FIG. 1

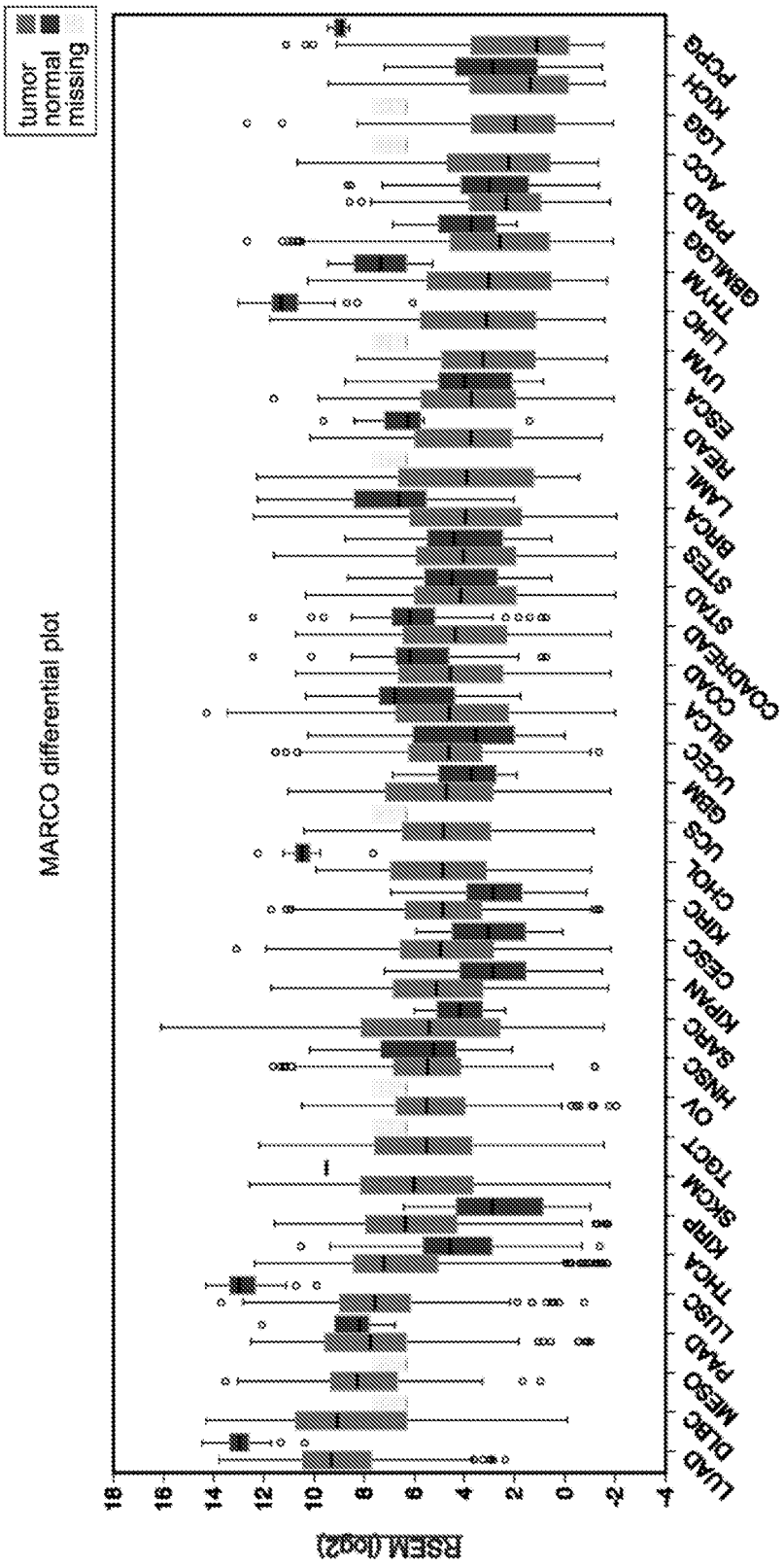

MARCO differential plot
tumor
normal
missing
RSEM (log2)
18
16
14
12
10
8
6
4
2
0
-2
-4
LUAD
DLBC
MESO
PAAD
LUSC
THCA
KIRP
SKCM
TGCT
OV
HNSC
SARC
KIPAN
CESC
KIRC
CHOL
UCS
GBM
UCEC
BLCA
COAD
COADREAD
STAD
STES
BRCA
LAML
READ
ESCA
UVM
LIHC
THYM
GBMLGG
PRAD
ACC
LGG
KICH
PCPG

FIG. 2

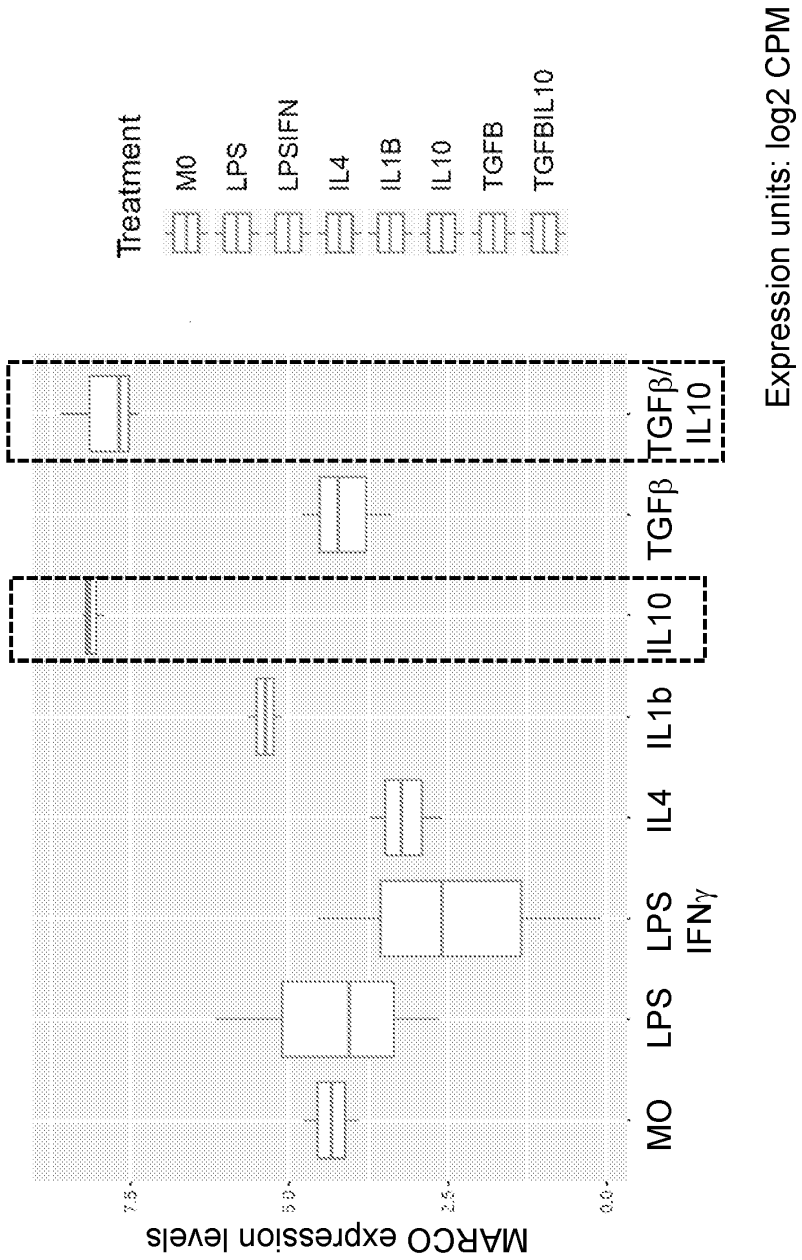

Treatment
M0
LPS
LPSIFN
IL4
IL1B
IL10
TGFB
TGFBIL10
Expression units: log2 CPM
MARCO expression levels
7.5
5.0
2.5
0.0
M0
LPS
LPS IFNγ
IL4
IL1b
IL10
TGFβ
TGFβ/ IL10

FIG. 3A

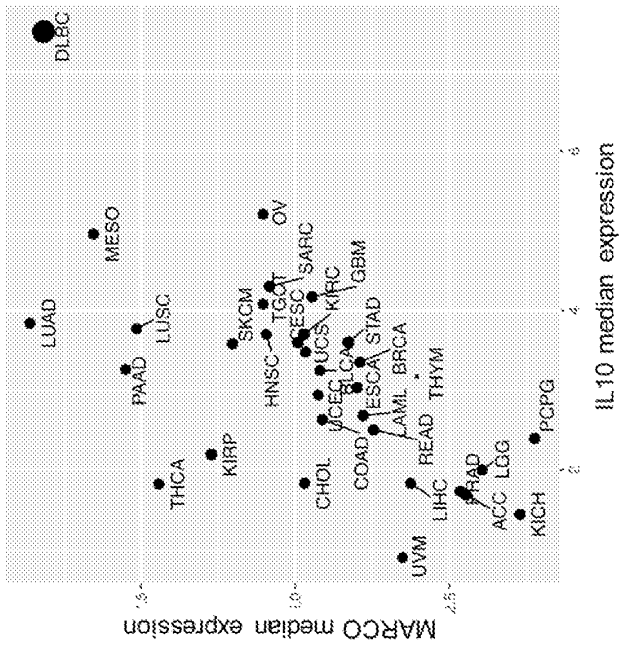

DLBC
MESO
LUAD
LUSC
PAAD
SKCM
OV
TGCT
SARC
CESC
KIRC
GBM
HNSC
UCS
STAD
BLCA
ESCA
BRCA
UCEC
LAML
THYM
READ
KIRP
THCA
CHOL
COAD
LIHC
UVM
PRAD
ACC
LGG
KICH
PCPG
MARCO median expression
IL10 median expression

FIG. 3B

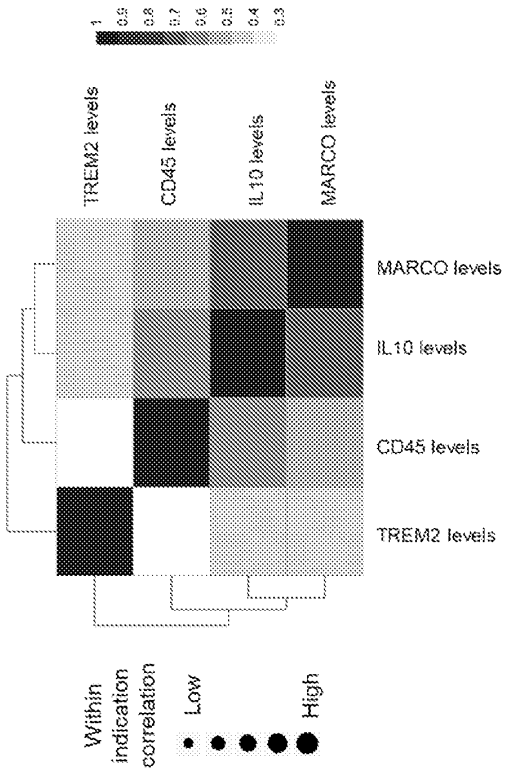

TREM2 levels
CD45 levels
IL10 levels
MARCO levels
MARCO levels
IL10 levels
CD45 levels
TREM2 levels
Within indication correlation
Low
High

FIG. 4A

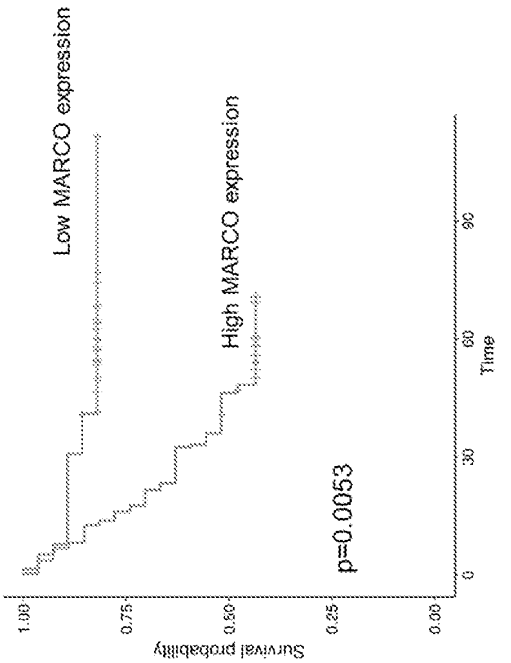


FIG. 4B

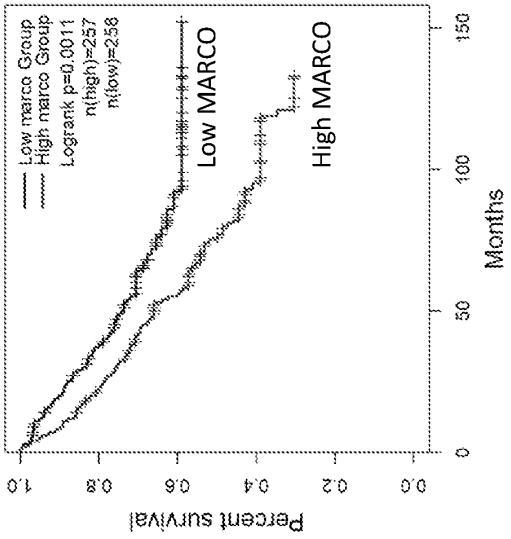


FIG. 4C

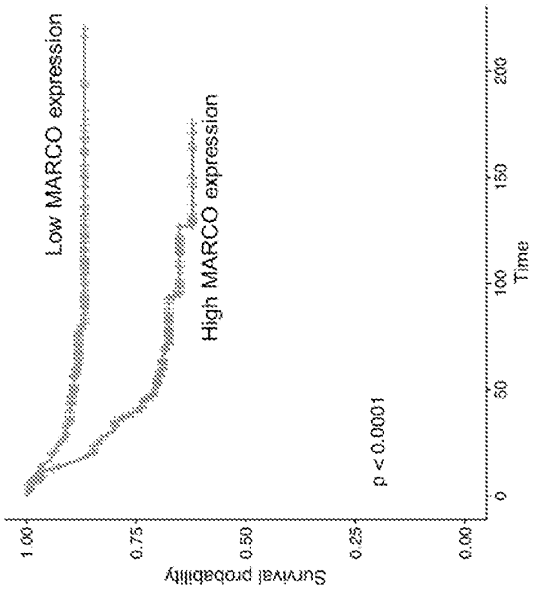
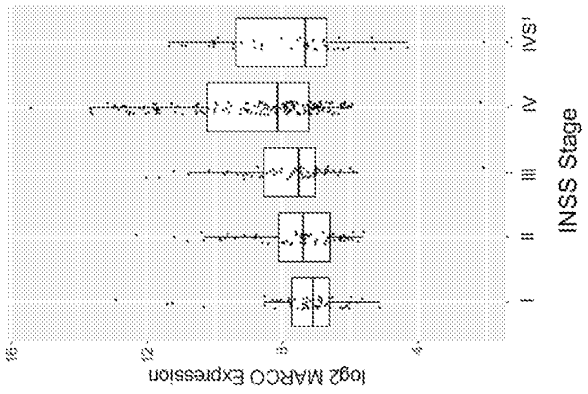


FIG. 4D



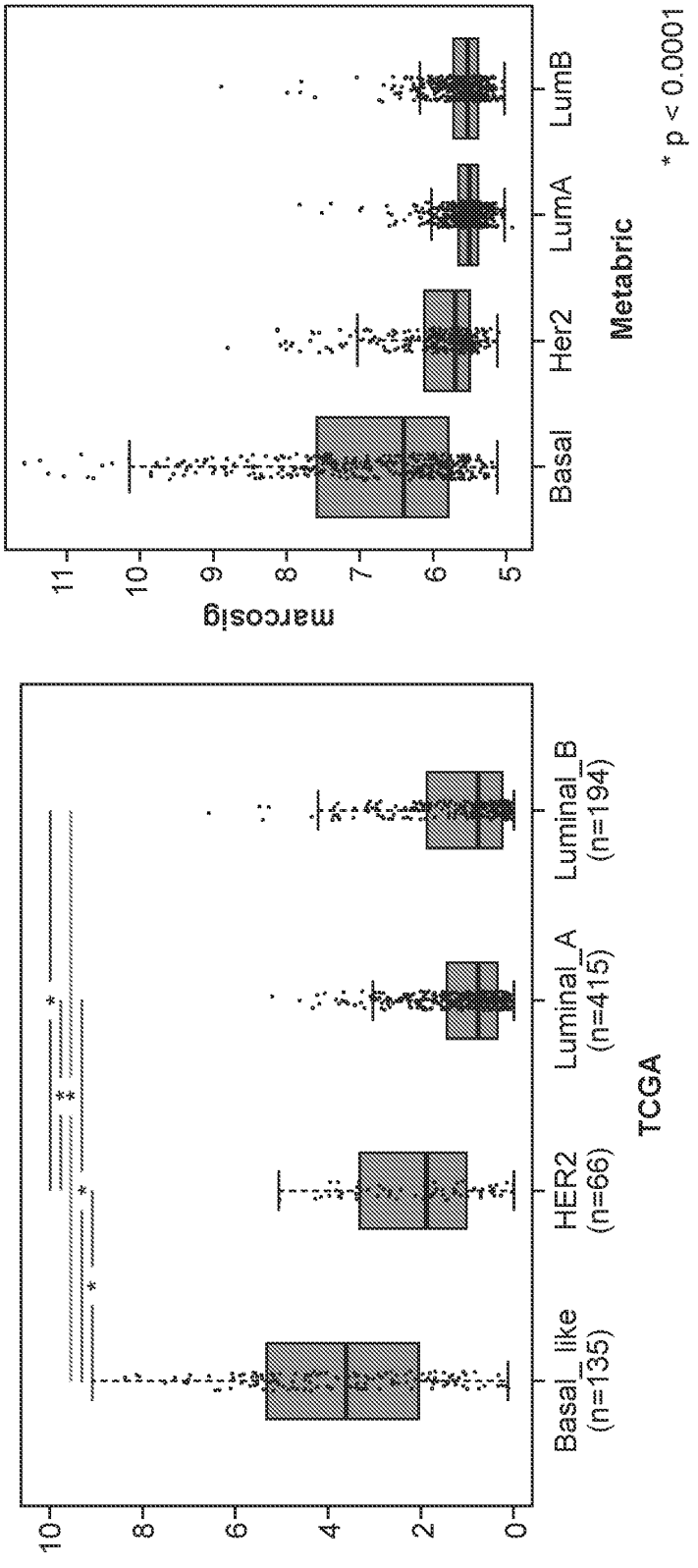

marcosig
11
10
9
8
7
6
5
Basal
Her2
LumA
LumB
Metabric
* p < 0.0001
0
2
4
6
8
10
Basal_like (n=135)
HER2 (n=66)
Luminal_A (n=415)
Luminal_B (n=194)
TCGA

