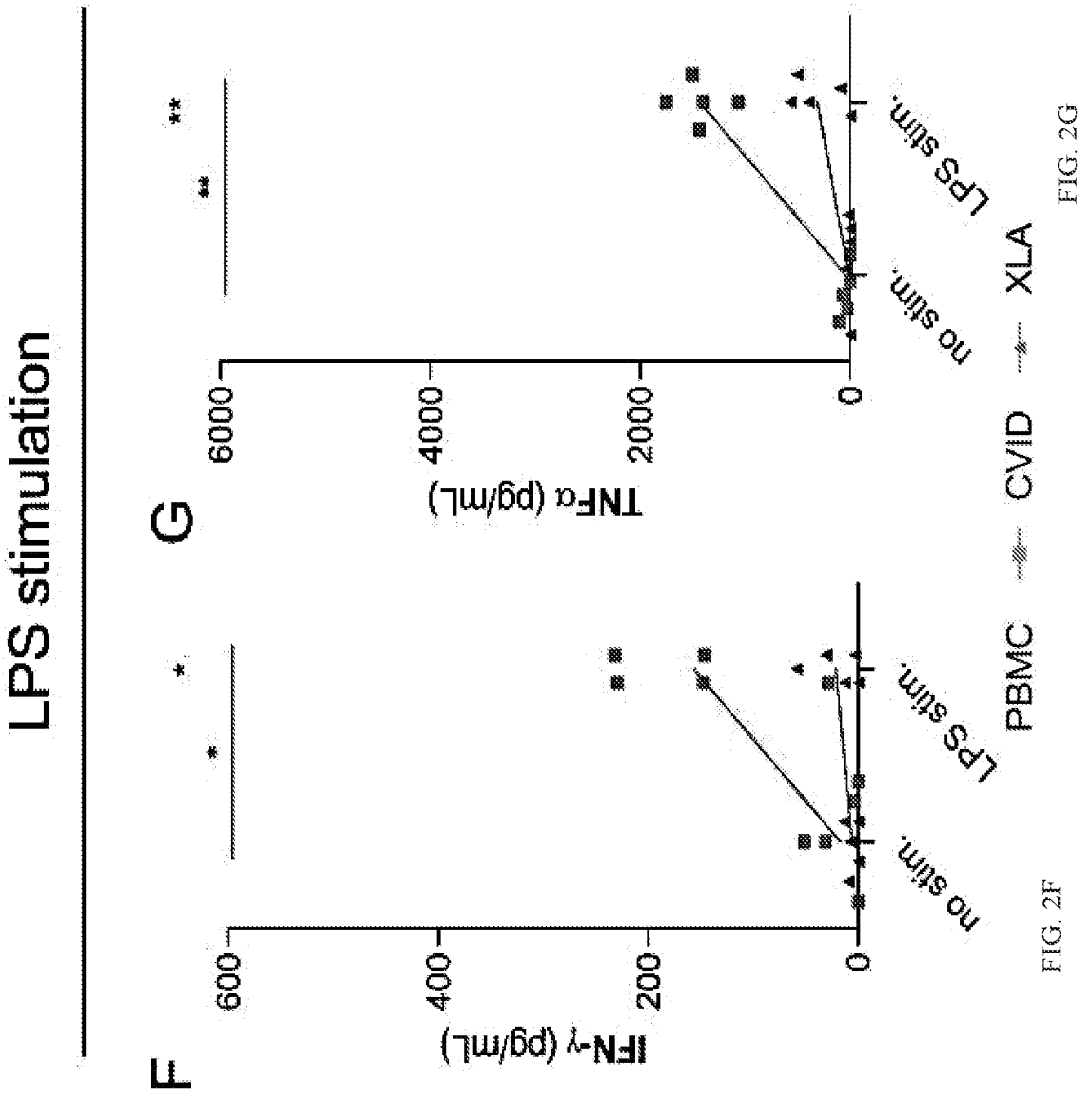

LPS stimulation
F
IFN-γ (pg/mL)
600
400
200
0
*
*
no stim.
LPS stim.
PBMC
CVID
XLA
G
TNFα (pg/mL)
6000
4000
2000
0
**
**
no stim.
LPS stim.

FIG. 2F

FIG. 2G

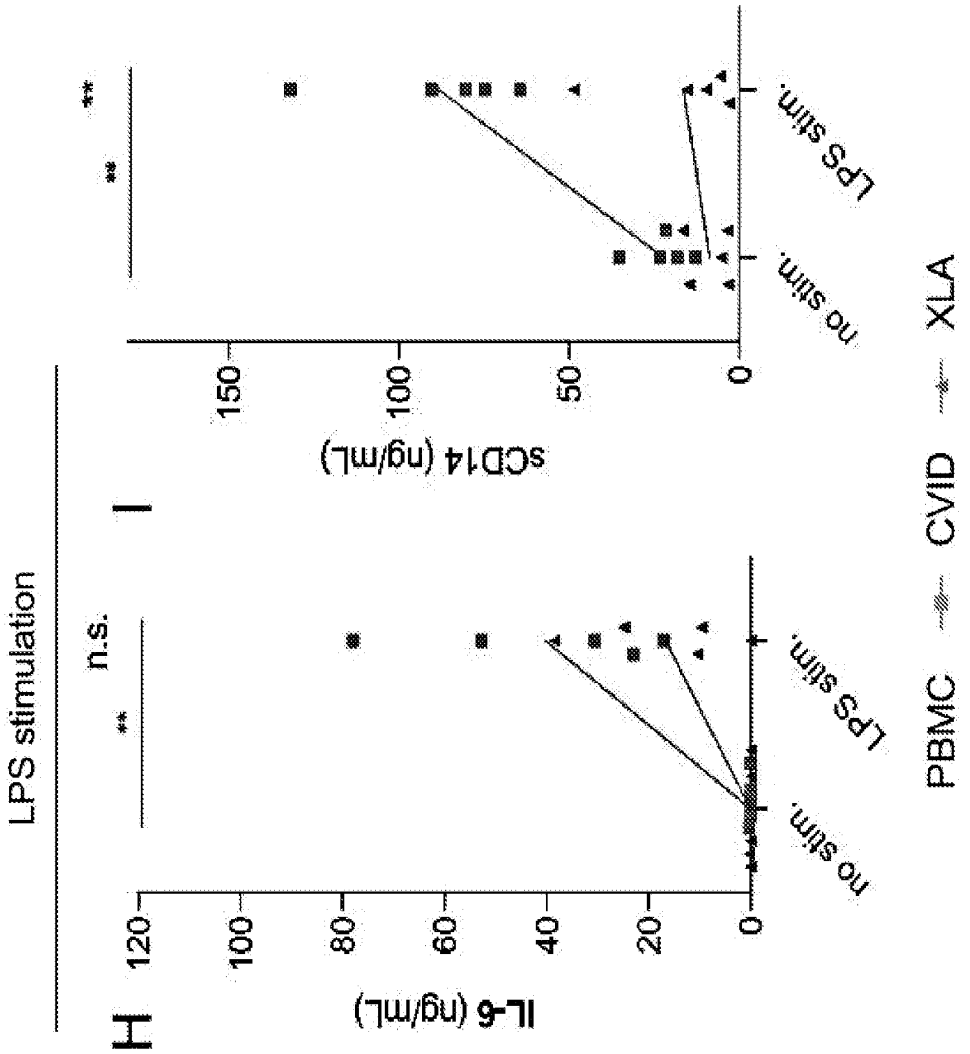

H
IL-6 (ng/mL)
120
100
80
60
40
20
0
n.s.
**
no stim.
LPS stim.
I
sCD14 (ng/mL)
150
100
50
0
**
**
no stim.
LPS stim.
LPS stimulation
PBMC
CVID
XLA

FIG. 2H

FIG. 2I

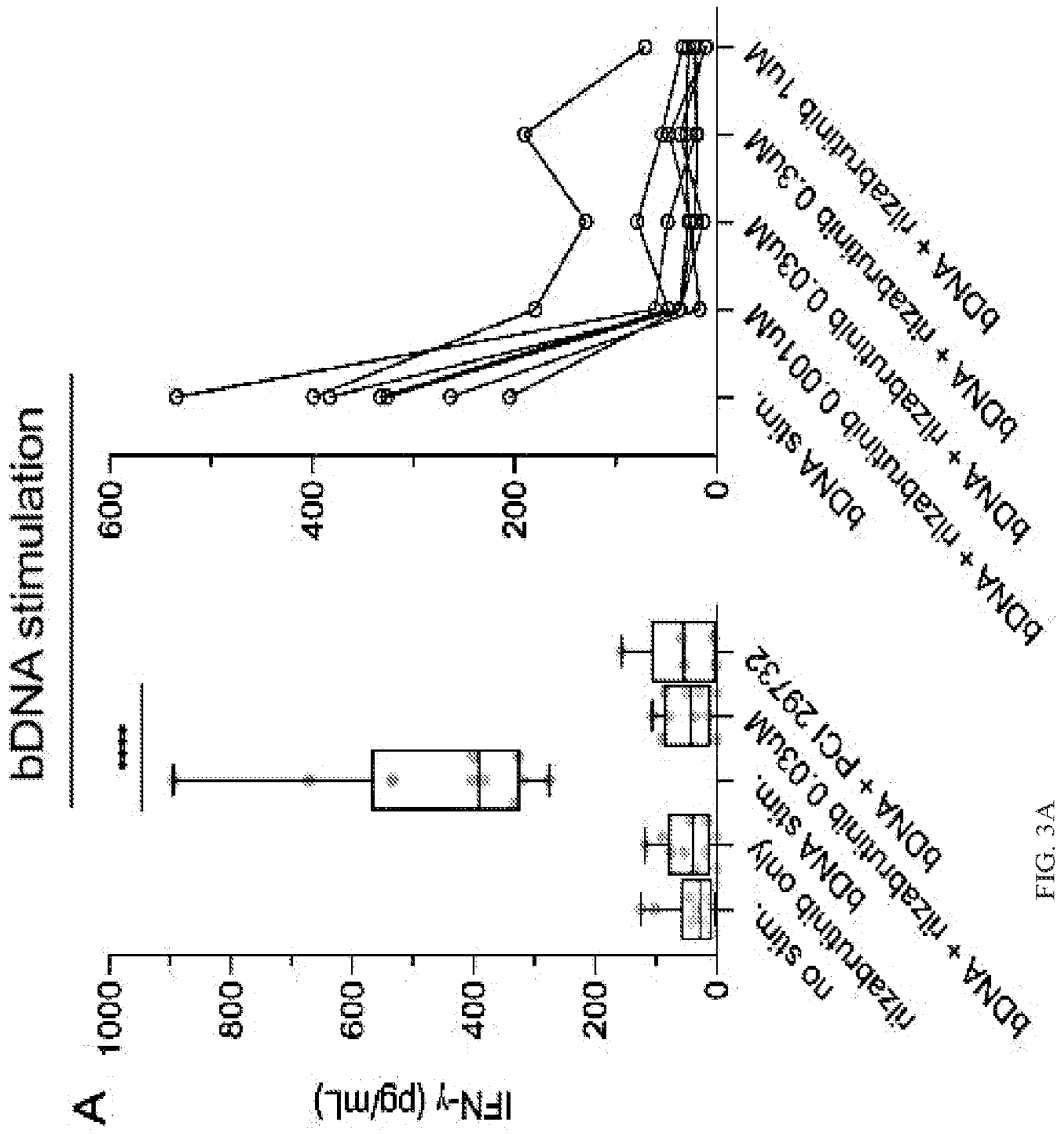

A
IFN-γ (pg/mL)
1000
800
600
400
200
0
no stim.
rizaburitinib only
bDNA stim.
bDNA + rizaburitinib 0.03uM
bDNA + PCI 29732
****
bDNA stim.
bDNA + rizaburitinib 0.001uM
bDNA + rizaburitinib 0.03uM
bDNA + rizaburitinib 0.3uM
bDNA + rizaburitinib 1uM
bDNA stimulation