FIG. 5

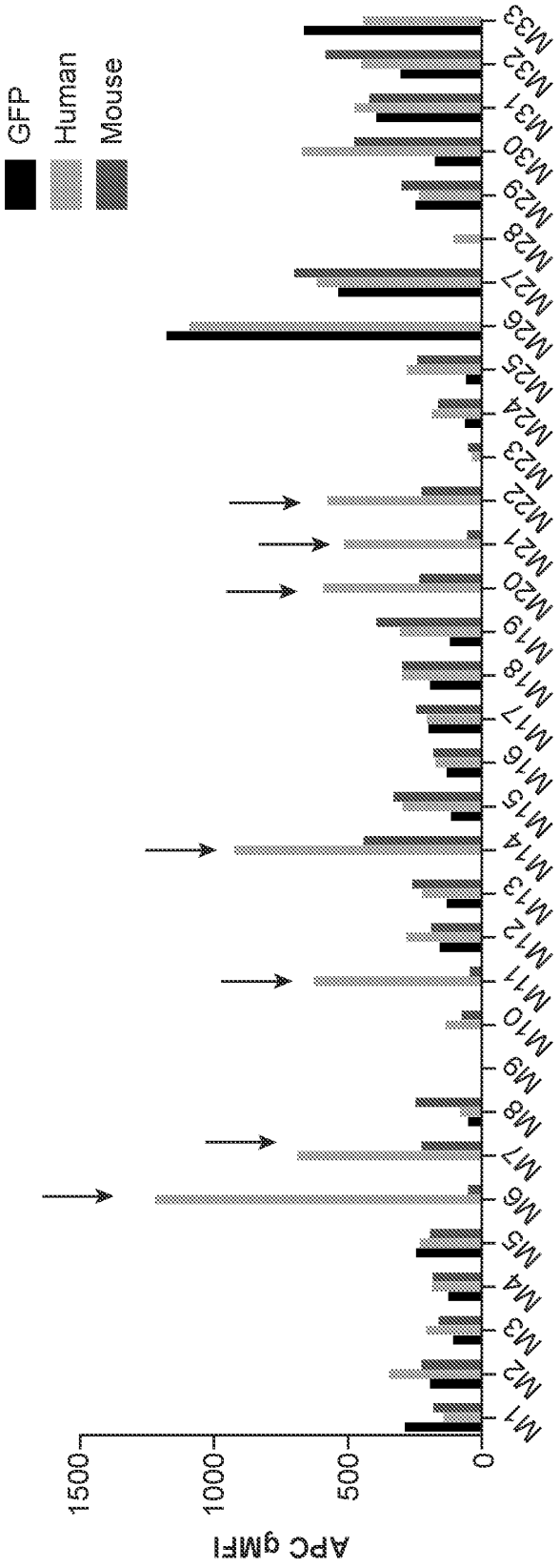

GFP
Human
Mouse
APC gMFI
1500
1000
500
0
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
M13
M14
M15
M16
M17
M18
M19
M20
M21
M22
M23
M24
M25
M26
M27
M28
M29
M30
M31
M32
M33

FIG. 6A

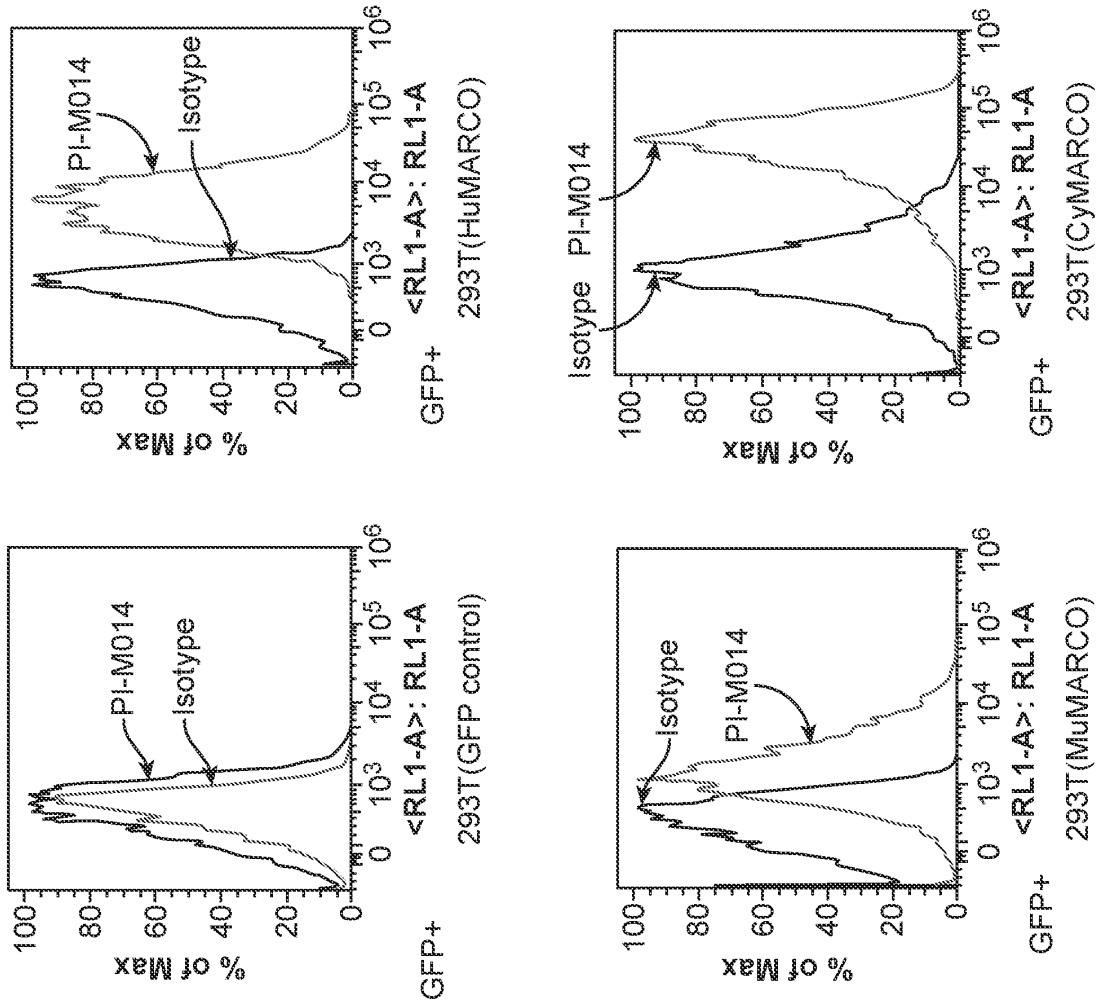

% of Max
PI-M014
Isotype
<RL1-A>: RL1-A
GFP+
293T(HuMARCO)
293T(CyMARCO)
293T(MuMARCO)
293T(GFP control)

FIG. 6B

FIG. 6C

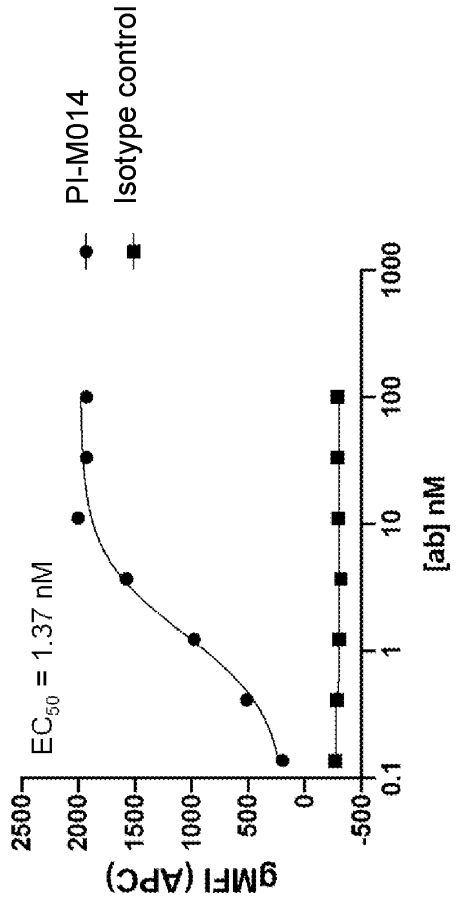

293T(huMARCO)
PI-M014
Isotype control
EC50 = 1.37 nM
gMFI (APC)
2500
2000
1500
1000
500
0
-500
0.1
1
10
100
1000
[ab] nM

FIG. 6D

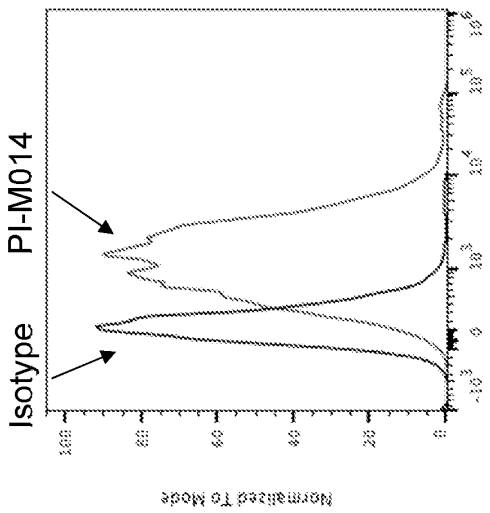
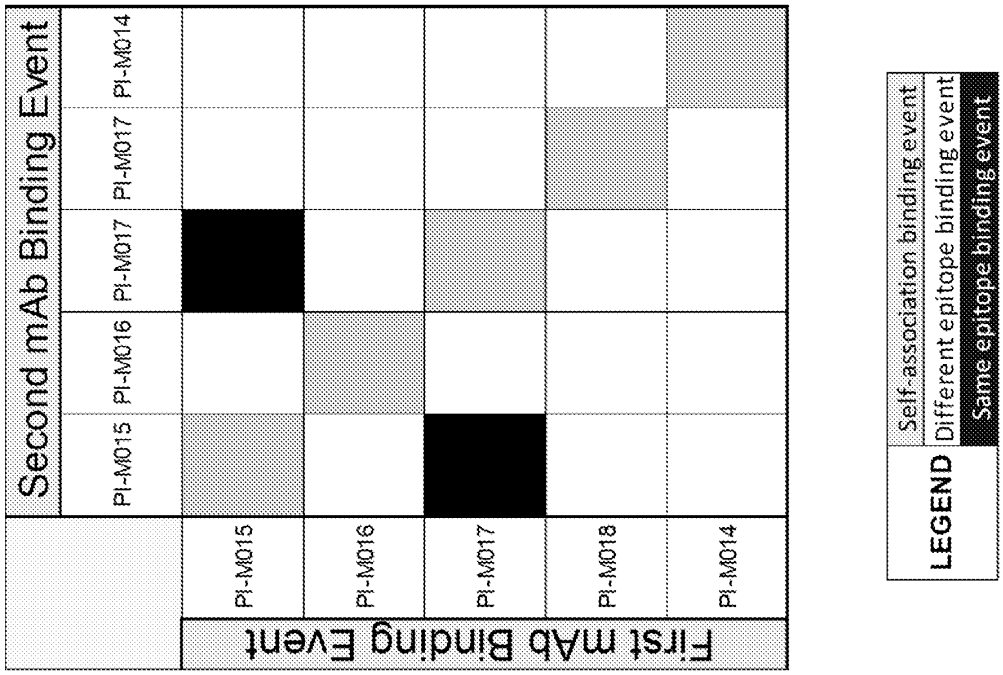

Human monocyte-derived macrophages (hMDMs)
Isotype
PI-M014
Normalized To Mode

FIG. 7


Second mAb Binding Event
PI-M015
PI-M016
PI-M017
PI-M017
PI-M014
First mAb Binding Event
PI-M015
PI-M016
PI-M017
PI-M018
PI-M014
LEGEND
Self-association binding event
Different epitope binding event
Same epitope binding event

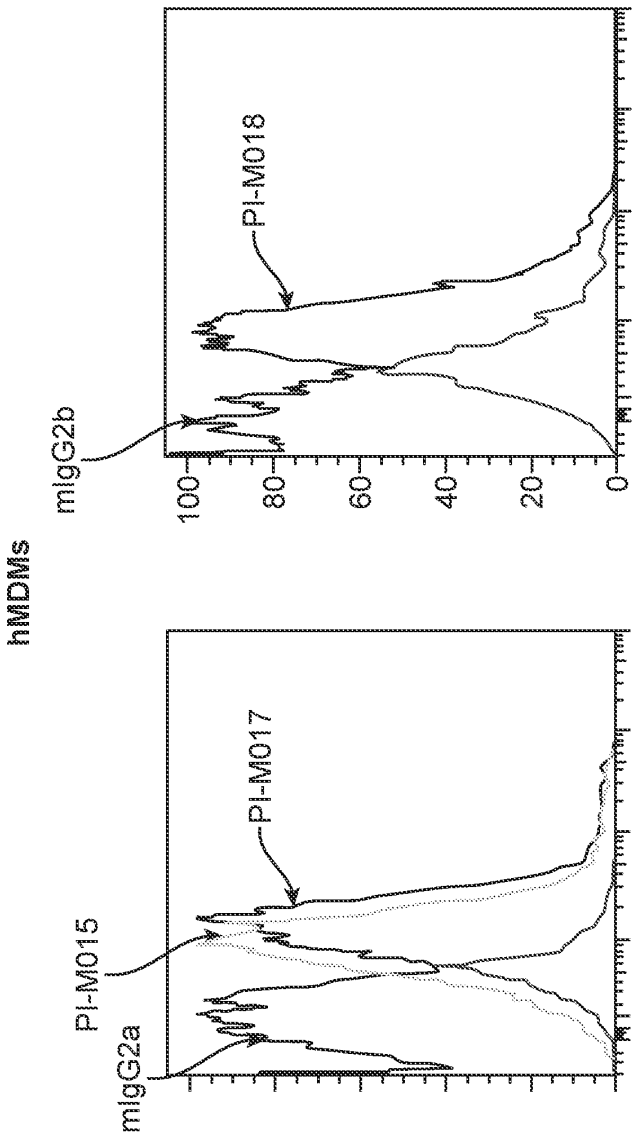


FIG. 8A

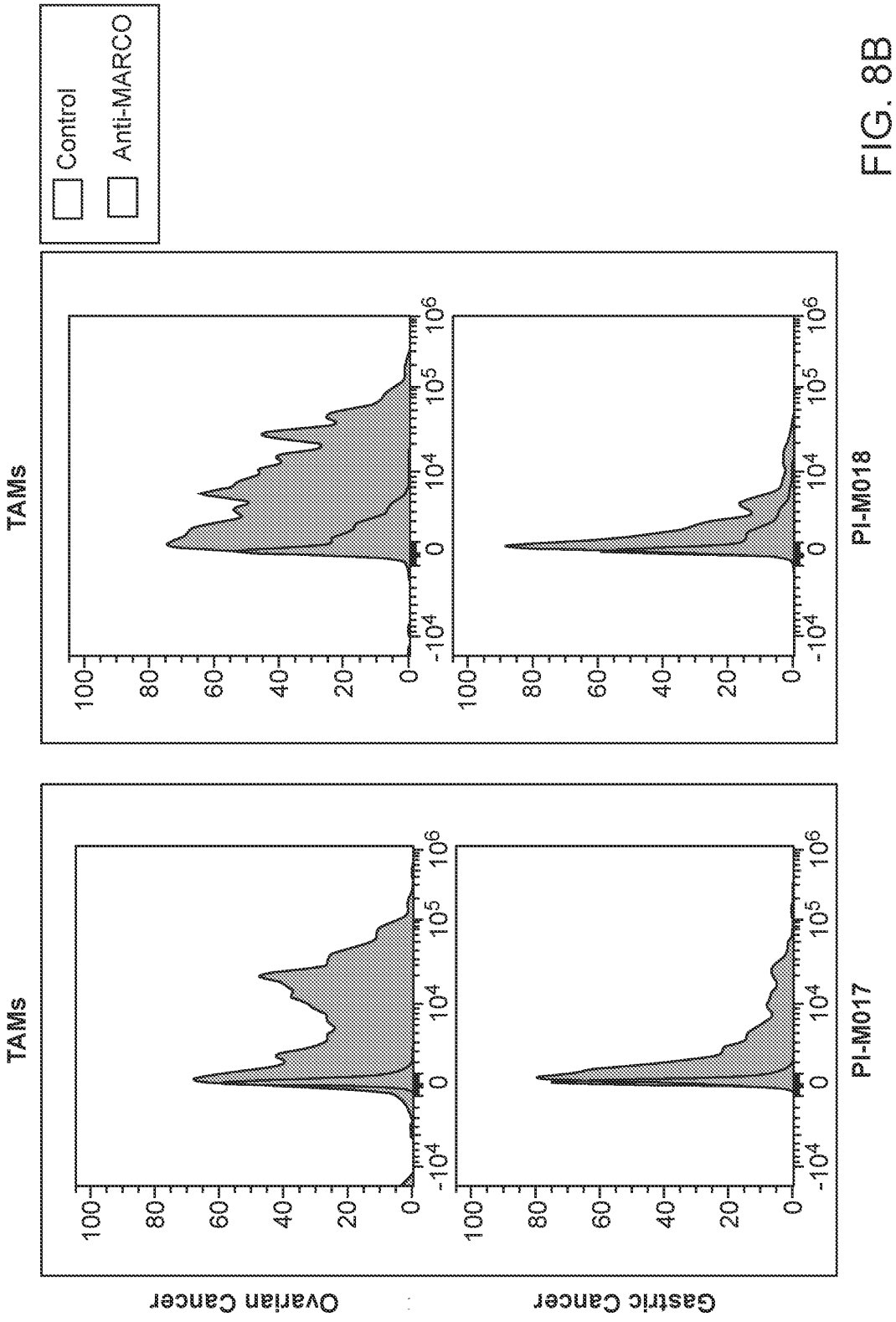
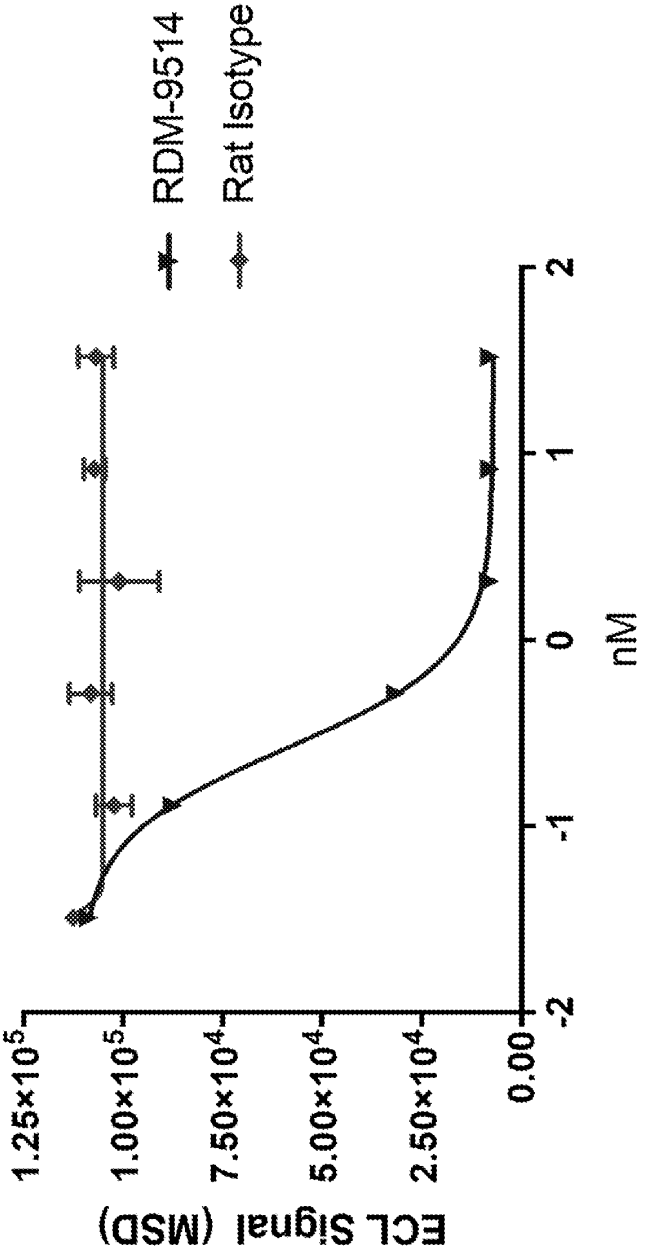