FIG. 3A

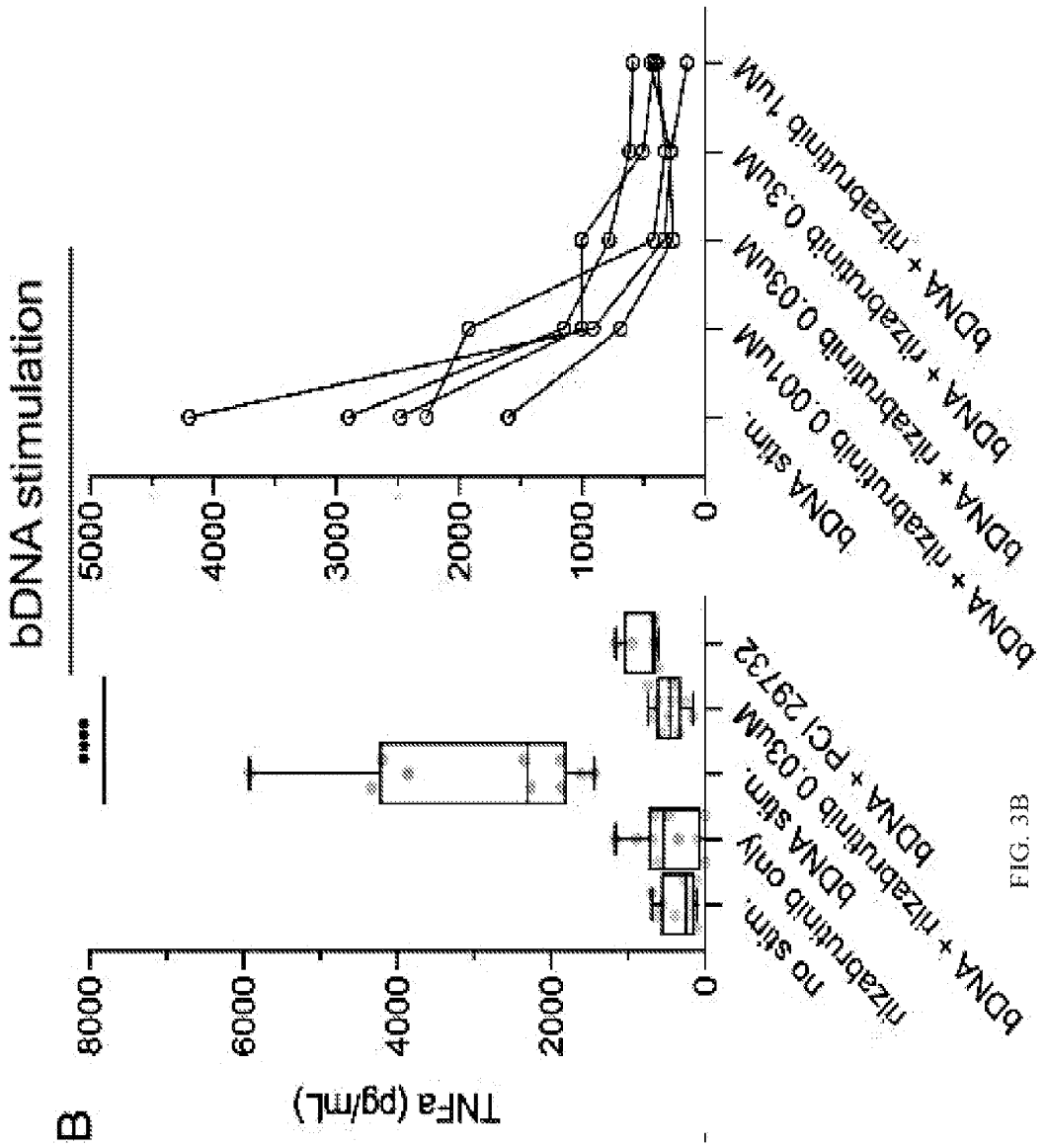

B
TNFa (pg/mL)
8000
6000
4000
2000
0
****
no stim.
rizaburitinib only
bDNA stim.
bDNA + rizaburitinib 0.03uM
bDNA + PCI 29732
bDNA stim.
bDNA + rizaburitinib 0.001uM
bDNA + rizaburitinib 0.03uM
bDNA + rizaburitinib 0.3uM
bDNA + rizaburitinib 1uM
bDNA stimulation
5000
4000
3000
2000
1000
0

FIG. 3B

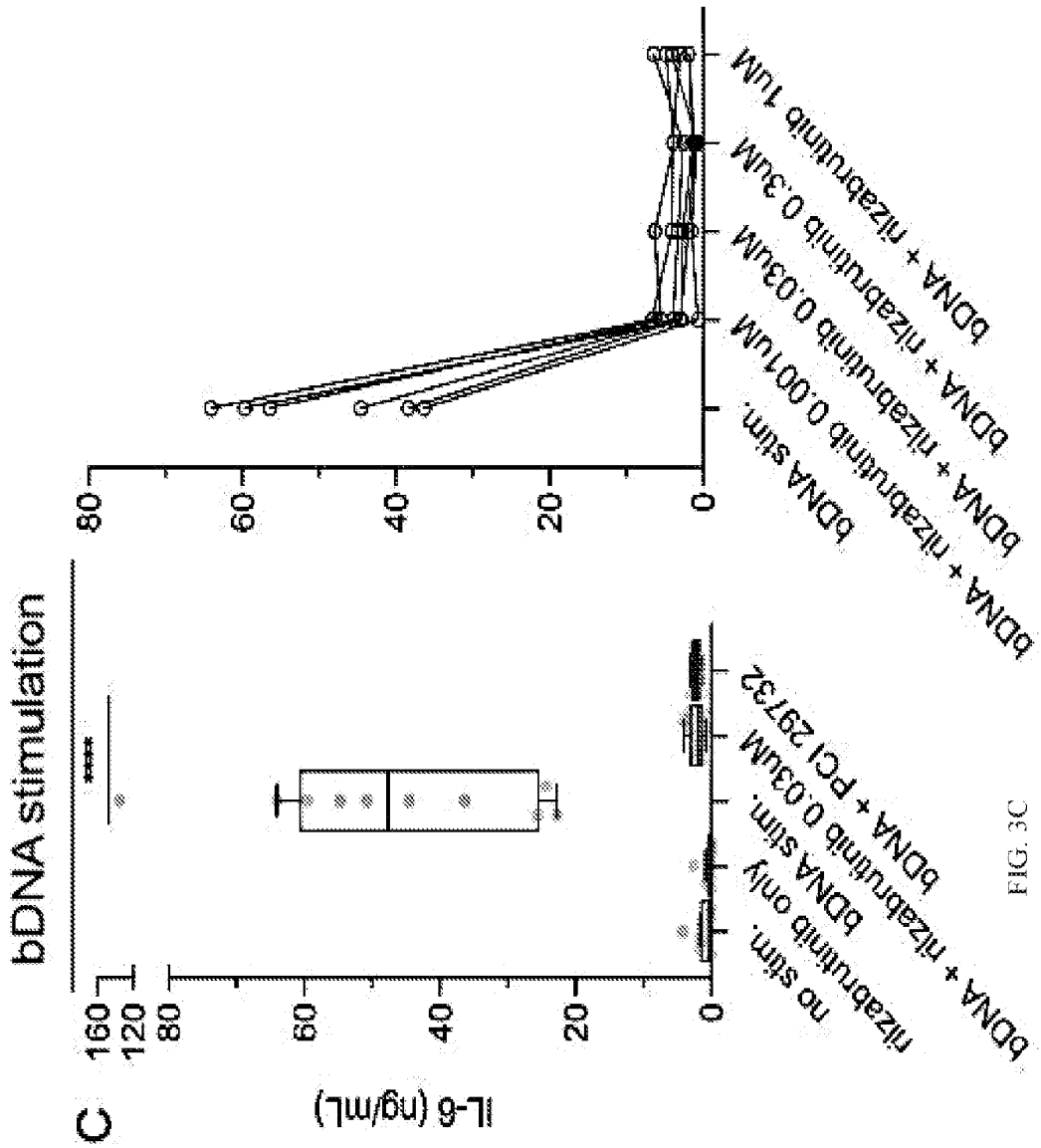

C
bDNA stimulation
IL-6 (ng/mL)
0
20
40
60
80
120
160
****
no stim.
rizaburitinib only
bDNA stim.
bDNA + rizaburitinib 0.03uM
bDNA + PCI 29732
bDNA stim.
bDNA + rizaburitinib 0.001uM
bDNA + rizaburitinib 0.03uM
bDNA + rizaburitinib 0.3uM
bDNA + rizaburitinib 1uM