Control
Anti-MARCO
TAMs
TAMs
PI-M018
PI-M017
Ovarian Cancer
Gastric Cancer
100
80
60
40
20
0
-10^4
0
10^4
10^5
10^6

FIG. 8B

FIG. 9


RDM-9514
Rat Isotype
ECL Signal (MSD)
1.25×10^5
1.00×10^5
7.50×10^4
5.00×10^4
2.50×10^4
0.00
-2
-1
0
1
2
nM

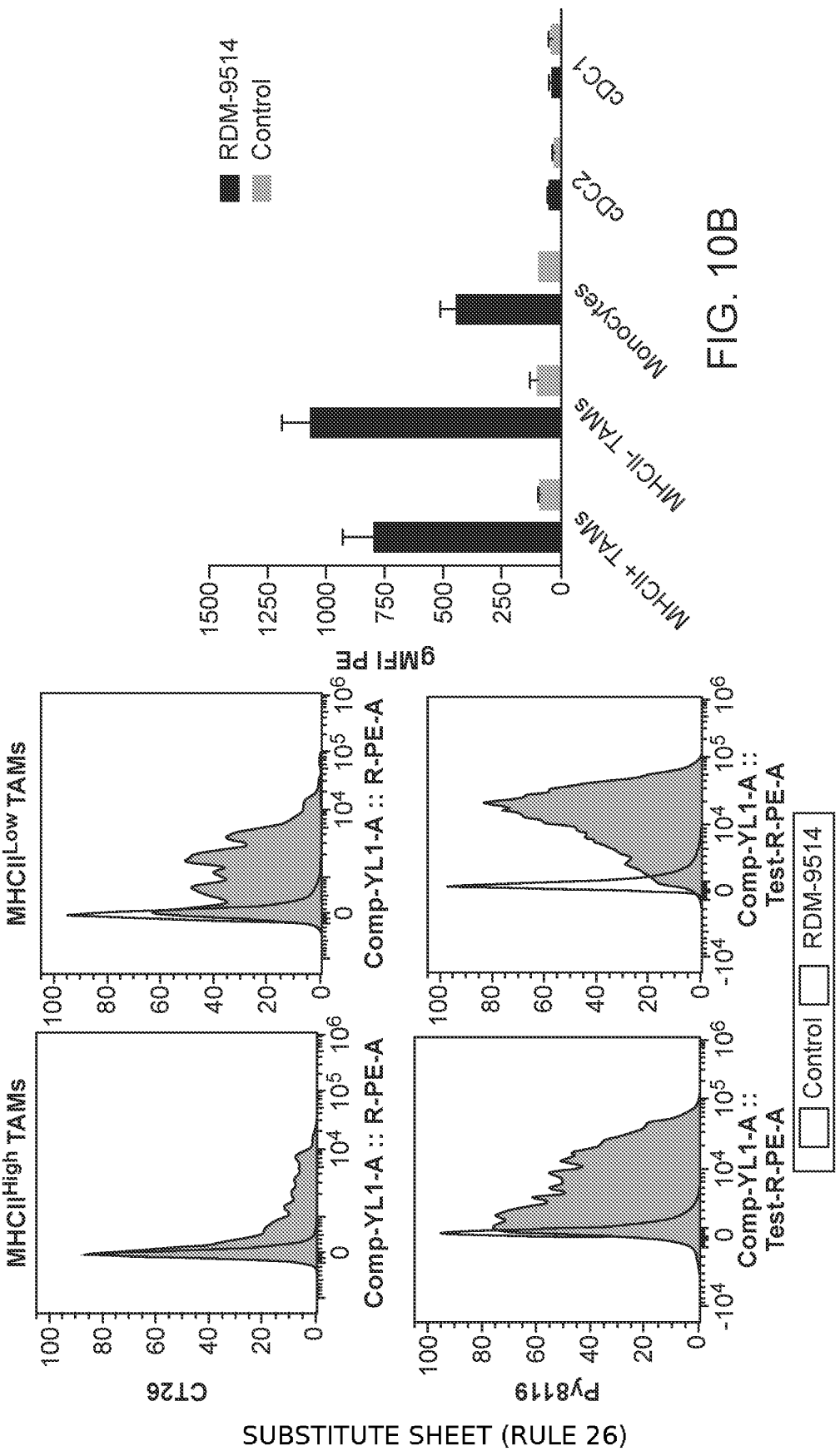


FIG. 10B

FIG. 10A

FIG. 11B

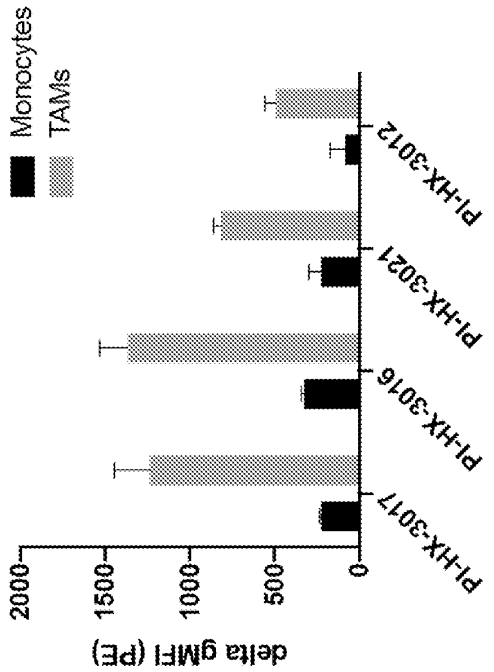


FIG. 11A

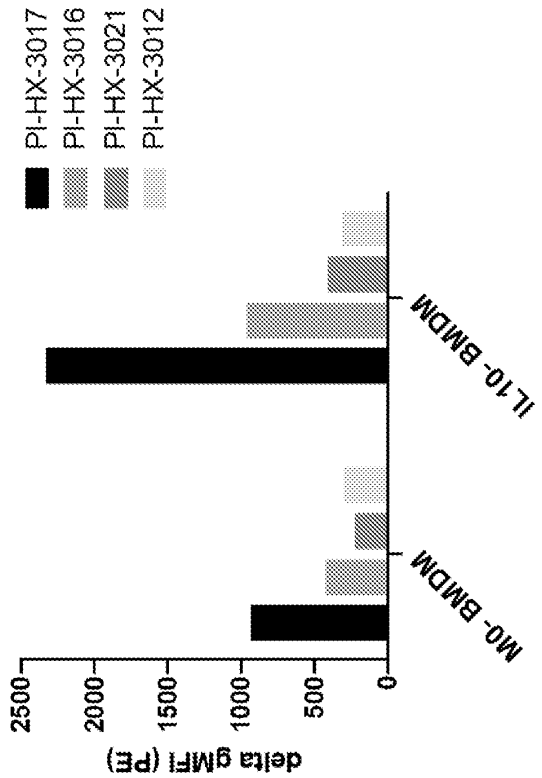


FIG. 12

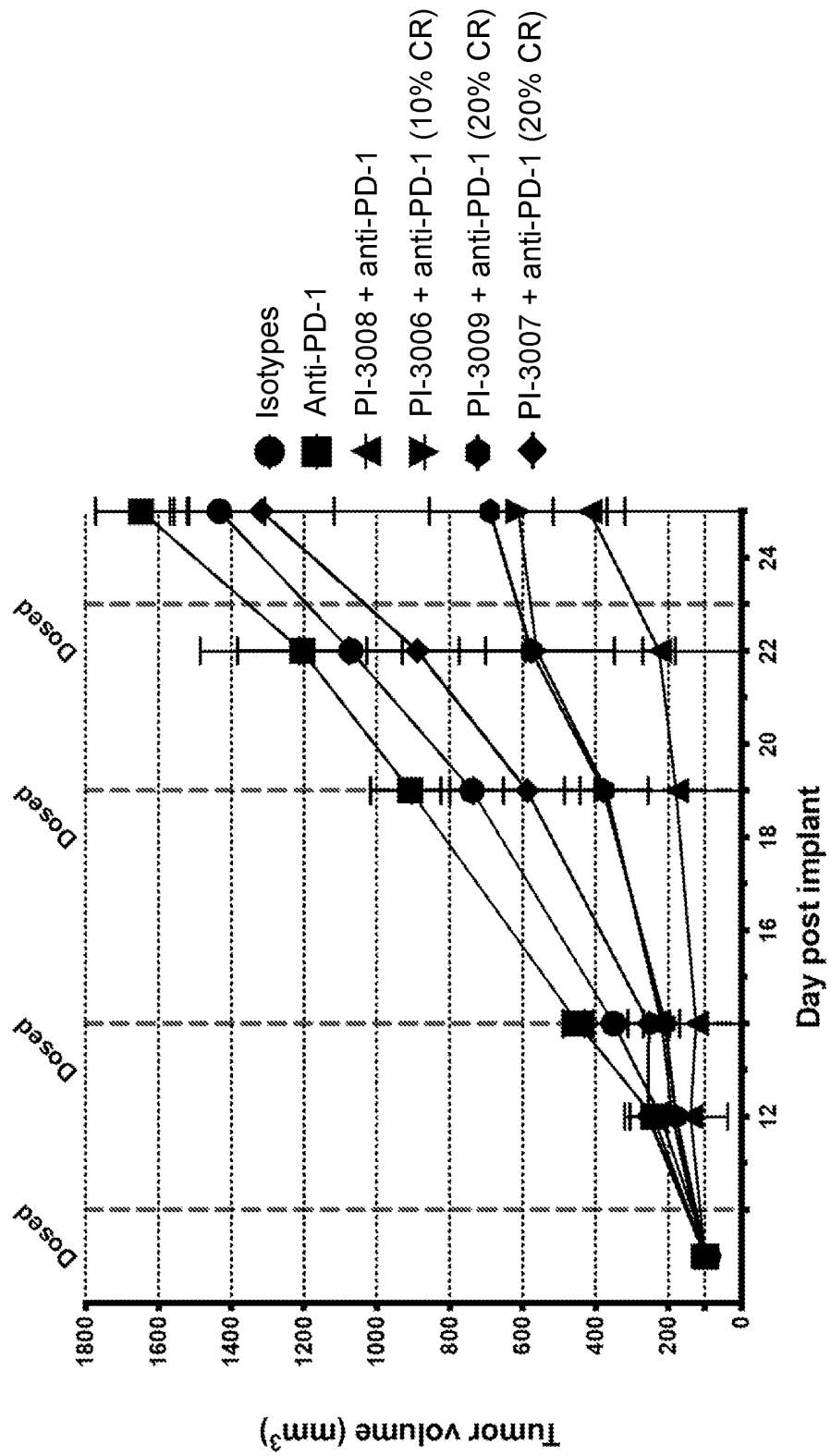

Isotypes
Anti-PD-1
PI-3008 + anti-PD-1
PI-3006 + anti-PD-1 (10% CR)
PI-3009 + anti-PD-1 (20% CR)
PI-3007 + anti-PD-1 (20% CR)
Dosed
Dosed
Dosed
Dosed
1800
1600
1400
1200
1000
800
600
400
200
0
12
16
18
20
22
24
Day post implant
Tumor volume (mm3)

FIG. 13A
Controls

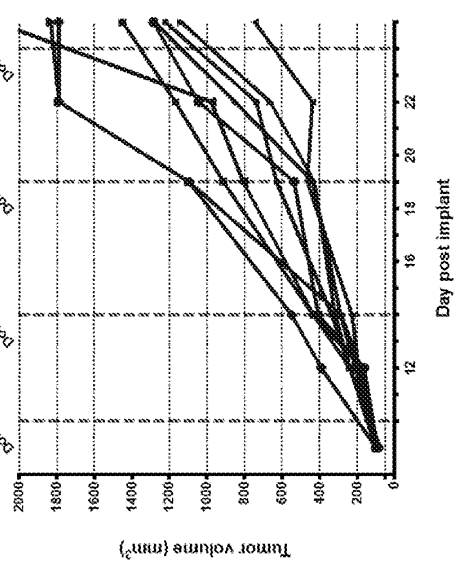


FIG. 13B
Anti-PD-1

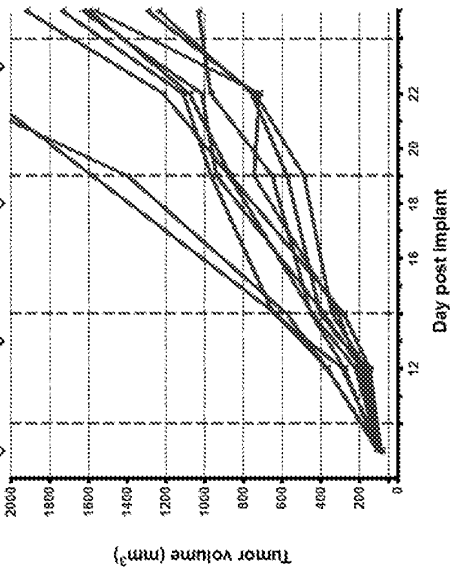


FIG. 13C
PI-3008 + anti-PD-1

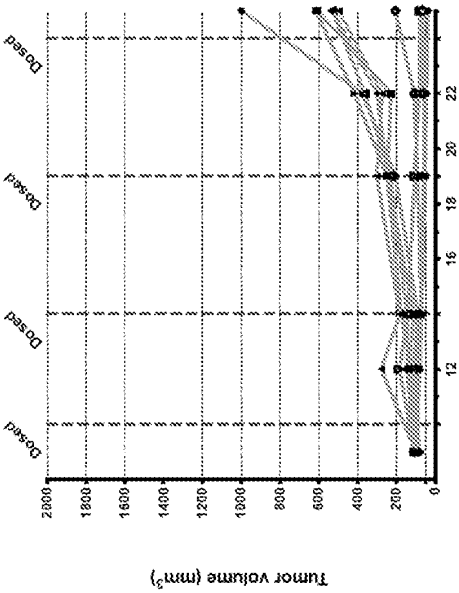


FIG. 13D
PI-3009 + anti-PD-1

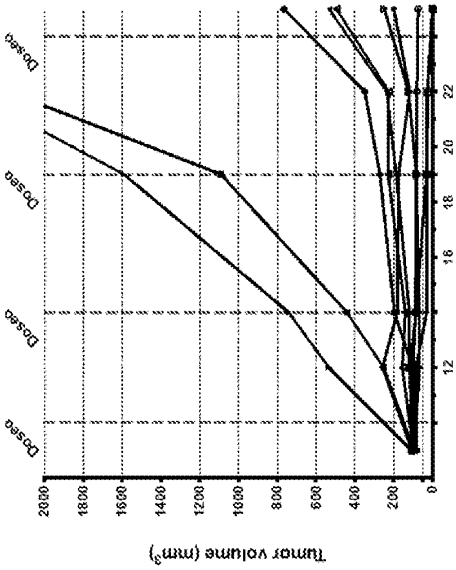


FIG. 13F
PI-3008

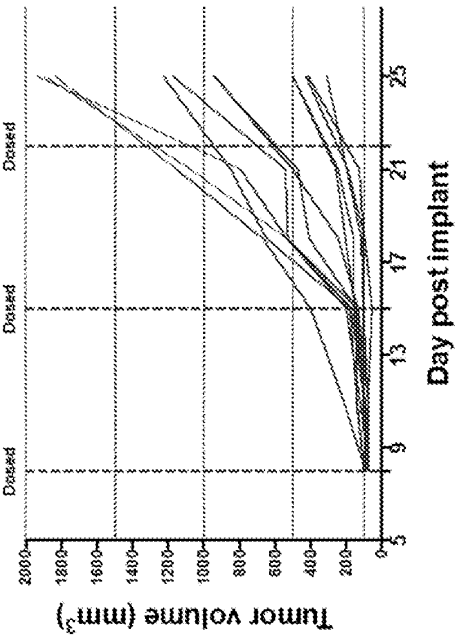


FIG. 13E
Isotype

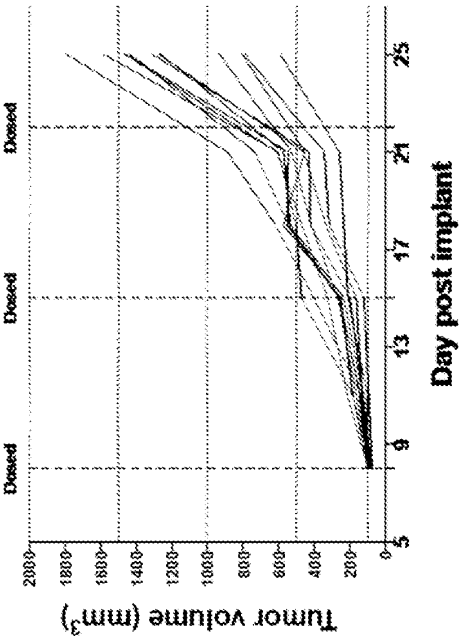
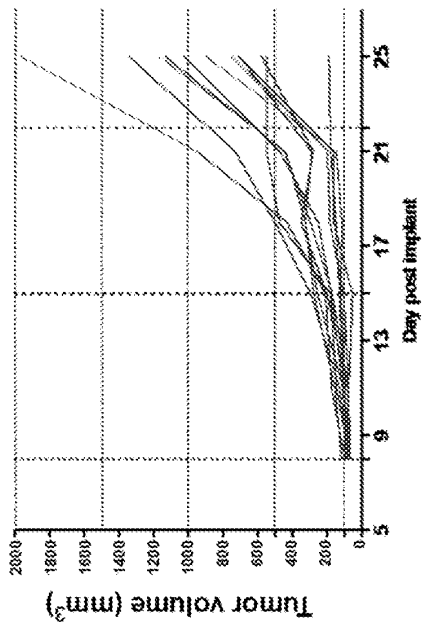


FIG. 13G
PI-3008 Afuc



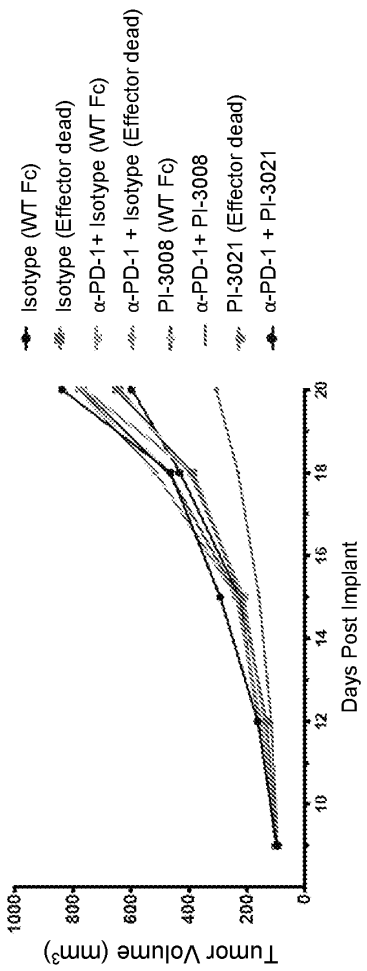


FIG. 13H

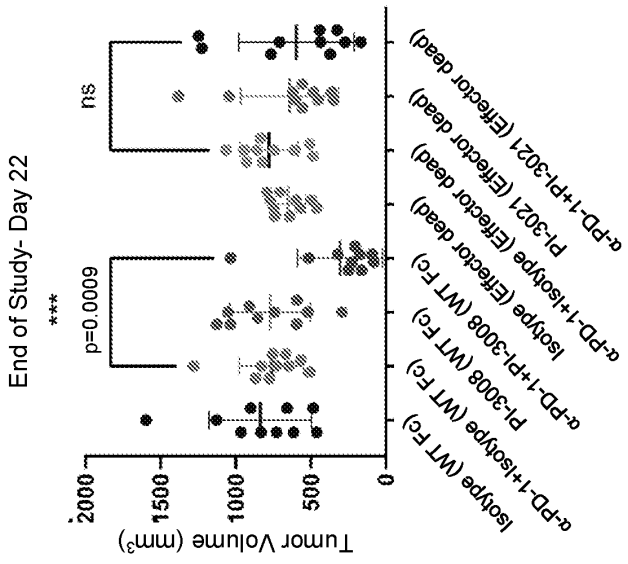


FIG. 13I

FIG. 13K

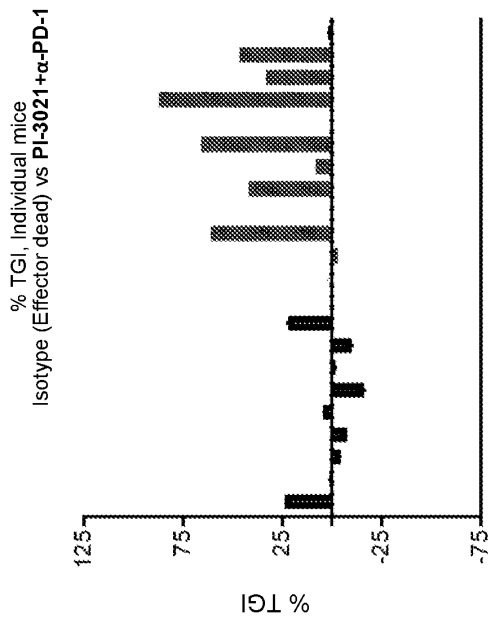


FIG. 13J

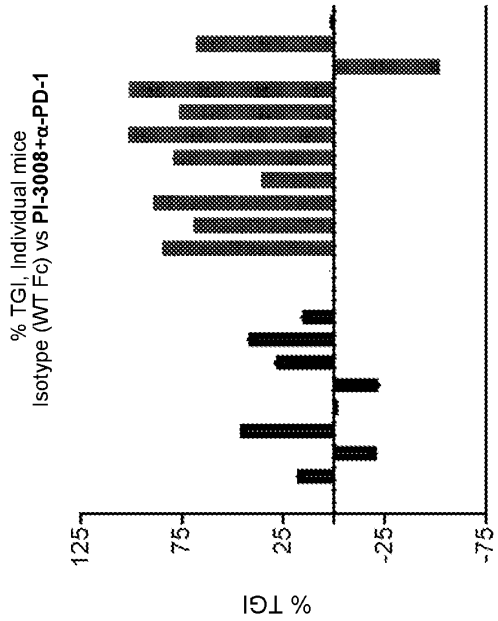


FIG. 14

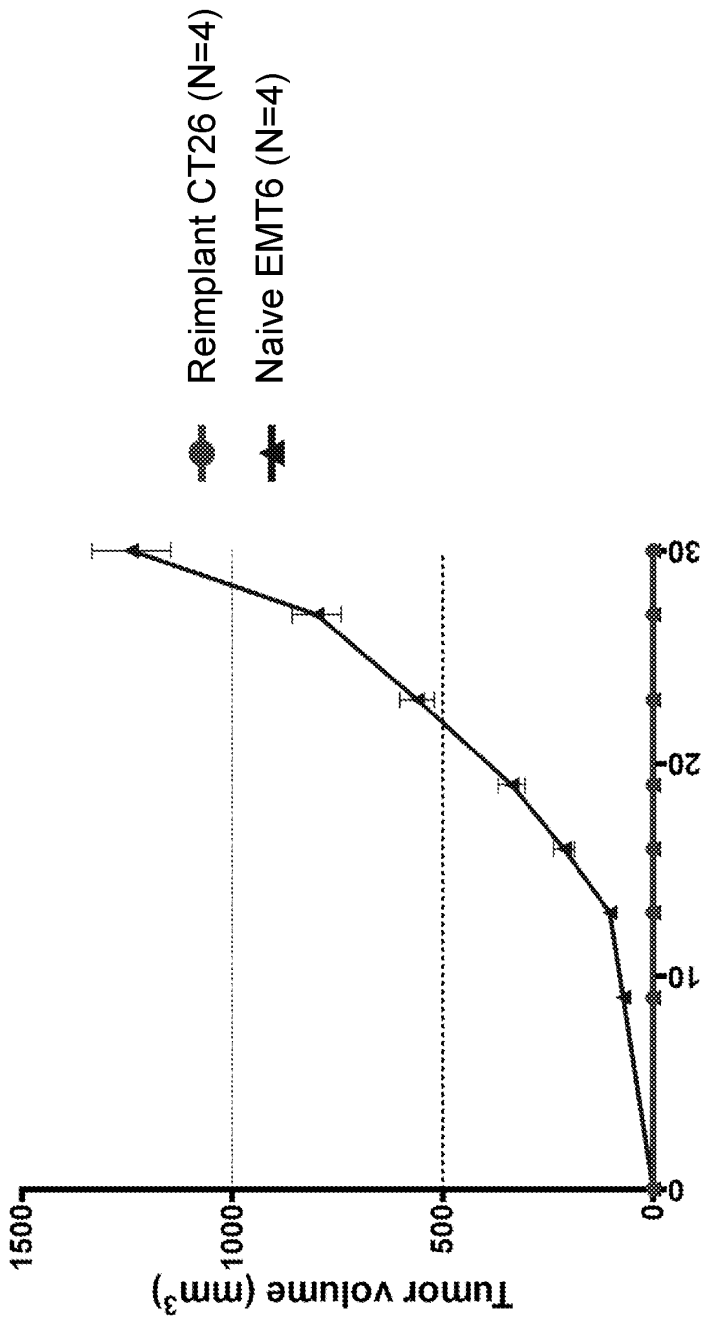

Reimplant CT26 (N=4)
Naive EMT6 (N=4)
Tumor volume (mm³)
1500
1000
500
0
0
10
20
30

FIG. 15A

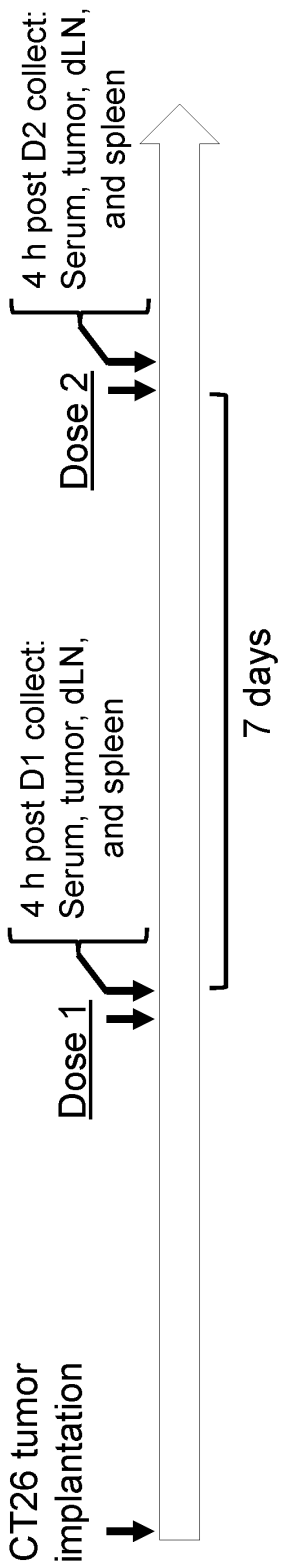


FIG. 15B

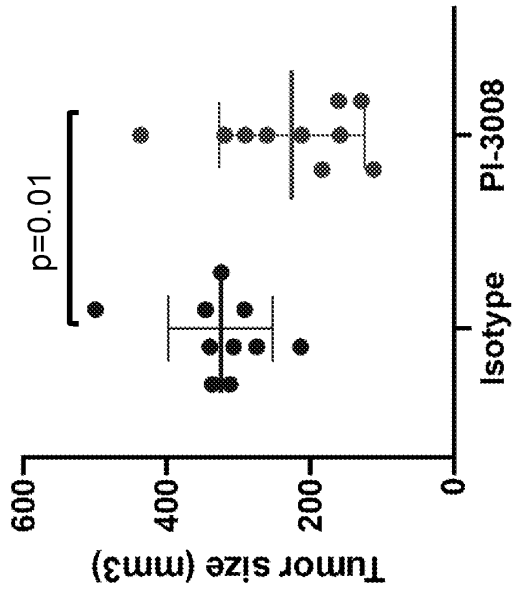
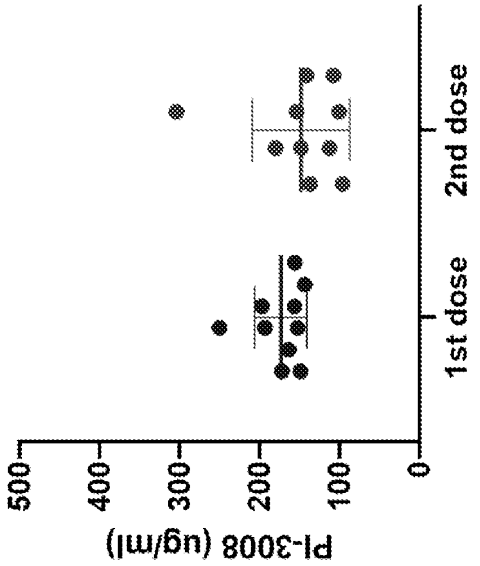


FIG. 15C



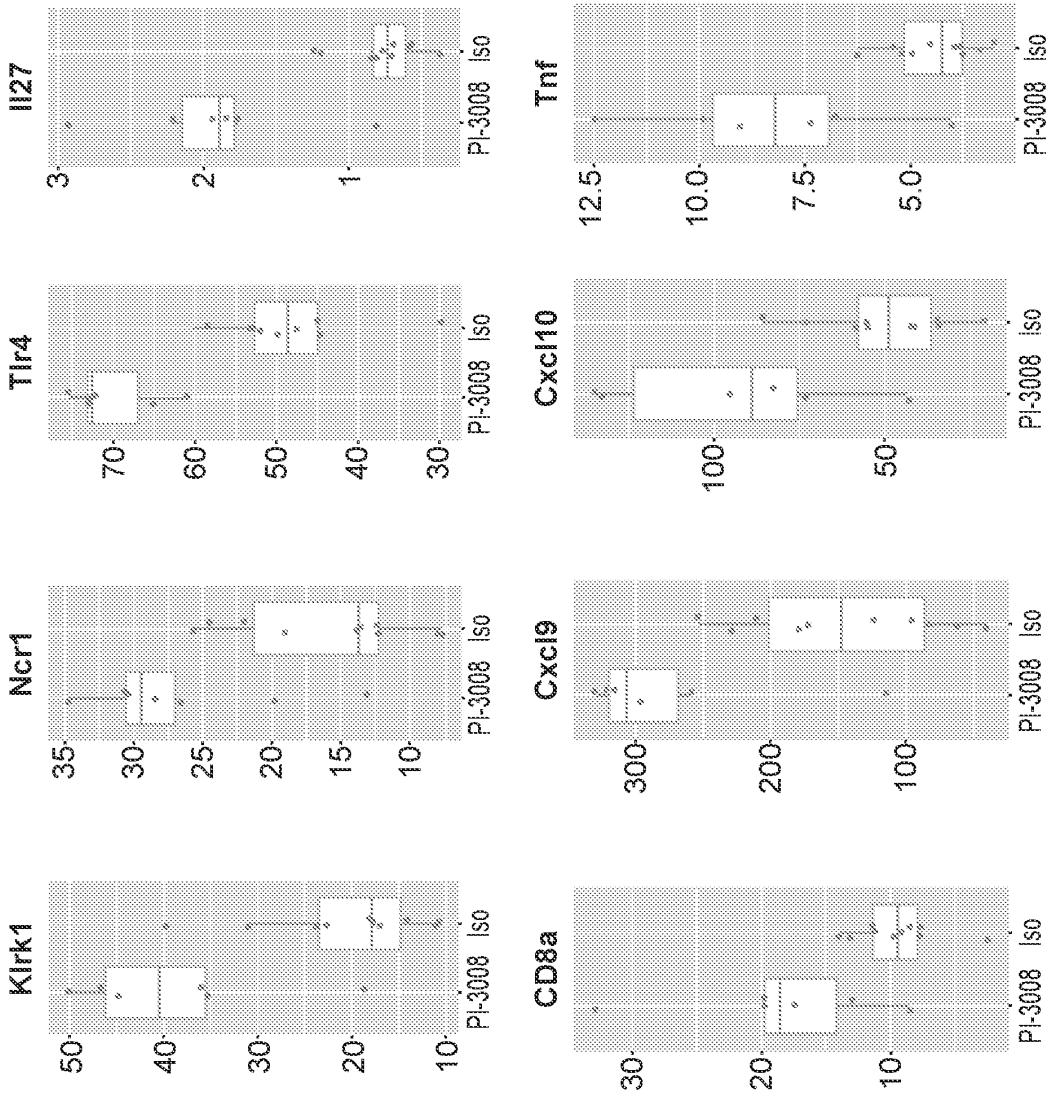


FIG. 16A

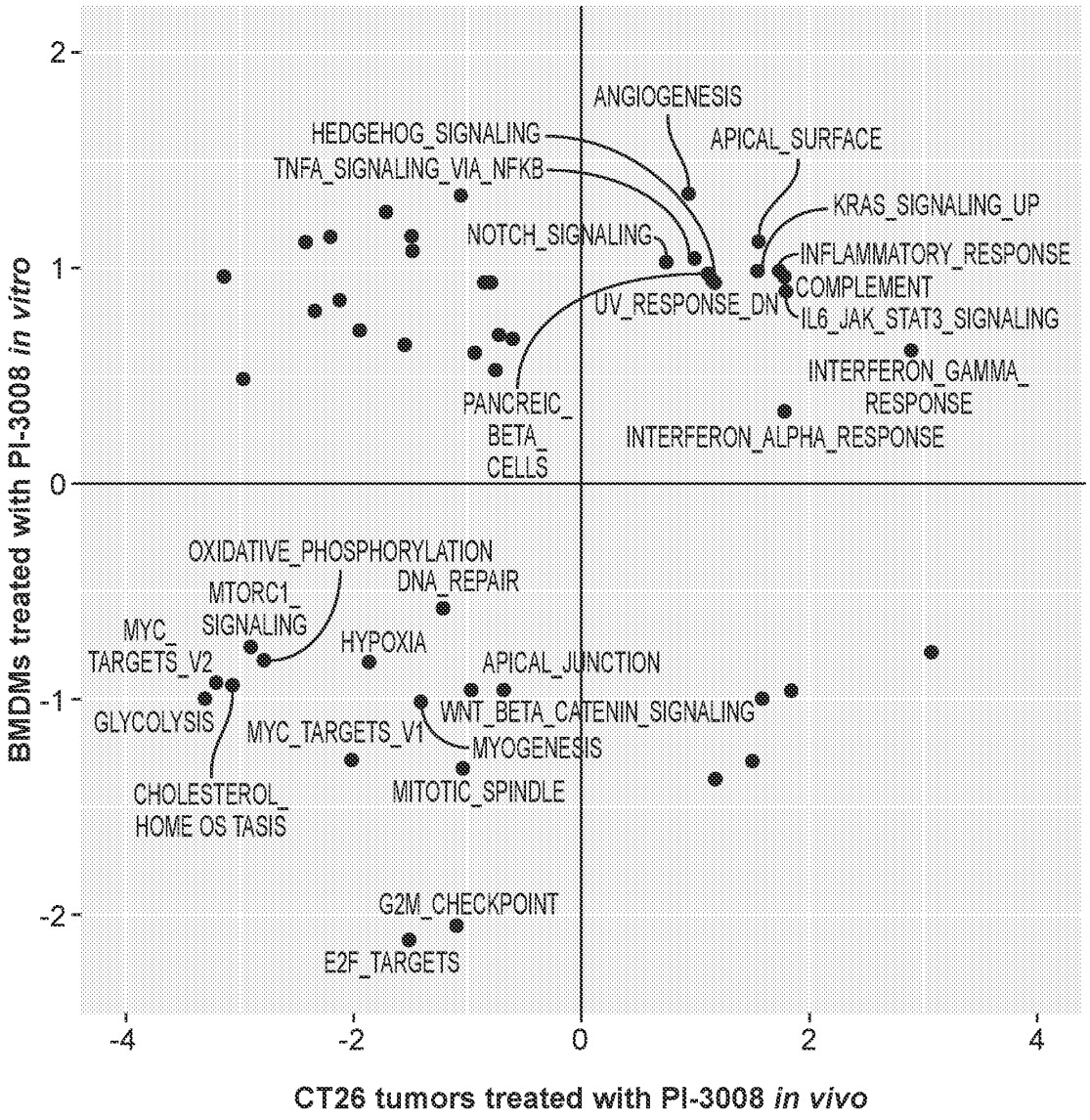

ANGIOGENESIS
HEDGEHOG_SIGNALING
APICAL_SURFACE
TNFA_SIGNALING_VIA_NFKB
KRAS_SIGNALING_UP
NOTCH_SIGNALING
INFLAMMATORY_RESPONSE
COMPLEMENT
UV_RESPONSE_DN
IL6_JAK_STAT3_SIGNALING
INTERFERON_GAMMA_RESPONSE
PANCREIC_BETA_CELLS
INTERFERON_ALPHA_RESPONSE
OXIDATIVE_PHOSPHORYLATION
DNA_REPAIR
MTORC1_SIGNALING
MYC_TARGETS_V2
HYPOXIA
APICAL_JUNCTION
GLYCOLYSIS
WNT_BETA_CATENIN_SIGNALING
MYC_TARGETS_V1
MYOGENESIS
CHOLESTEROL_HOMEOSTASIS
MITOTIC_SPINDLE
G2M_CHECKPOINT
E2F_TARGETS
BMDMs treated with PI-3008 in vitro
CT26 tumors treated with PI-3008 in vivo
2
1
0
-1
-2
-4
-2
0
2
4