FIG. 3C

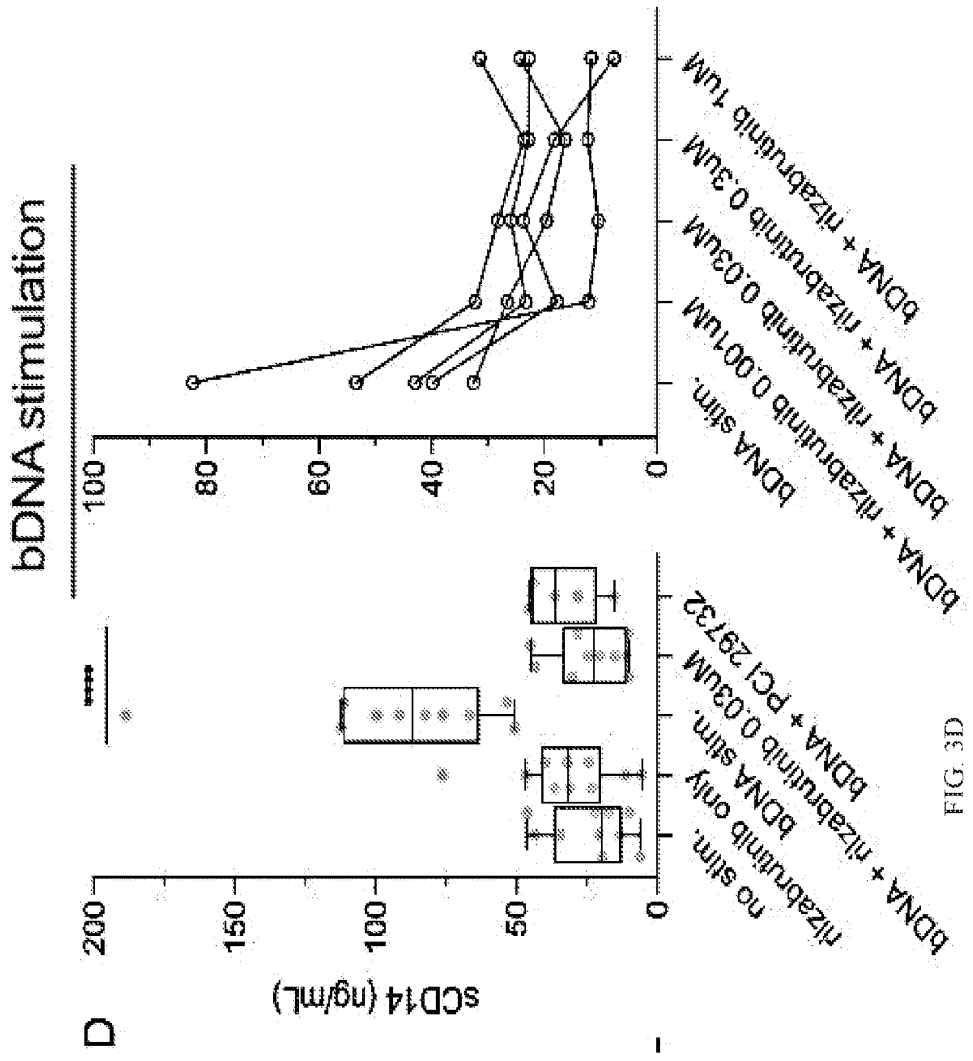

D
sCD14 (ng/mL)
200
150
100
50
0
***
no stim.
rizaburitinib only
bDNA stim.
bDNA + rizaburitinib 0.03uM
bDNA + PCI 29732
bDNA stim.
bDNA + rizaburitinib 0.001uM
bDNA + rizaburitinib 0.03uM
bDNA + rizaburitinib 0.3uM
bDNA + rizaburitinib 1uM
bDNA stimulation
100
80
60
40
20
0

FIG. 3D

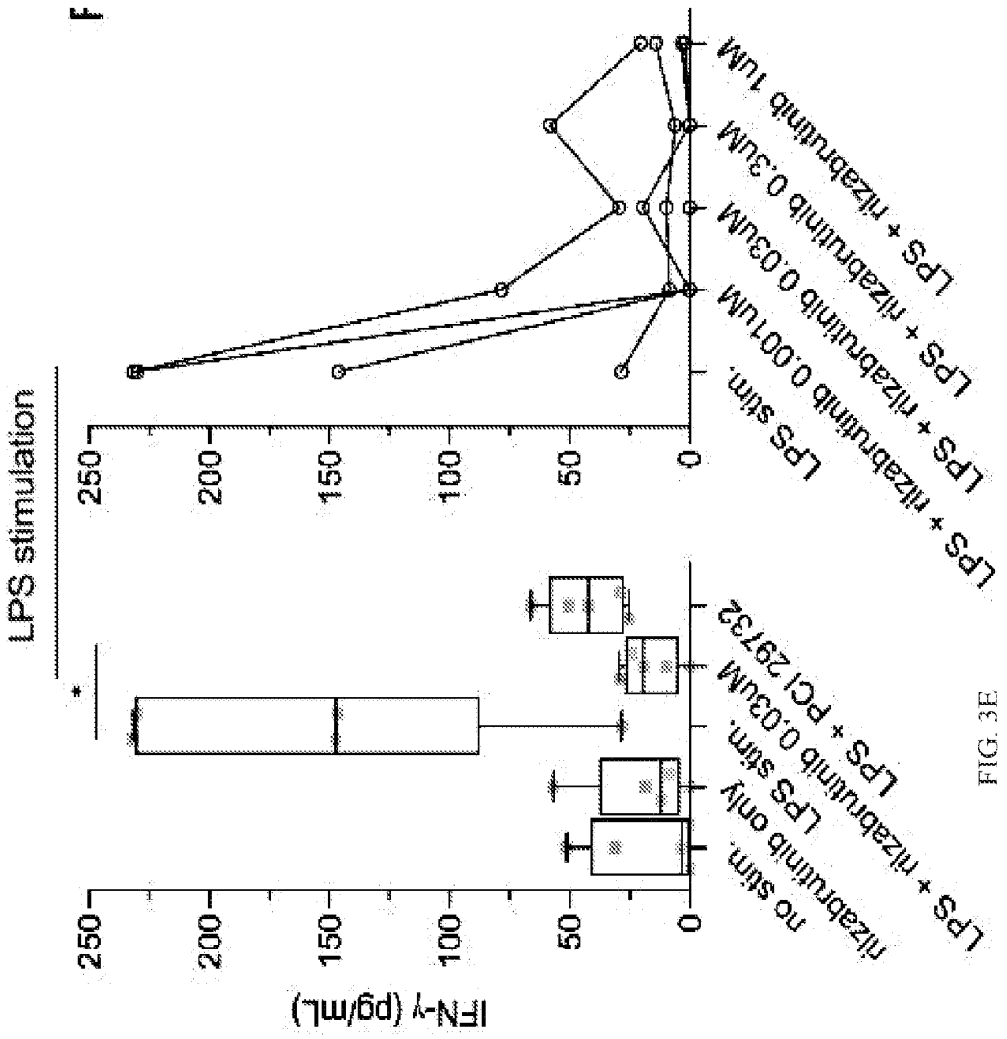

F
LPS stimulation
IFN-γ (pg/mL)
250
200
150
100
50
0
*
no stim.
ribociclib only
LPS stim.
LPS + ribociclib 0.03uM
LPS + PCI 29732
LPS stim.
LPS + ribociclib 0.001uM
LPS + ribociclib 0.03uM
LPS + ribociclib 0.3uM
LPS + ribociclib 1uM