FIG. 16B

FIG. 17A

```
seq                 10        20        30        40        50
AbM                 10        20        30        40        50  a
3061        EVQLVESGGGLVQPGGSLKLSCVAS KFTFSNYGMN WIRQAPKKGLEWIA LIYYNSNNKY
                          *  *   *              *    *     **
3-23*04     EVQLVESGGGLVQPGGSLRLSCAAS GFTFSSYAMS WVRQAPGKGLEWVS AISGSGGSTY
h3061-H1    EVQLVESGGGLVQPGGSLRLSCAAS KFTFSNYGMN WVRQAPGKGLEWVS LIYYNSNNKY
h3061-H2    EVQLVESGGGLVQPGGSLRLSCAAS KFTFSNYGMN WIRQAPGKGLEWIA LIYYNSNNKY
h3061-H3    EVQLVESGGGLVQPGGSLRLSCAAS GFTFSNYGMN WIRQAPGKGLEWIA LIYYNSNNKY
                                      #                          @ ##

seq         60        70        80        90        100       110       120
AbM          60        70        80  abc      90                    110
3061        YADSVKGRFTISRDNSKNTLYLEMNSLRSEDTAMYYCAK SLTGGSDYFDS WGQGVMVTVSS
                                    *     *    *                   **
3-23*04     YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK             WGQGTLVTVSS
h3061-H1    YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK SLTGGSDYFDS WGQGTLVTVSS
h3061-H2    YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK SLTGGSDYFDS WGQGTLVTVSS
h3061-H3    YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK SLTGGSDYFDS WGQGTLVTVSS
                                              M                      V

@ isoaspartate formation substitutions: S/Q/A
# asparagine deamidation substitutions: Q/S/A
```

FIG. 17B

```
seq                 10        20        30        40        50
AbM                 10        20        30        40        50
3061        DVQMTQSPSYLAASPGESVSISC KASKSIGTFLA WYQEKPEKTNKLLIY SGSTLQS
             *       * *  * ** * *                 *   * **
1-39*01     DIQMTQSPSSLSASVGDRVTITC RASQSISSYLN WYQQKPGKAPKLLIY AASSLQS
h3061-L1    DIQMTQSPSSLSASVGDRVTITC RASKSIGTFLA WYQQKPGKAPKLLIY SGSTLQS
             V                      K              E    TN

seq          60        70        80        90        100
AbM          60        70        80        90        100
3061        GTPSRFSGSGSGTDFTLTIRNLEPEDFAVYYC QQHDEYPFT FGSGTKLEIK
             *                  ** *     *              *
1-39*01     GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC QQSYSTPP  FGQGTKLEIK
h3061-L1    GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC QQHDEYPFT FGQGTKLEIK
             T
```

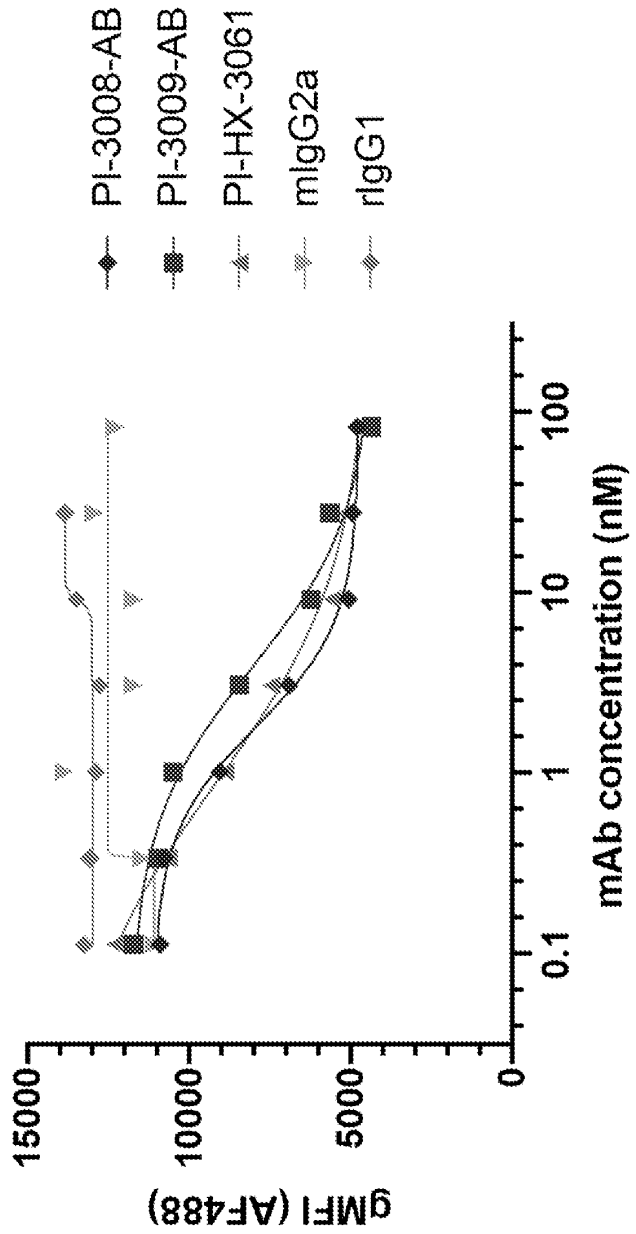
FIG. 18

```
seq                 10        20        30        40        50
AbM                 10        20        30        40        50
                 b b b    p p     b b b  b   b   bi bi i    ii ibbi
3031             DIQMTQSPASLSTSLGETVSIEC LASEGISNDLA WYQQKSGKSPQLLIY AA
                       *   * * ** * *                 *   * *
1-39*01          DIQMTQSPSSLSASVGDRVTITC RASQSISSYLN WYQQKPGKAPKLLIY AA
h3031-L1         DIQMTQSPSSLSASVGDRVTITC %ASEGISNDLA WYQQKPGKAPKLLIY AA
h3031-L2         DIQMTQSPSSLSASVGDRVTITC %ASEGISNDLA WYQQKPGKAPKLLIY AA
h3031-L3         DIQMTQSPSSLSASVGDRVTITC %ASEGISNDLA WYQQKPGKAPKLLIY AA
h3031-L2b        DIQMTQSPSSLSASVGDRVTITC %ASEGISNDLA WYQQKPGKAPKLLIY AA
h3031-L2c        DIQMTQSPSSLS%SVGDRVTITC %ASEGISNDLA WYQQKPGK%PKLLIY AA
h3031-L2d        DIQMTQSPSSLS%SVGDRVTITC %ASEGISNDLA WYQQKPGK%PKLLIY AA
                            T           L      #            S

seq               60        70        80        90        100
AbM               60        70        80        90        100
                 b   b        b b b  b    ib bib  ibii-ib  i   b b b
3031             GVPSRFSGSGSGTRYSLKISGMQPEDEADYFC QQSYKYPLT FGSGTKLEIK
                          *** *  **    * * *                 *
1-39*01          GVPSRFSGSGSGTD#TLTISSLQPEDFATYYC QQSYSTPP  FGQGTKLEIK
h3031-L1         GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC QQSYKYPLT FGQGTKLEIK
h3031-L2         GVPSRFSGSGSGTD%TLTISSLQPEDFATYYC QQSYKYPLT FGQGTKLEIK
h3031-L3         GVPSRFSGSGSGTD%TLTISS%QPEDFATYYC QQSYKYPLT FGQGTKLEIK
h3031-L2b        GVPSRFSGSGSGTD%TLTISSLQPEDFATYYC QQSYKYPLT FGQGTKLEIK
h3031-L2c        GVPSRFSGSGSGTD%TLTISSLQPEDFATY#C QQSYKYPLT FGQGTKLEIK
h3031-L2d        GVPSRFSGSGSGTD%TLTISSLQPED%ATY#C QQSYKYPLT FGQGTKLEIK
                                        E   F

# deamidation substitutions: Q/S/A/D
```

FIG. 19


PI-3008-AB
PI-3009-AB
PI-HX-3061
mIgG2a
rIgG1
gMFI (AF488)
15000
10000
5000
0
0.1
1
10
100
mAb concentration (nM)

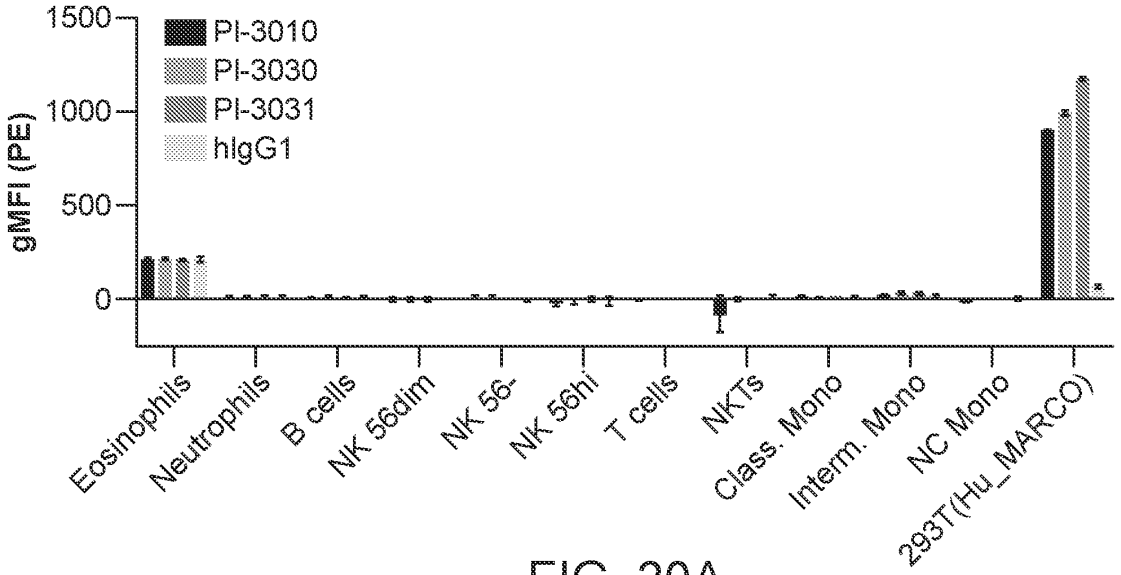


FIG. 20A

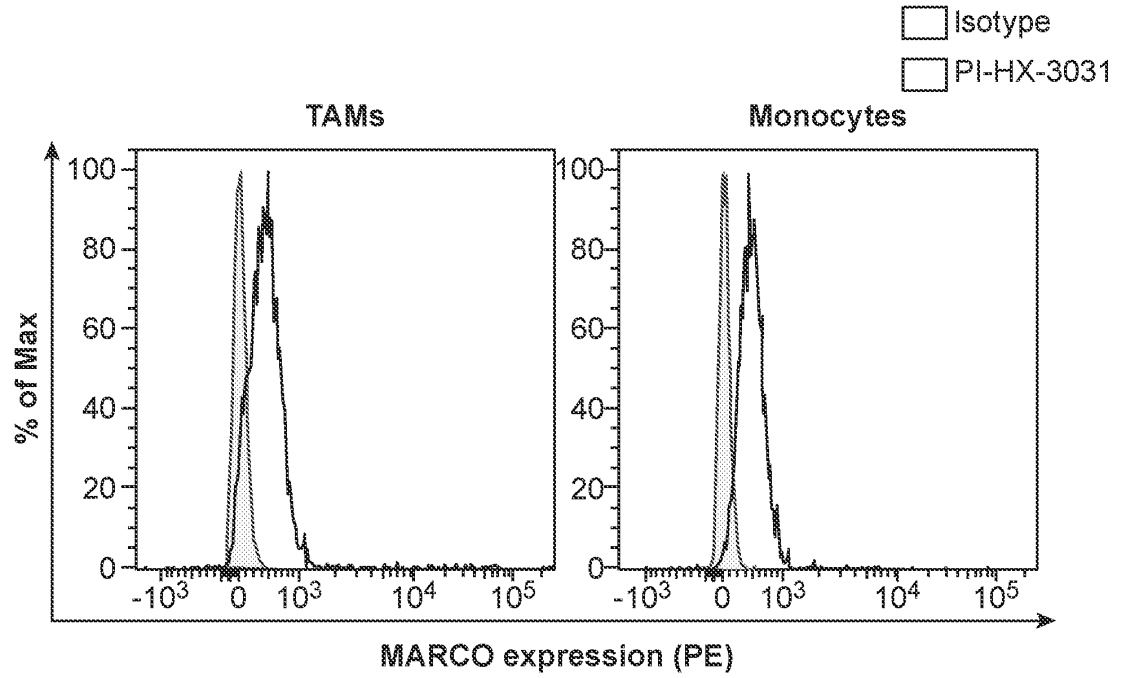
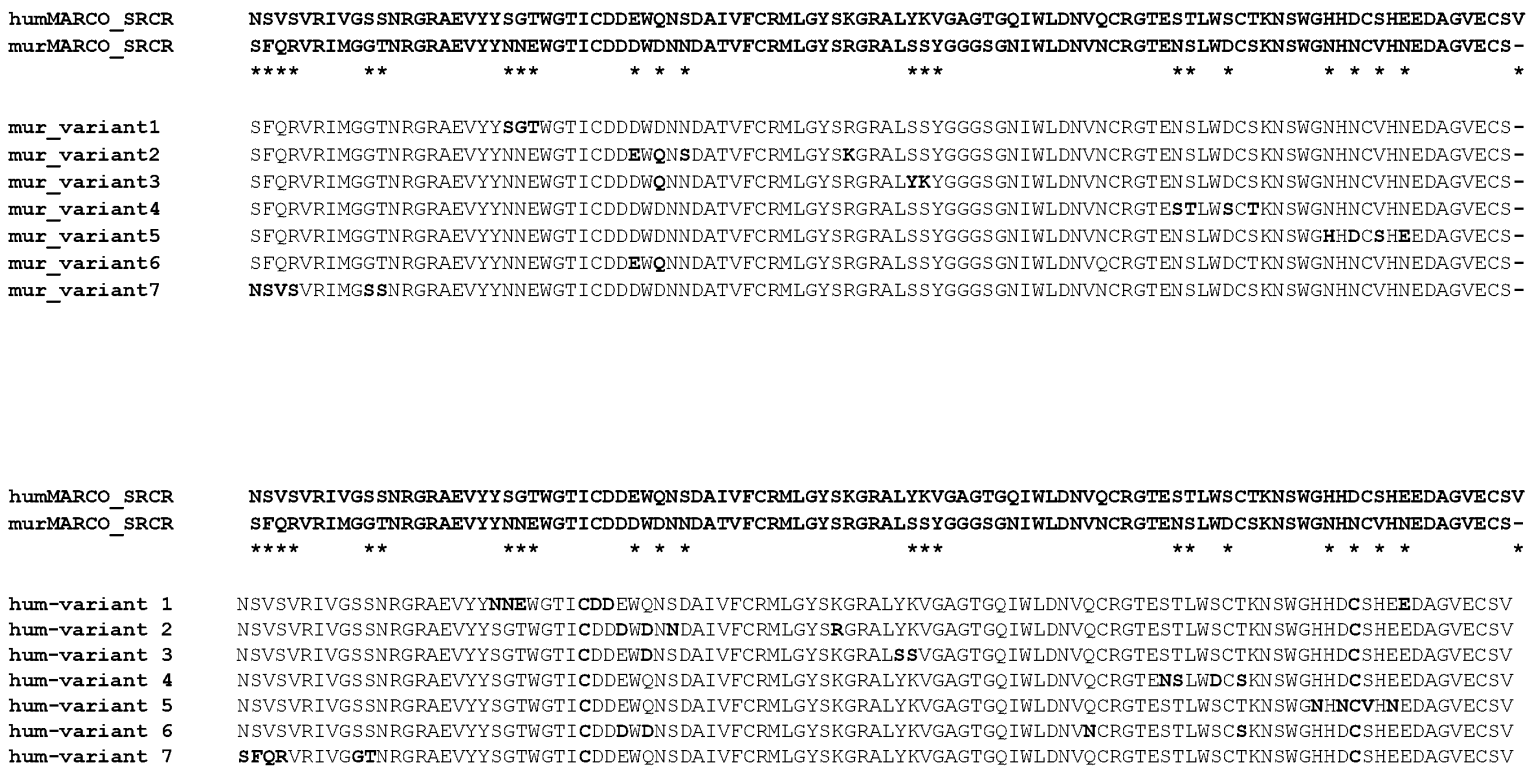


FIG. 20B

FIG. 21


humMARCO_SRCR NSVSVRIVGSSNRGRAEVYYSGTWGTICDDEWQNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGHHDCSHEEDAGVECSV
murMARCO_SRCR SFQRVRIMGGTNRGRAEVYYNNEWGTICDDDWDNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVNCRGTENSLWDCSKNSWGNHNCVHNEDAGVECS-
mur_variant1 SFQRVRIMGGTNRGRAEVYYSGTWGTICDDDWDNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVNCRGTENSLWDCSKNSWGNHNCVHNEDAGVECS-
mur_variant2 SFQRVRIMGGTNRGRAEVYYNNEWGTICDDEWQNSDATVFCRMLGYSKGRALSSYGGGSGNIWLDNVNCRGTENSLWDCSKNSWGNHNCVHNEDAGVECS-
mur_variant3 SFQRVRIMGGTNRGRAEVYYNNEWGTICDDDWQNNDATVFCRMLGYSRGRALYKYGGGSGNIWLDNVNCRGTENSLWDCSKNSWGNHNCVHNEDAGVECS-
mur_variant4 SFQRVRIMGGTNRGRAEVYYNNEWGTICDDDWDNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVNCRGTESTLWSCTKNSWGNHNCVHNEDAGVECS-
mur_variant5 SFQRVRIMGGTNRGRAEVYYNNEWGTICDDDWDNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVNCRGTENSLWDCSKNSWGHHDCSHEEDAGVECS-
mur_variant6 SFQRVRIMGGTNRGRAEVYYNNEWGTICDDEWQNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVQCRGTENSLWDCTKNSWGNHNCVHNEDAGVECS-
mur_variant7 NSVSVRIMGSSNRGRAEVYYNNEWGTICDDDWDNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVNCRGTENSLWDCSKNSWGNHNCVHNEDAGVECS-
humMARCO_SRCR NSVSVRIVGSSNRGRAEVYYSGTWGTICDDEWQNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGHHDCSHEEDAGVECSV
murMARCO_SRCR SFQRVRIMGGTNRGRAEVYYNNEWGTICDDDWDNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVNCRGTENSLWDCSKNSWGNHNCVHNEDAGVECS-
hum-variant 1 NSVSVRIVGSSNRGRAEVYYNNEWGTICDDEWQNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGHHDCSHEEDAGVECSV
hum-variant 2 NSVSVRIVGSSNRGRAEVYYSGTWGTICDDDWDNNDAIVFCRMLGYSRGRALYKVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGHHDCSHEEDAGVECSV
hum-variant 3 NSVSVRIVGSSNRGRAEVYYSGTWGTICDDEWDNSDAIVFCRMLGYSKGRALSSVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGHHDCSHEEDAGVECSV
hum-variant 4 NSVSVRIVGSSNRGRAEVYYSGTWGTICDDEWQNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVQCRGTENSLWDCSKNSWGHHDCSHEEDAGVECSV
hum-variant 5 NSVSVRIVGSSNRGRAEVYYSGTWGTICDDEWQNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGNHNCVHNEDAGVECSV
hum-variant 6 NSVSVRIVGSSNRGRAEVYYSGTWGTICDDDWDNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVNCRGTESTLWSCSKNSWGHHDCSHEEDAGVECSV
hum-variant 7 SFQRVRIVGGTNRGRAEVYYSGTWGTICDDEWQNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGHHDCSHEEDAGVECSV

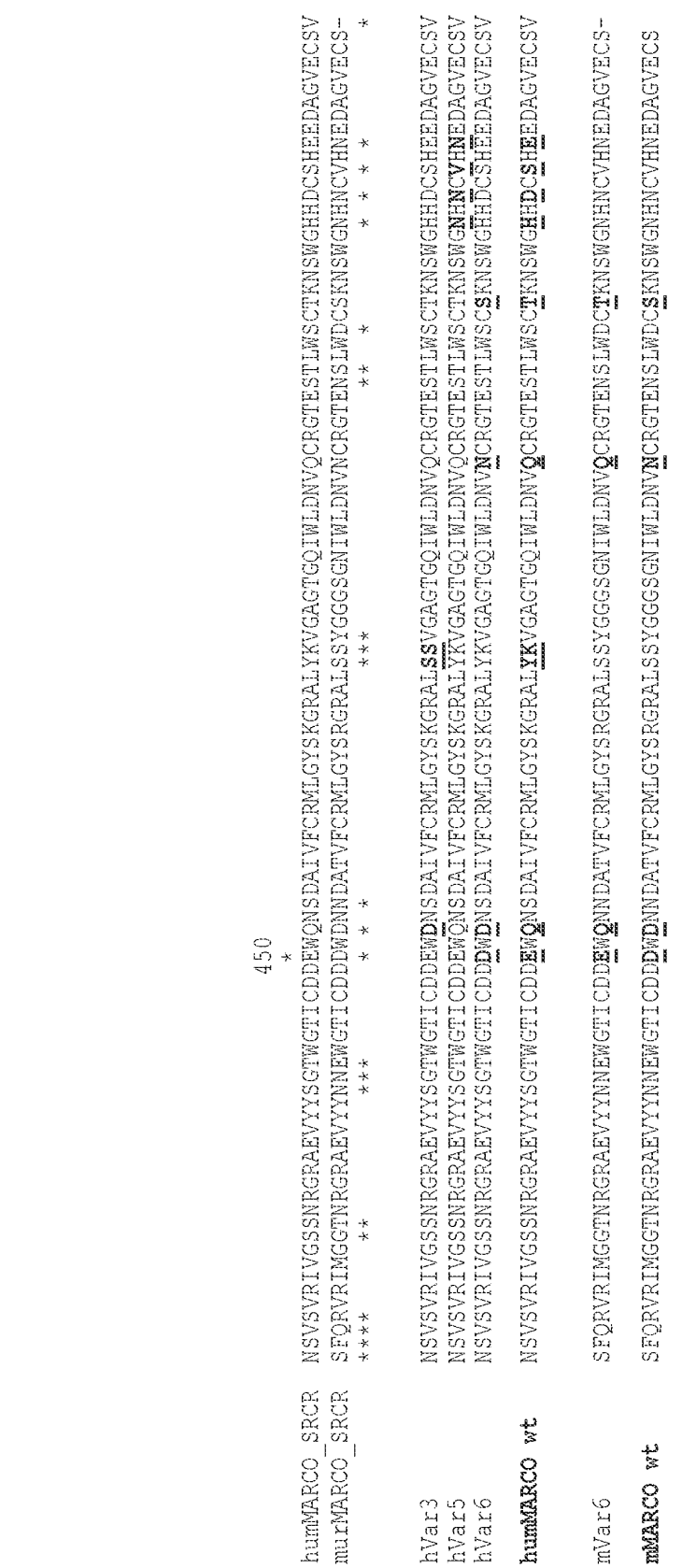
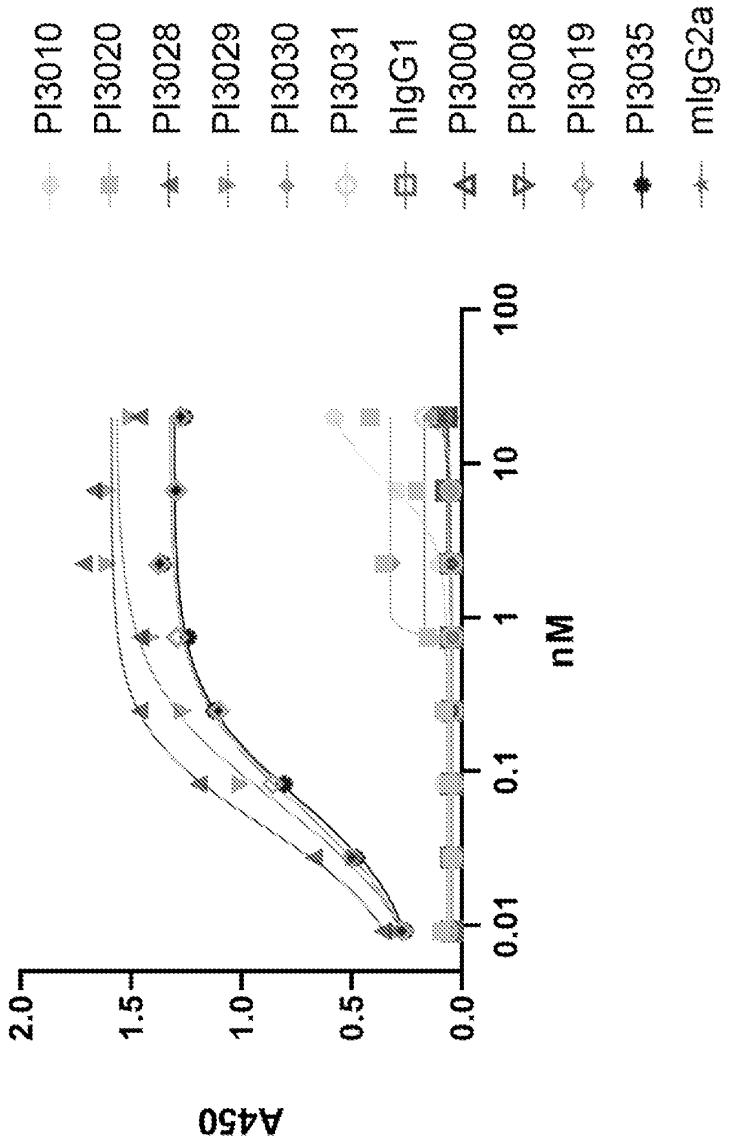

450
humMARCO_SRCR NSVSVRIVGSSNRGRAEVYYSGTWGTICDDEWQNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGHHDCSHEEDAGVECSV
murMARCO_SRCR SFQRVRIMGGTNRGRAEVYYNNEWGTICDDDWDNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVNCRGTENSLWDCSKNSWGNHNCVHNEDAGVECS-
hVar3 NSVSVRIVGSSNRGRAEVYYSGTWGTICDDEWDNSDAIVFCRMLGYSKGRALSSVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGHHDCSHEEDAGVECSV
hVar5 NSVSVRIVGSSNRGRAEVYYSGTWGTICDDEWQNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGNEHNCVHNEDAGVECSV
hVar6 NSVSVRIVGSSNRGRAEVYYSGTWGTICDDDWDNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVNCRGTESTLWSCSKNSWGHHDCSHEEDAGVECSV
humMARCO wt NSVSVRIVGSSNRGRAEVYYSGTWGTICDDEWQNSDAIVFCRMLGYSKGRALYKVGAGTGQIWLDNVQCRGTESTLWSCTKNSWGHEDCSHEEDAGVECSV
mVar6 SFQRVRIMGGTNRGRAEVYYNNEWGTICDDEWQNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVQCRGTENSLWDCTKNSWGNHNCVHNEDAGVECS-
mMARCO wt SFQRVRIMGGTNRGRAEVYYNNEWGTICDDDWDNNDATVFCRMLGYSRGRALSSYGGGSGNIWLDNVNCRGTENSLWDCSKNSWGNHNCVHNEDAGVECS

FIG. 22

FIG. 23


PI3010
PI3020
PI3028
PI3029
PI3030
PI3031
hIgG1
PI3000
PI3008
PI3019
PI3035
mIgG2a
A450
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
nM

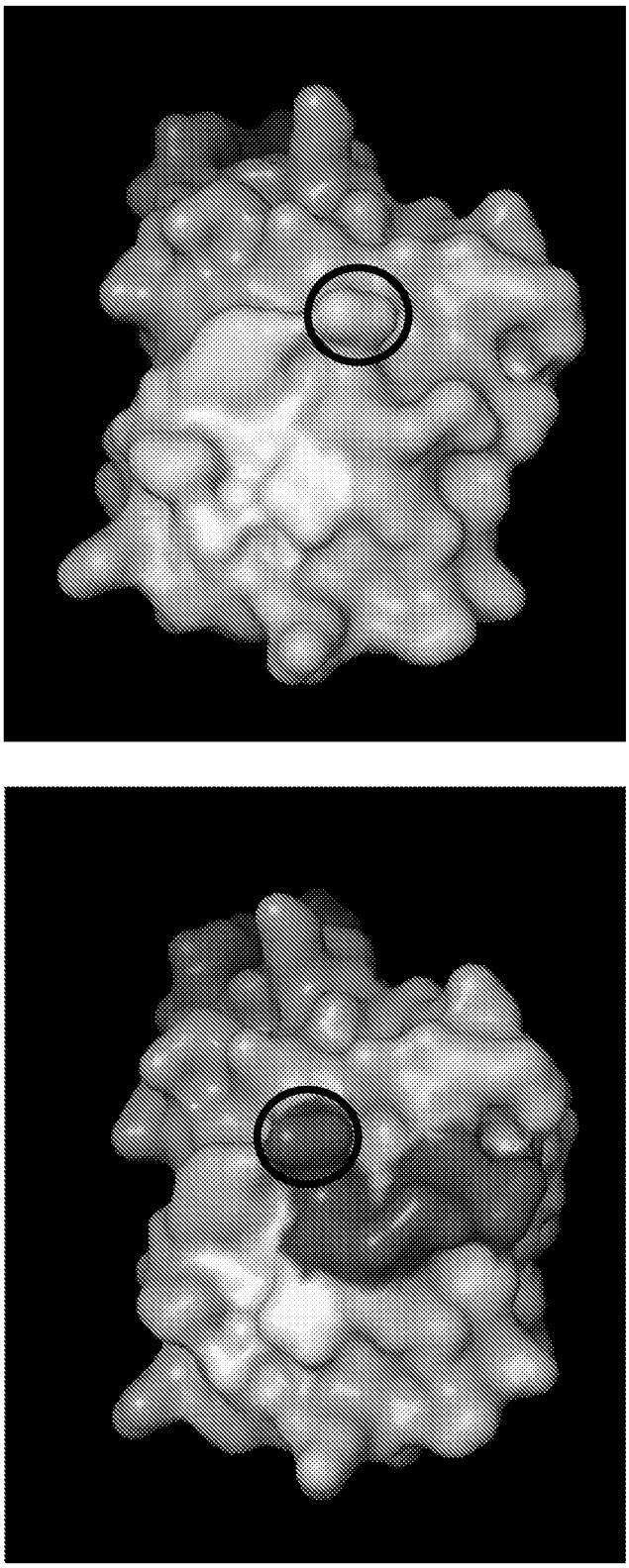


FIG. 24

FIG. 25A

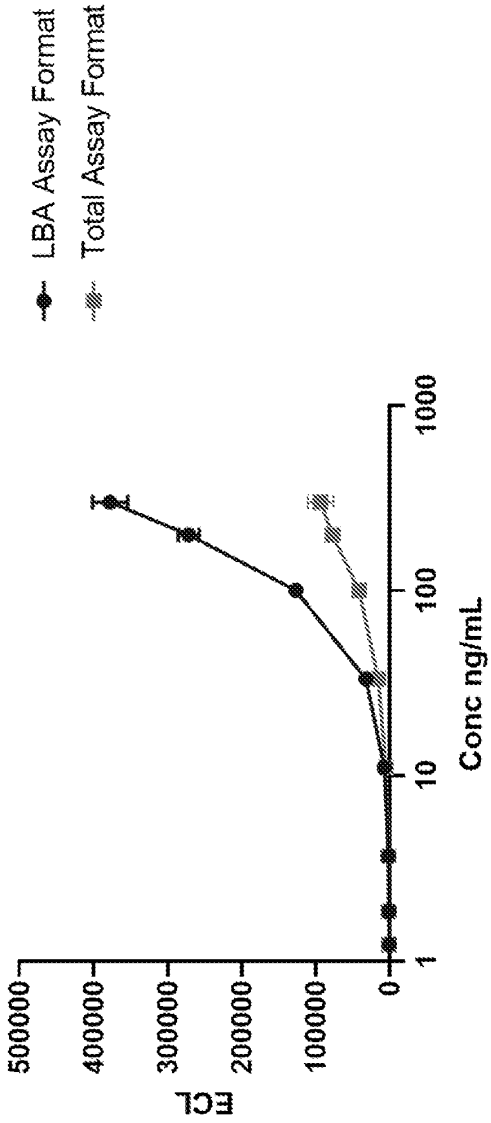
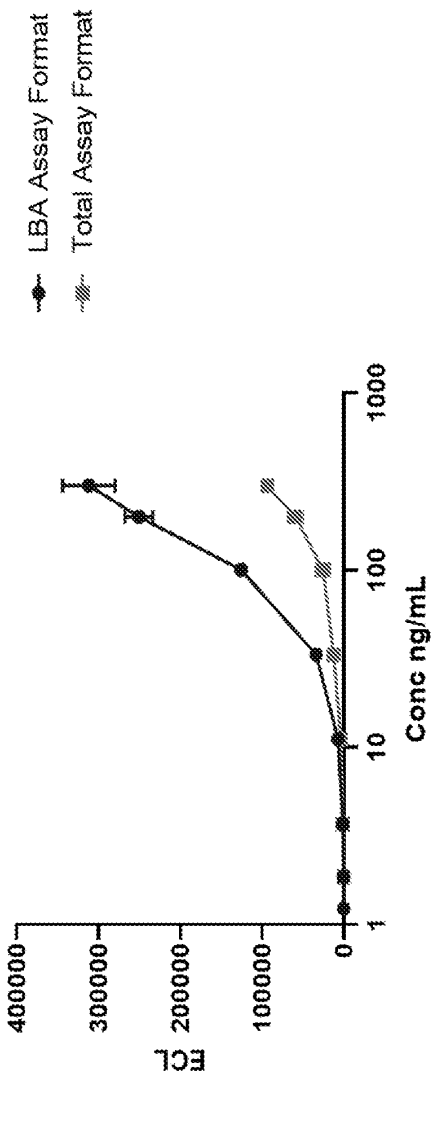