FIG. 3E

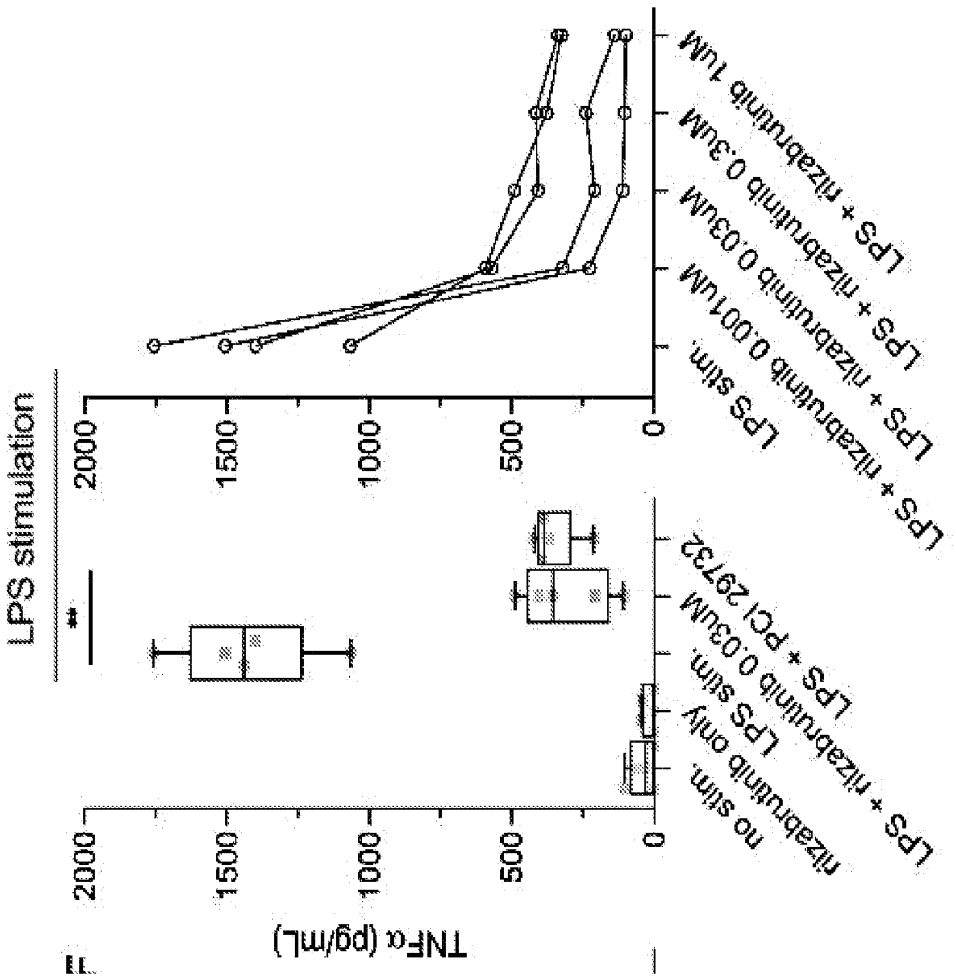

LPS stimulation
TNFα (pg/mL)
2000
1500
1000
500
0
no stim.
rizabrutinib only
LPS stim.
LPS + rizabrutinib 0.03uM
LPS + PCI 29732
LPS stim.
LPS + rizabrutinib 0.001uM
LPS + rizabrutinib 0.03uM
LPS + rizabrutinib 0.3uM
LPS + rizabrutinib 1uM

FIG. 3F

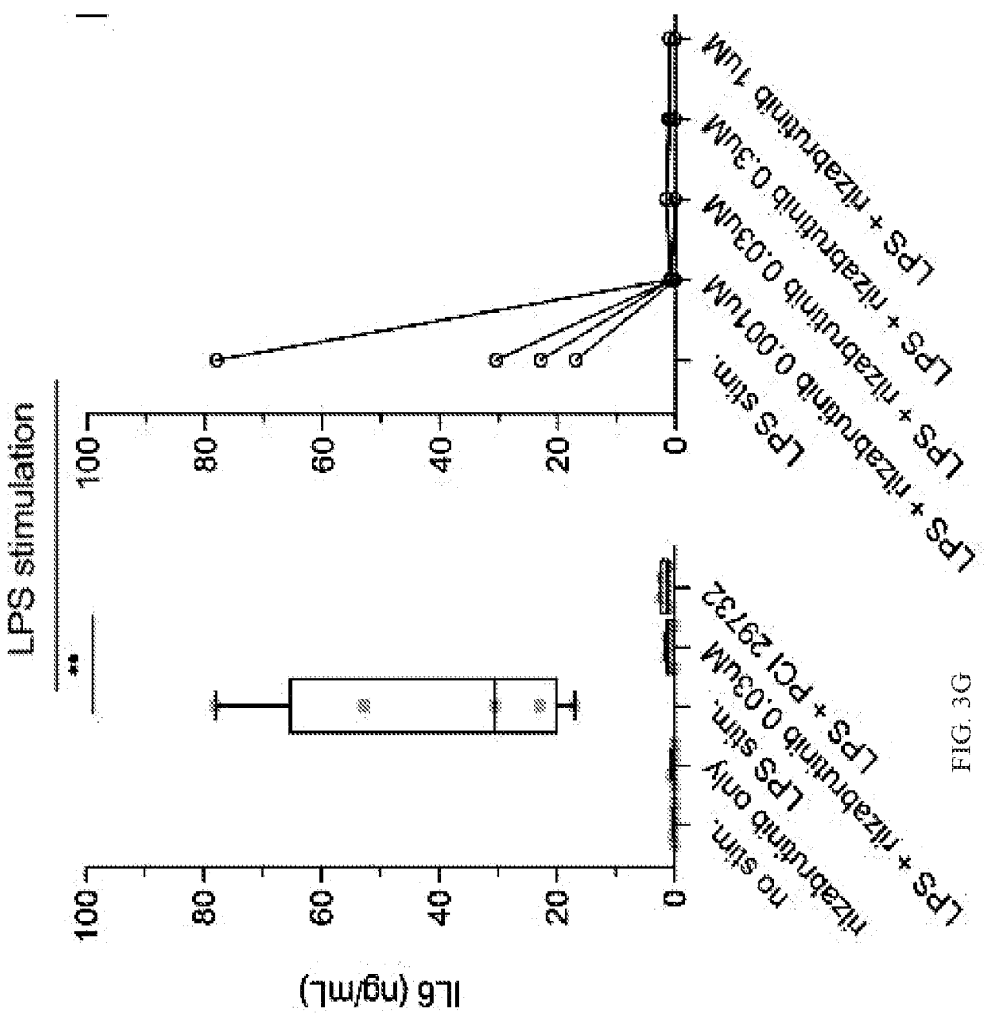

IL6 (ng/mL)
0
20
40
60
80
100
LPS stimulation
**
no stim.
rizabrutinib only
LPS stim.
LPS + rizabrutinib 0.03uM
LPS + PCI 29732
LPS stim.
LPS + rizabrutinib 0.001uM
LPS + rizabrutinib 0.03uM
LPS + rizabrutinib 0.3uM
LPS + rizabrutinib 1uM

FIG. 3G

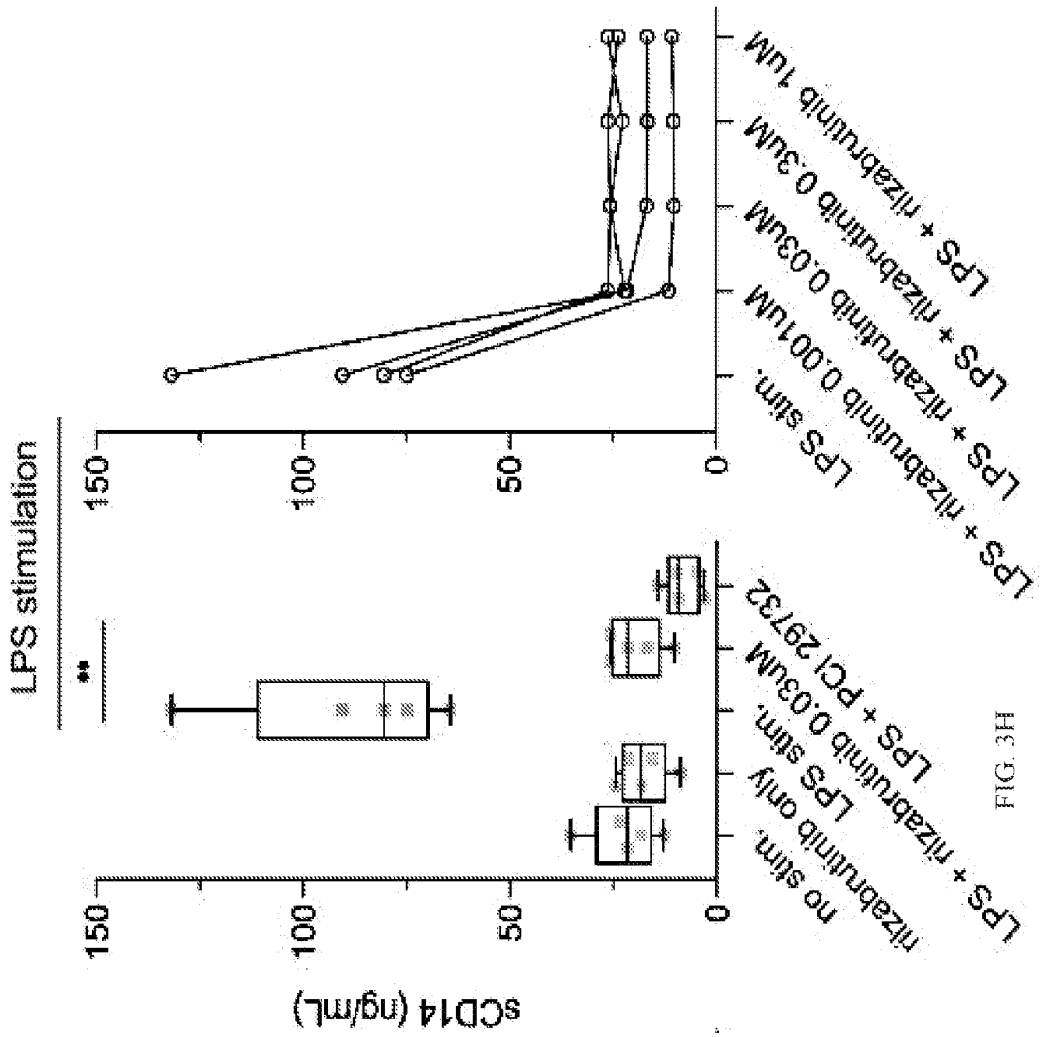

LPS stimulation
**
sCD14 (ng/mL)
150
100
50
0
no stim.
mizaburitinib only
LPS stim.
LPS + mizaburitinib 0.03uM
LPS + PCI 29732
LPS stim.
LPS + mizaburitinib 0.001uM
LPS + mizaburitinib 0.03uM
LPS + mizaburitinib 0.3uM
LPS + mizaburitinib 1uM

FIG. 3H

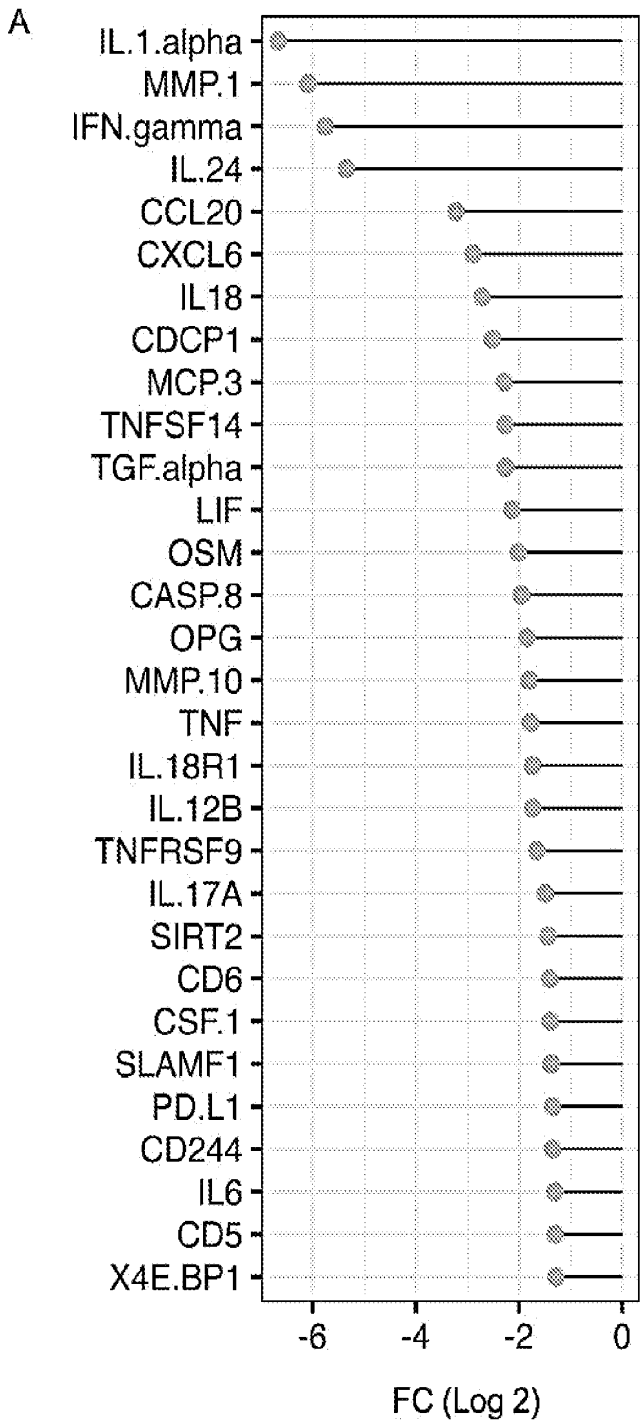

A
IL.1.alpha
MMP.1
IFN.gamma
IL.24
CCL20
CXCL6
IL18
CDCP1
MCP.3
TNFSF14
TGF.alpha
LIF
OSM
CASP.8
OPG
MMP.10
TNF
IL.18R1
IL.12B
TNFRSF9
IL.17A
SIRT2
CD6
CSF.1
SLAMF1
PD.L1
CD244
IL6
CD5
X4E.BP1
-6
-4
-2
0
FC (Log 2)

FIG. 4A

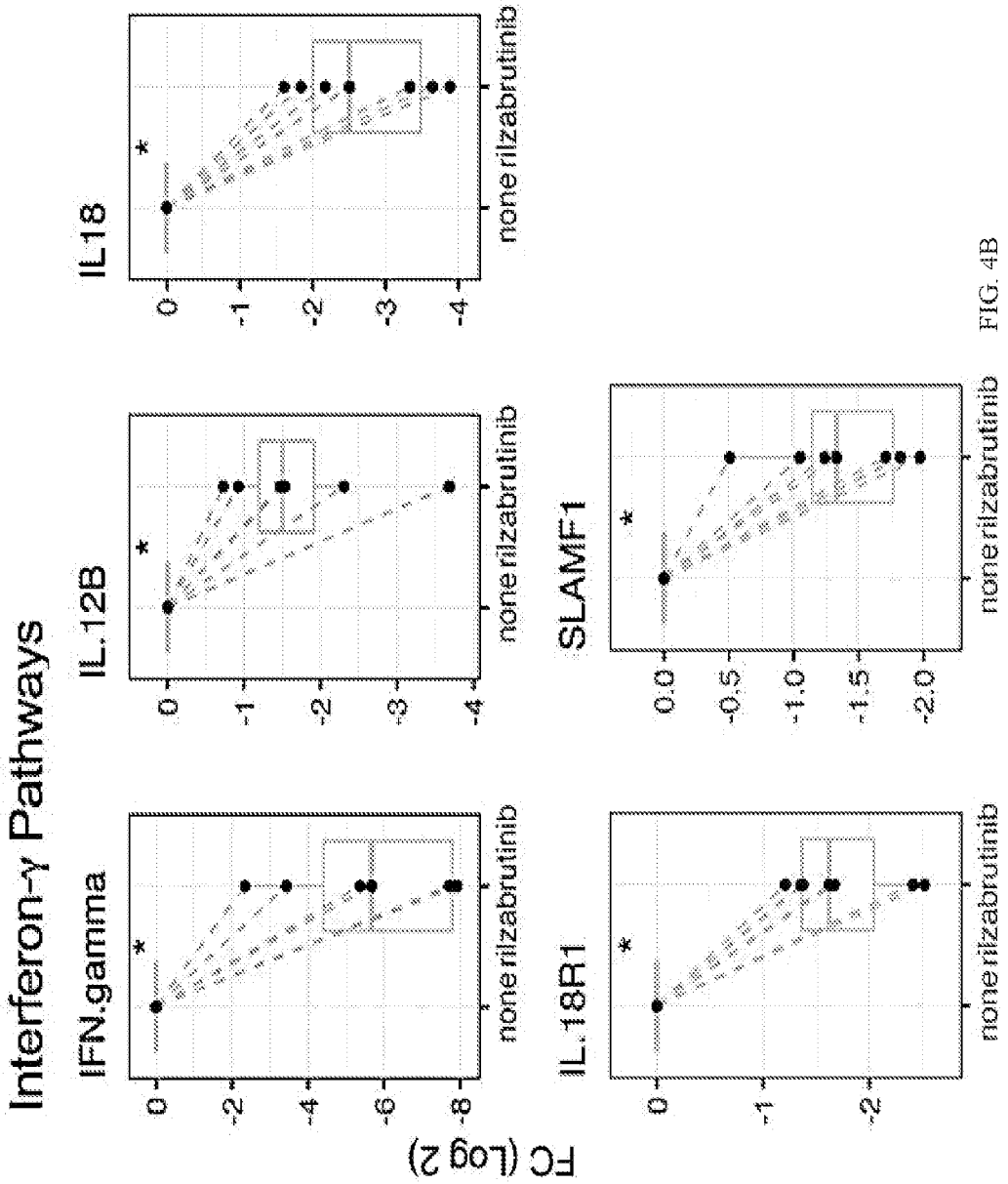

Interferon-γ Pathways
IFN.gamma
IL.12B
IL18
IL.18R1
SLAMF1
FC (Log 2)
none
rilzabrutinib
*