FIG. 25B



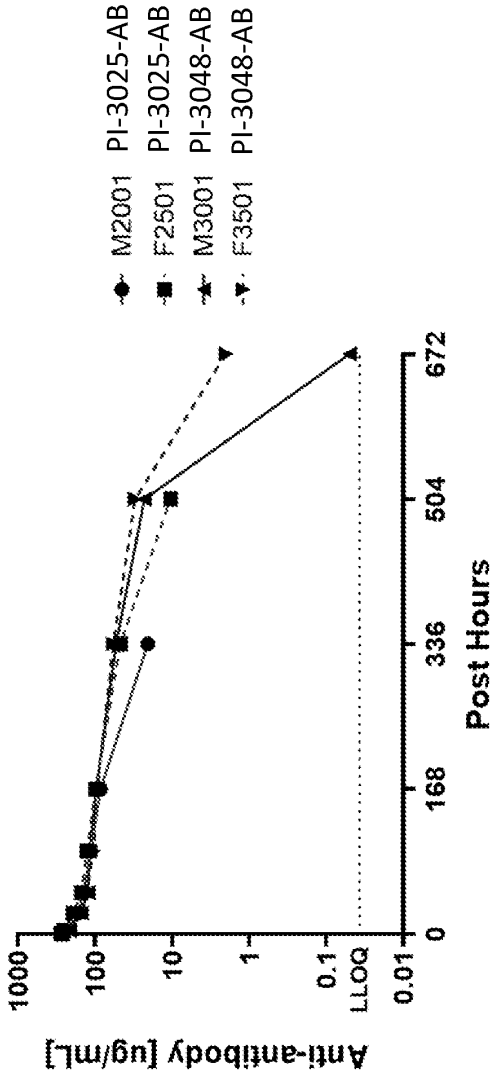


FIG. 26A

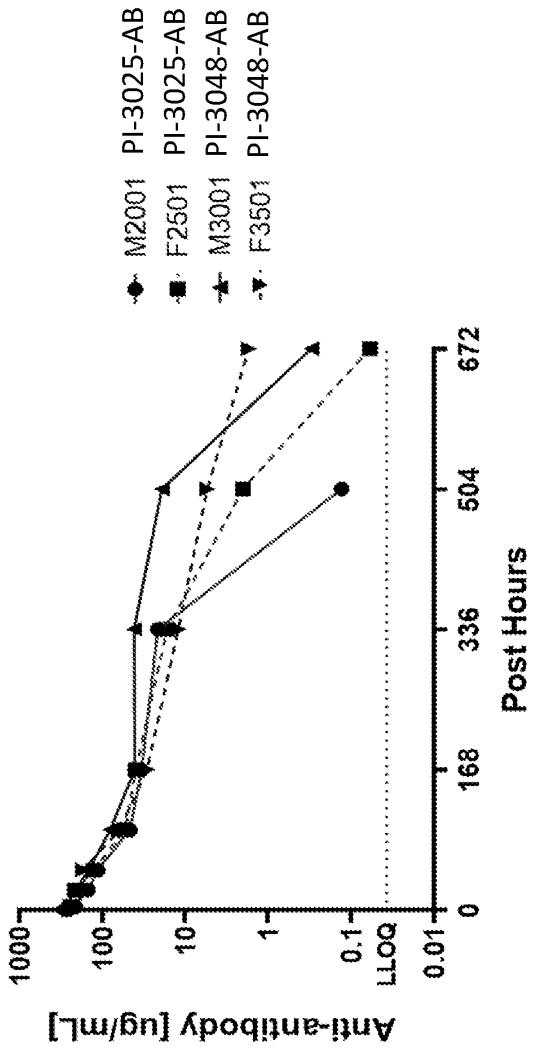
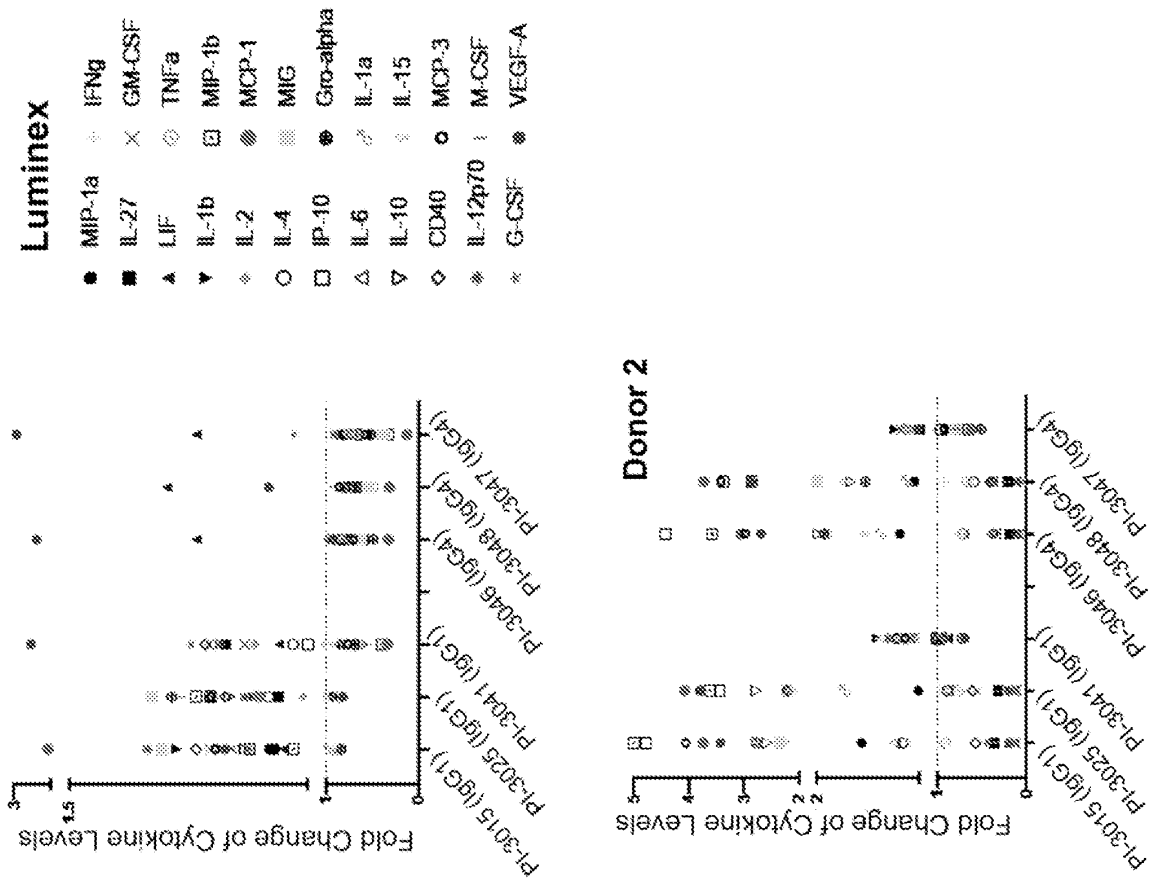


FIG. 26B

FIG. 27


Donor 1
Donor 2
Luminex
MIP-1a
IFNg
IL-27
GM-CSF
LIF
TNFa
IL-1b
MIP-1b
IL-2
MCP-1
IL-4
MIG
IP-10
Gro-alpha
IL-6
IL-1a
IL-10
IL-15
CD40
MCP-3
IL-12p70
M-CSF
G-CSF
VEGF-A
Fold Change of Cytokine Levels
PI-3015 (IgG1)
PI-3025 (IgG1)
PI-3041 (IgG1)
PI-3046 (IgG4)
PI-3048 (IgG4)
PI-3047 (IgG4)

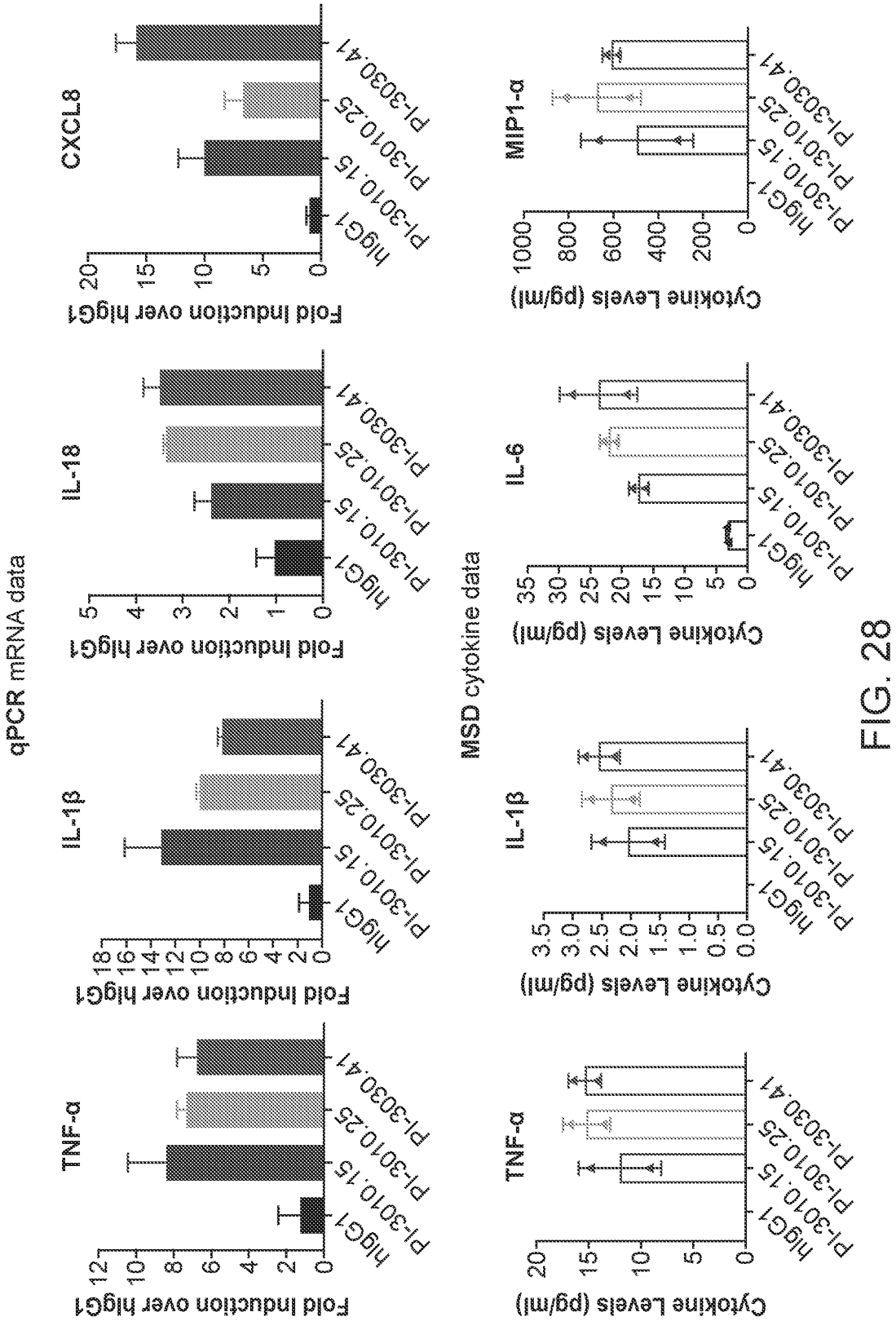

qPCR mRNA data
MSD cytokine data
TNF-α
IL-1β
IL-18
CXCL8
IL-6
MIP1-α
Fold Induction over hIgG1
Cytokine Levels (pg/ml)
hIgG1
Pl-3010.15
Pl-3010.25
Pl-3030.41

FIG. 28

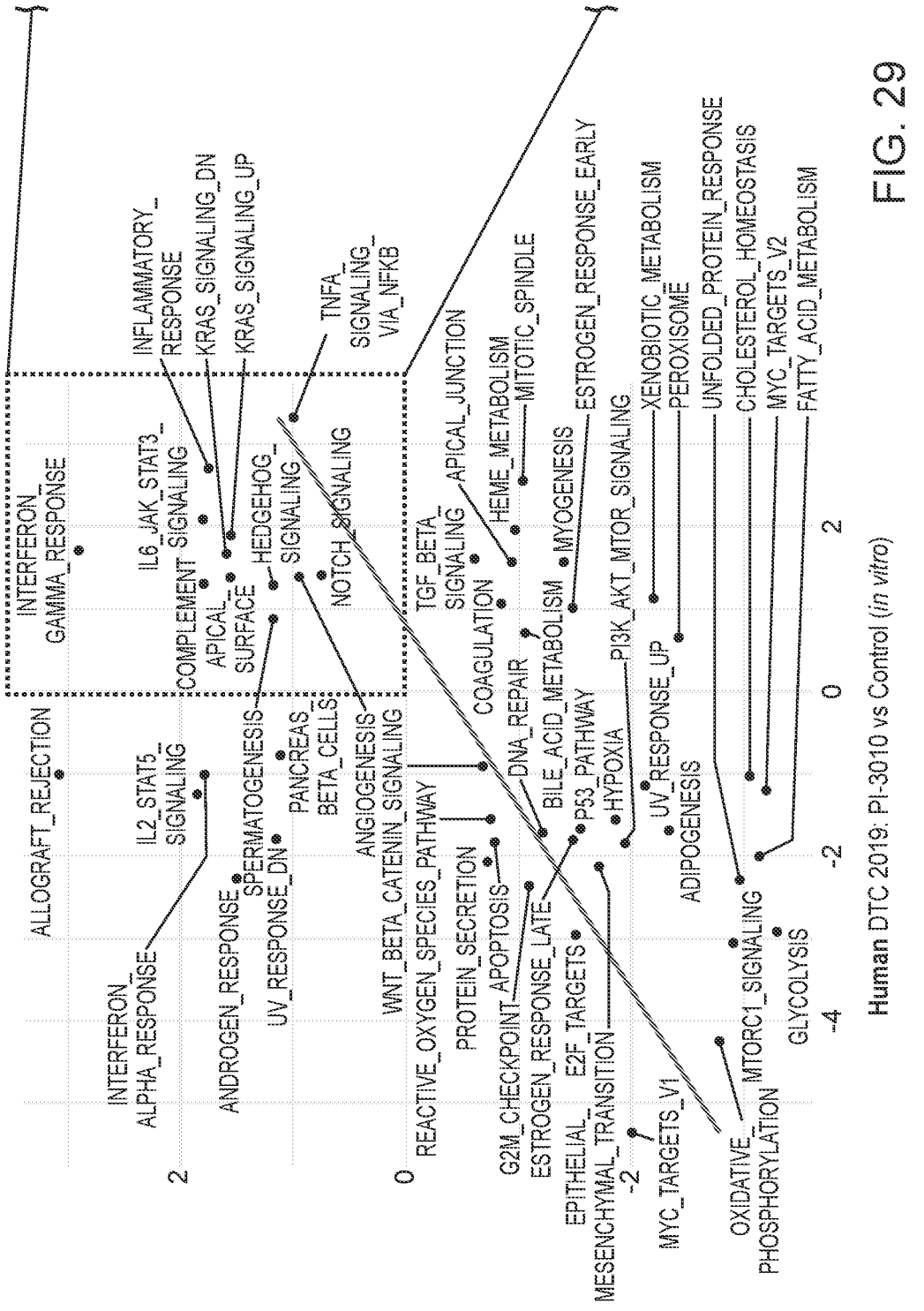

ALLOGRAFT_REJECTION
INTERFERON_GAMMA_RESPONSE
IL2_STAT5_SIGNALING
INFLAMMATORY_RESPONSE
IL6_JAK_STAT3_SIGNALING
KRAS_SIGNALING_DN
COMPLEMENT
APICAL_SURFACE
KRAS_SIGNALING_UP
INTERFERON_ALPHA_RESPONSE
HEDGEHOG_SIGNALING
TNFA_SIGNALING_VIA_NFKB
ANDROGEN_RESPONSE
SPERMATOGENESIS
UV_RESPONSE_DN
PANCREAS_BETA_CELLS
NOTCH_SIGNALING
ANGIOGENESIS
WNT_BETA_CATENIN_SIGNALING
TGF_BETA_SIGNALING
APICAL_JUNCTION
REACTIVE_OXYGEN_SPECIES_PATHWAY
COAGULATION
HEME_METABOLISM
MITOTIC_SPINDLE
PROTEIN_SECRETION
DNA_REPAIR
MYOGENESIS
ESTROGEN_RESPONSE_EARLY
G2M_CHECKPOINT
APOPTOSIS
BILE_ACID_METABOLISM
ESTROGEN_RESPONSE_LATE
P53_PATHWAY
HYPOXIA
PI3K_AKT_MTOR_SIGNALING
XENOBIOTIC_METABOLISM
EPITHELIAL_MESENCHYMAL_TRANSITION
E2F_TARGETS
UV_RESPONSE_UP
PEROXISOME
MYC_TARGETS_V1
ADIPOGENESIS
UNFOLDED_PROTEIN_RESPONSE
OXIDATIVE_PHOSPHORYLATION
MTORC1_SIGNALING
CHOLESTEROL_HOMEOSTASIS
GLYCOLYSIS
MYC_TARGETS_V2
FATTY_ACID_METABOLISM
2
0
-2
-4
2
0
-2
Human DTC 2019: PI-3010 vs Control (in vitro)
Mouse CT26: PI-3008 vs Control (in vivo)

FIG. 29

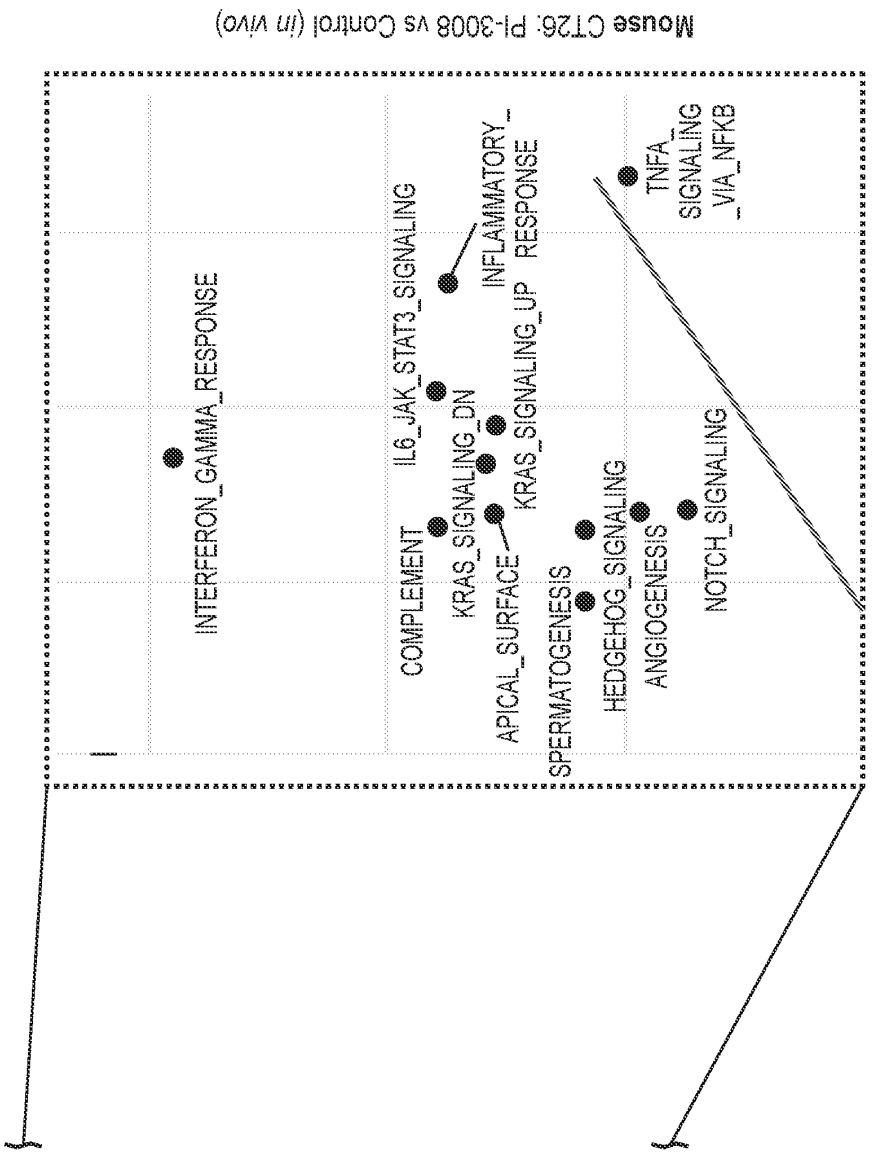
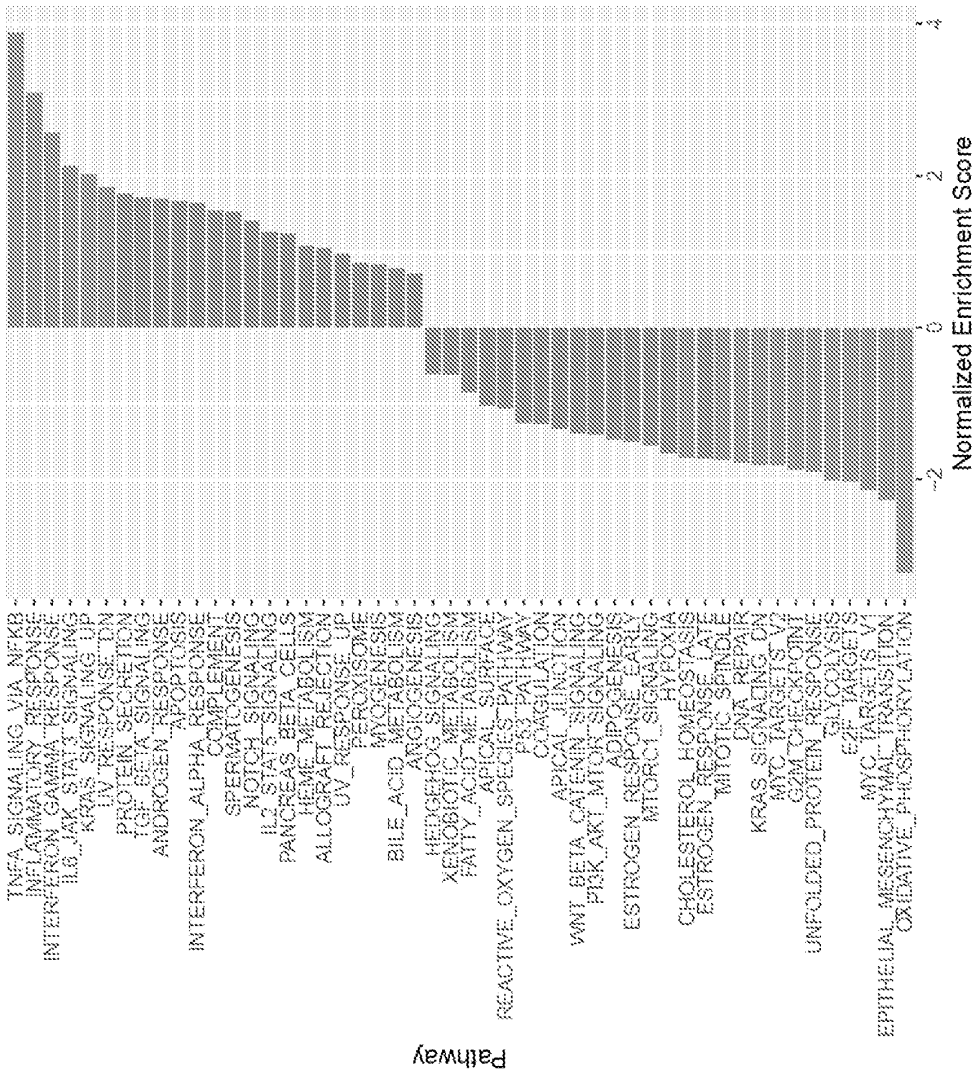

Mouse CT26: PI-3008 vs Control (in vivo)
INTERFERON_GAMMA_RESPONSE
COMPLEMENT
IL6_JAK_STAT3_SIGNALING
KRAS_SIGNALING_DN
APICAL_SURFACE
INFLAMMATORY_
KRAS_SIGNALING_UP RESPONSE
SPERMATOGENESIS
HEDGEHOG_SIGNALING
ANGIOGENESIS
NOTCH_SIGNALING
TNFA_
SIGNALING
_VIA_NFKB
Human DTC 2019: PI-3010 vs Control (in vitro)

FIG. 29 (Cont.)