FIG. 4B

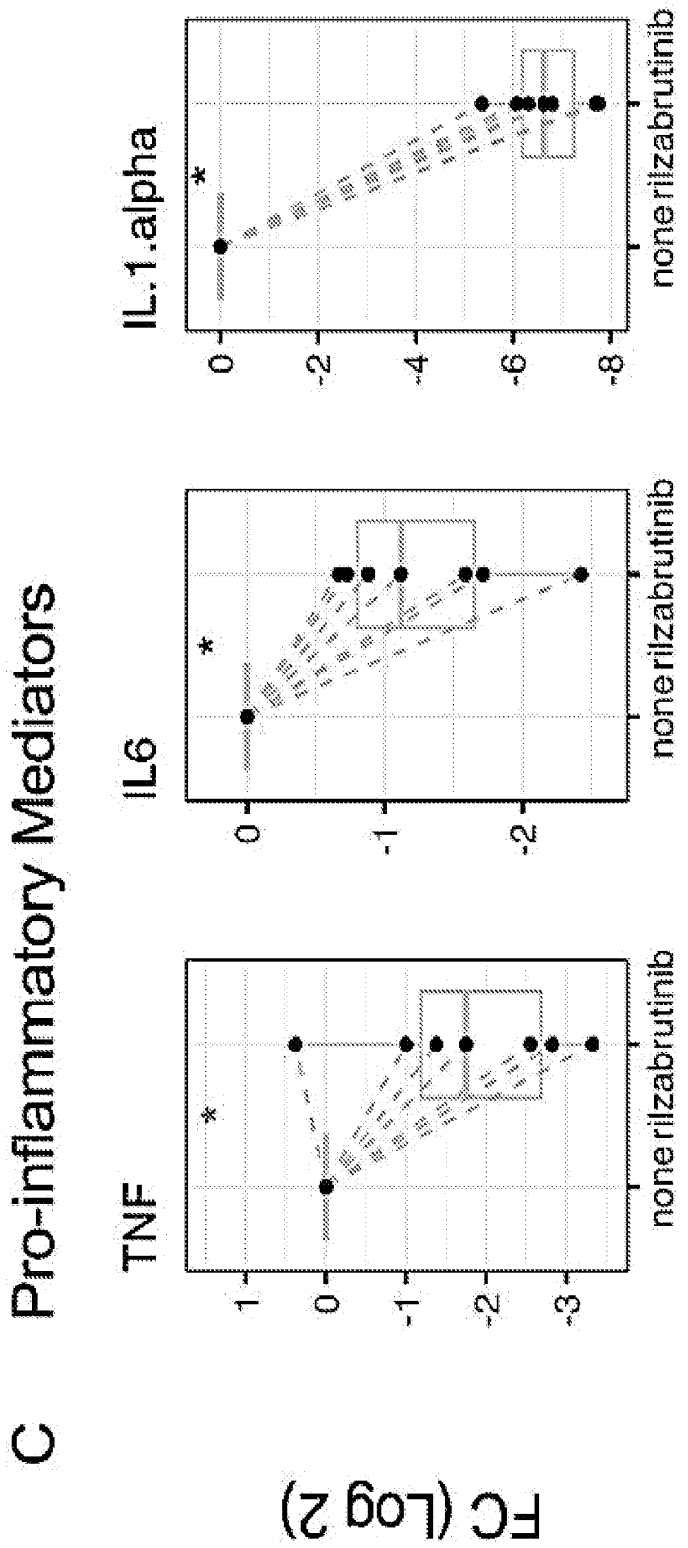

C
Pro-inflammatory Mediators
TNF
IL6
IL.1.alpha
FC (Log 2)
1
0
-1
-2
-3
-4
-6
-8
*
none
rilzabrutinib

FIG. 4C

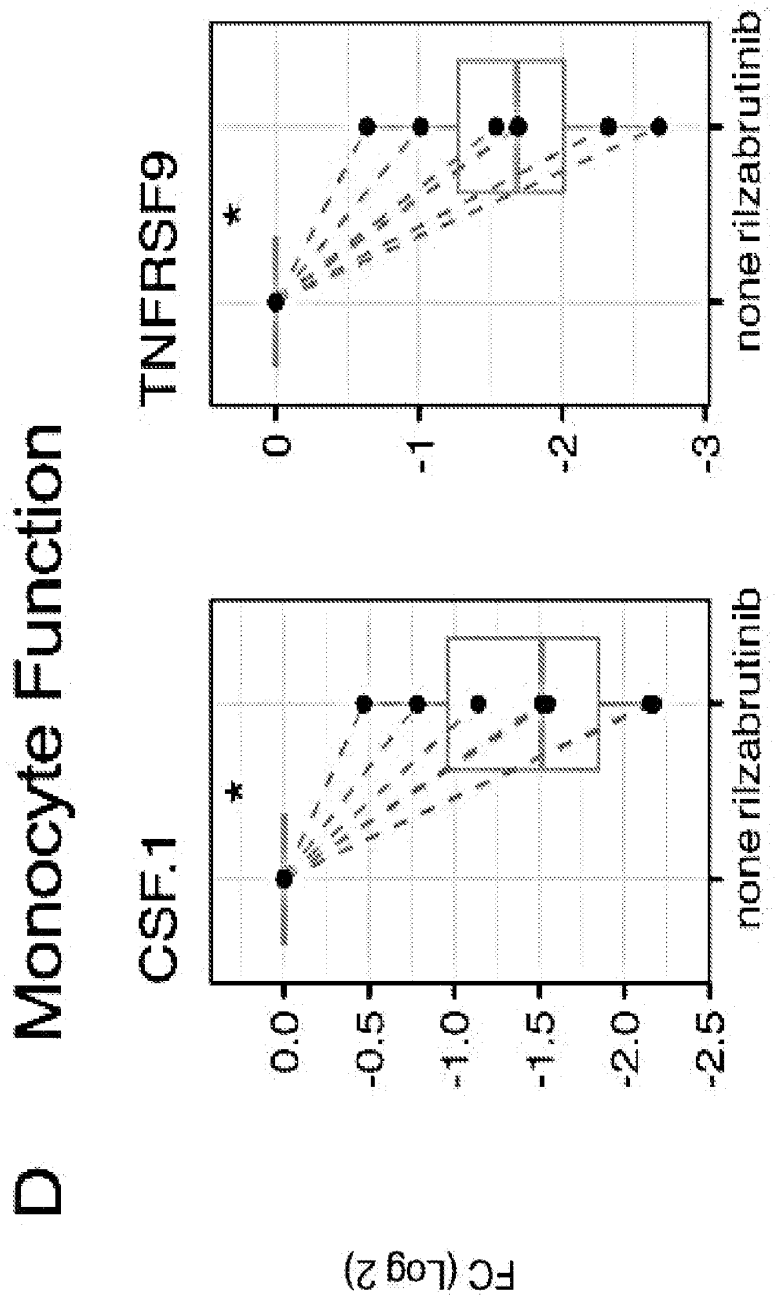

D
Monocyte Function
CSF.1
TNFRSF9
FC (Log 2)
0.0
-0.5
-1.0
-1.5
-2.0
-2.5
0
-1
-2
-3
*
*
none
rilzabrutinib
none
rilzabrutinib

FIG. 4D

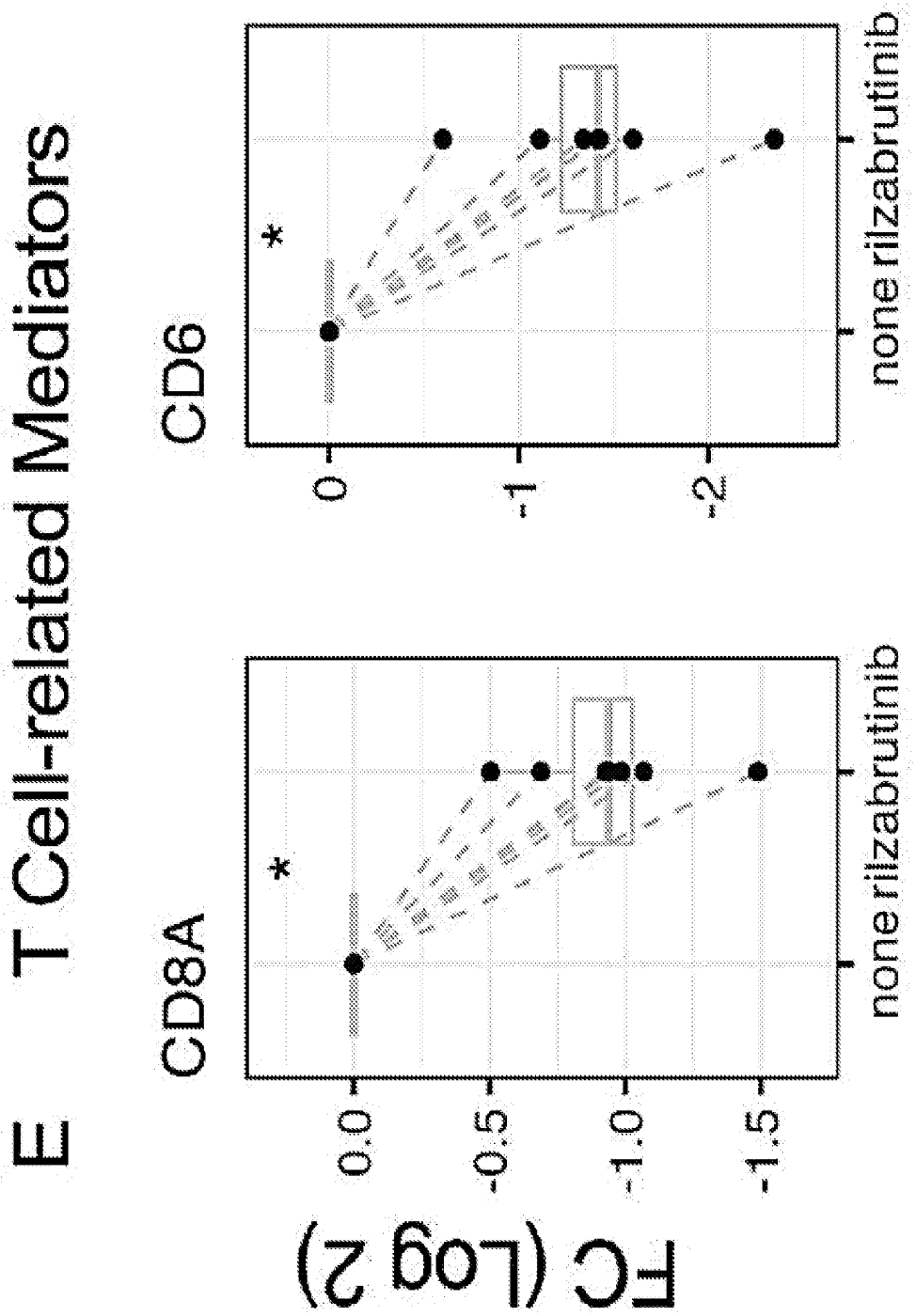

E T Cell-related Mediators
CD8A
CD6
FC (Log 2)
0.0
-0.5
-1.0
-1.5
0
-1
-2
*
*
none
rilzabrutinib
none
rilzabrutinib

FIG. 4E

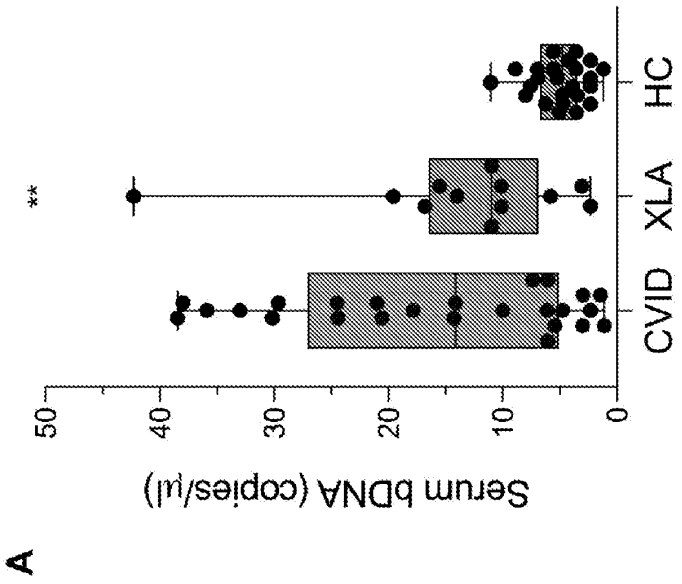

A
Serum bDNA (copies/μl)
50
40
30
20
10
0
**
CVID
XLA
HC

FIG. 5A

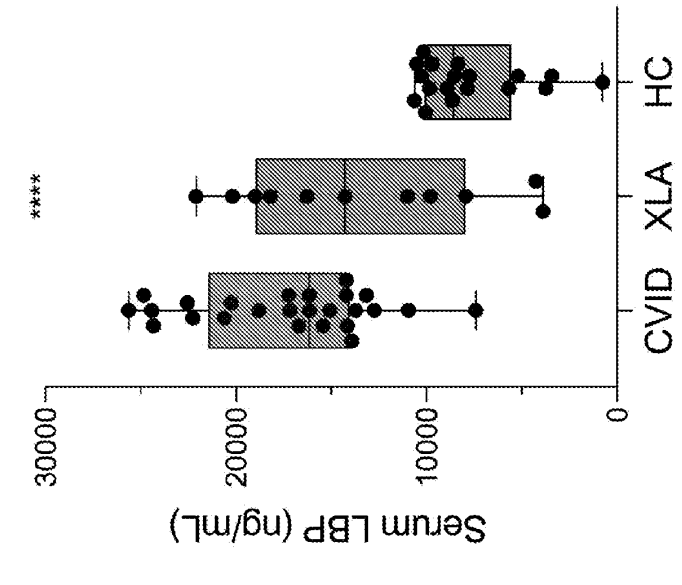

B
Serum LBP (ng/mL)
30000
20000
10000
0
****
CVID
XLA
HC

FIG. 5B