FIG. 30


TNFA_SIGNALING_VIA_NFKB
INFLAMMATORY_RESPONSE
INTERFERON_GAMMA_RESPONSE
IL6_JAK_STAT3_SIGNALING
KRAS_SIGNALING_UP
UV_RESPONSE_DN
PROTEIN_SECRETION
TGF_BETA_SIGNALING
ANDROGEN_RESPONSE
APOPTOSIS
INTERFERON_ALPHA_RESPONSE
COMPLEMENT
SPERMATOGENESIS
NOTCH_SIGNALING
IL2_STAT5_SIGNALING
PANCREAS_BETA_CELLS
HEME_METABOLISM
ALLOGRAFT_REJECTION
UV_RESPONSE_UP
PEROXISOME
MYOGENESIS
BILE_ACID_METABOLISM
ANGIOGENESIS
HEDGEHOG_SIGNALING
XENOBIOTIC_METABOLISM
FATTY_ACID_METABOLISM
APICAL_SURFACE
REACTIVE_OXYGEN_SPECIES_PATHWAY
P53_PATHWAY
COAGULATION
APICAL_JUNCTION
WNT_BETA_CATENIN_SIGNALING
PI3K_AKT_MTOR_SIGNALING
ADIPOGENESIS
ESTROGEN_RESPONSE_EARLY
MTORC1_SIGNALING
HYPOXIA
CHOLESTEROL_HOMEOSTASIS
ESTROGEN_RESPONSE_LATE
MITOTIC_SPINDLE
DNA_REPAIR
KRAS_SIGNALING_DN
MYC_TARGETS_V2
G2M_CHECKPOINT
UNFOLDED_PROTEIN_RESPONSE
GLYCOLYSIS
E2F_TARGETS
MYC_TARGETS_V1
EPITHELIAL_MESENCHYMAL_TRANSITION
OXIDATIVE_PHOSPHORYLATION
Pathway
−2
0
2
4
Normalized Enrichment Score

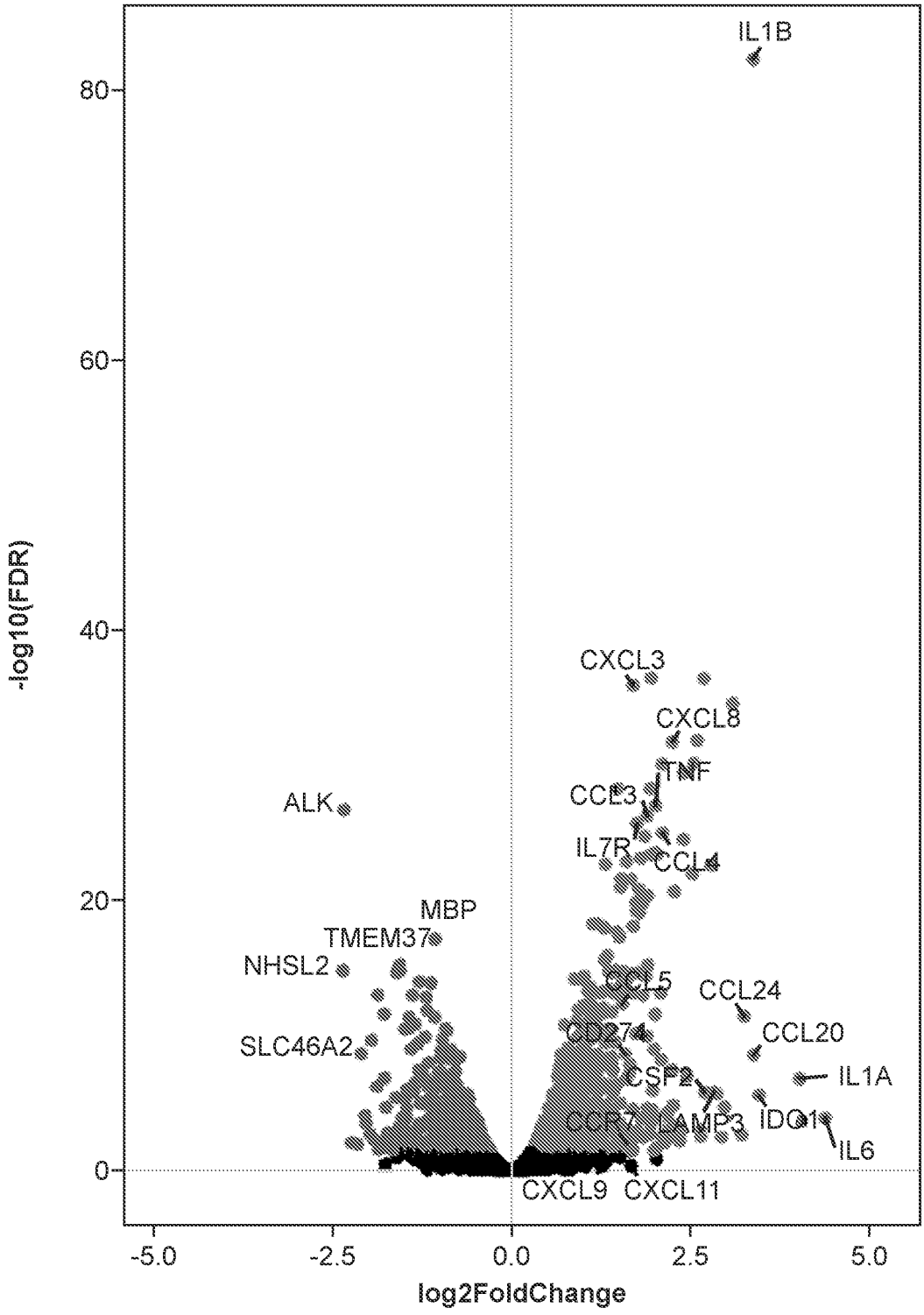

IL1B
80
60
40
20
0
-log10(FDR)
CXCL3
CXCL8
TNF
CCL3
ALK
IL7R
CCL4
MBP
TMEM37
NHSL2
CCL5
CCL24
CCL20
CD274
SLC46A2
IL1A
CSF2
IDO1
CCR7
LAMP3
IL6
CXCL9
CXCL11
-5.0
-2.5
0.0
2.5
5.0
log2FoldChange

FIG. 31


TNFA_SIGNALING_VIA_NFKB
INFLAMMATORY_RESPONSE
INTERFERON_GAMMA_RESPONSE
MYC_TARGETS_V2
HYPOXIA
MYC_TARGETS_V1
IL6_JAK_STAT3_SIGNALING
UNFOLDED_PROTEIN_RESPONSE
INTERFERON_ALPHA_RESPONSE
IL2_STAT5_SIGNALING
UV_RESPONSE_UP
ALLOGRAFT_REJECTION
EPITHELIAL_MESENCHYMAL
_TRANSITION
APOPTOSIS
MTORC1_SIGNALING
ESTROGEN_RESPONSE_EARLY
KRAS_SIGNALING_UP
CHOLESTEROL_HOMEOSTASIS
APICAL_JUNCTION
NOTCH_SIGNALING
WNT_BETA_CATENIN_SIGNALING
OXIDATIVE_PHOSPHORYLATION
COMPLEMENT
PI3K_AKT_MTOR_SIGNALING
REACTIVE_OXYGEN_
SPECIES_PATHWAY
HEDGEHOG_SIGNALING
ANGIOGENESIS
GLYCOLYSIS
KRAS_SIGNALING_DN
DNA_REPAIR
P53_PATHWAY
MYOGENESIS
COAGULATION
APICAL_SURFACE
ANDROGEN_RESPONSE
TGF_BETA_SIGNALING
FATTY_ACID_METABOLISM
XENOBIOTIC_METABOLISM
BILE_ACID_METABOLISM
ESTROGEN_RESPONSE_LATE
ADIPOGENESIS
PEROXISOME
HEME_METABOLISM
UV_RESPONSE_DN
MITOTIC_SPINDLE
PROTEIN_SECRETION
SPERMATOGENESIS
G2M_CHECKPOINT
E2F_TARGETS

FIG. 31 (Cont.)

FIG. 32

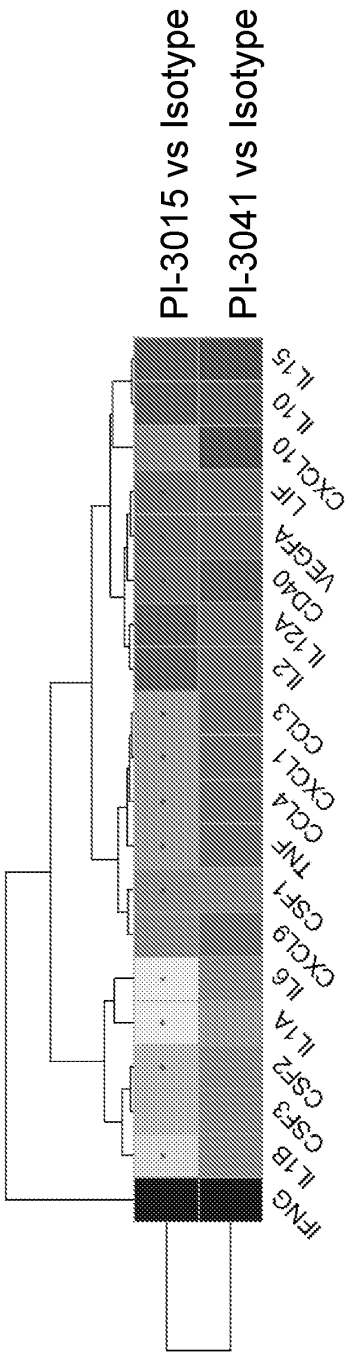

PI-3015 vs Isotype
PI-3041 vs Isotype
IL15
IL10
CXCL10
LIF
VEGFA
CD40
IL12A
IL2
CCL3
CXCL1
CCL4
TNF
CSF1
CXCL9
IL6
IL1A
CSF2
CSF3
IL1B
IFNG

FIG. 33A

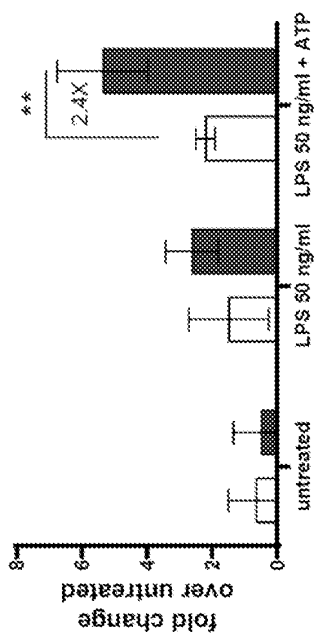


FIG. 33B

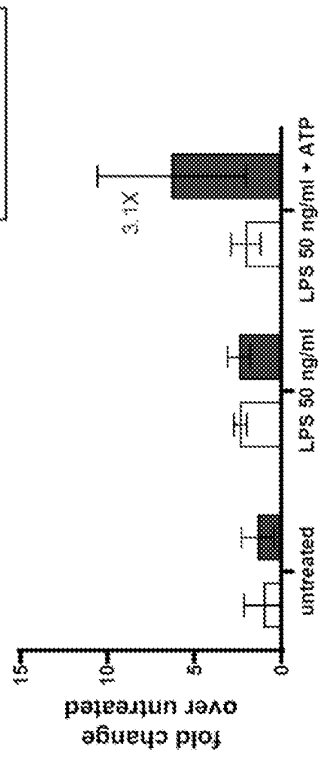


FIG. 33C

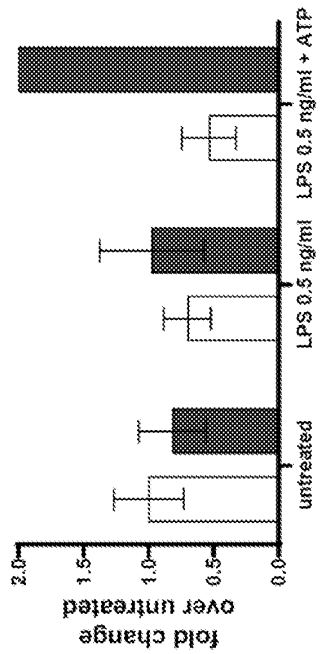
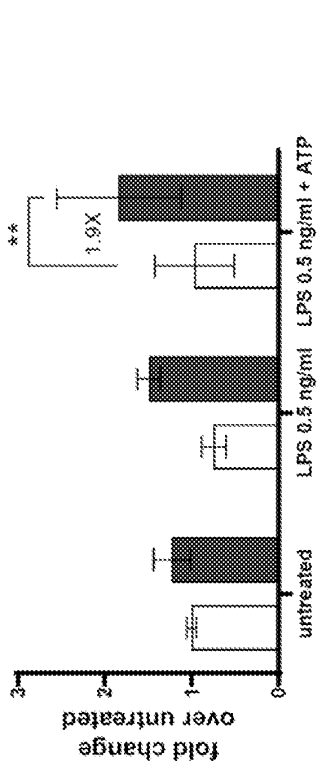


FIG. 33D



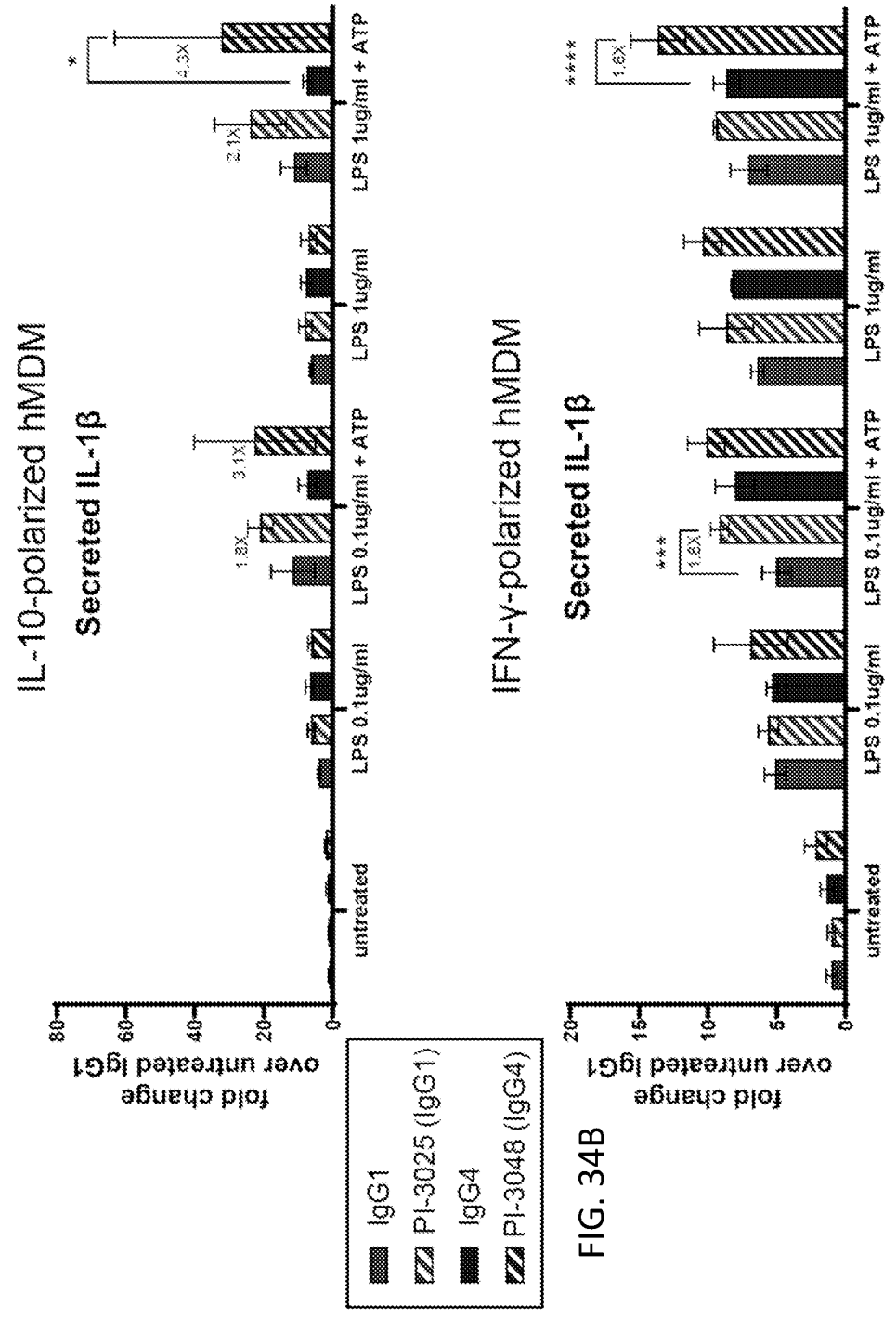


FIG. 34A

FIG. 34B

FIG. 35

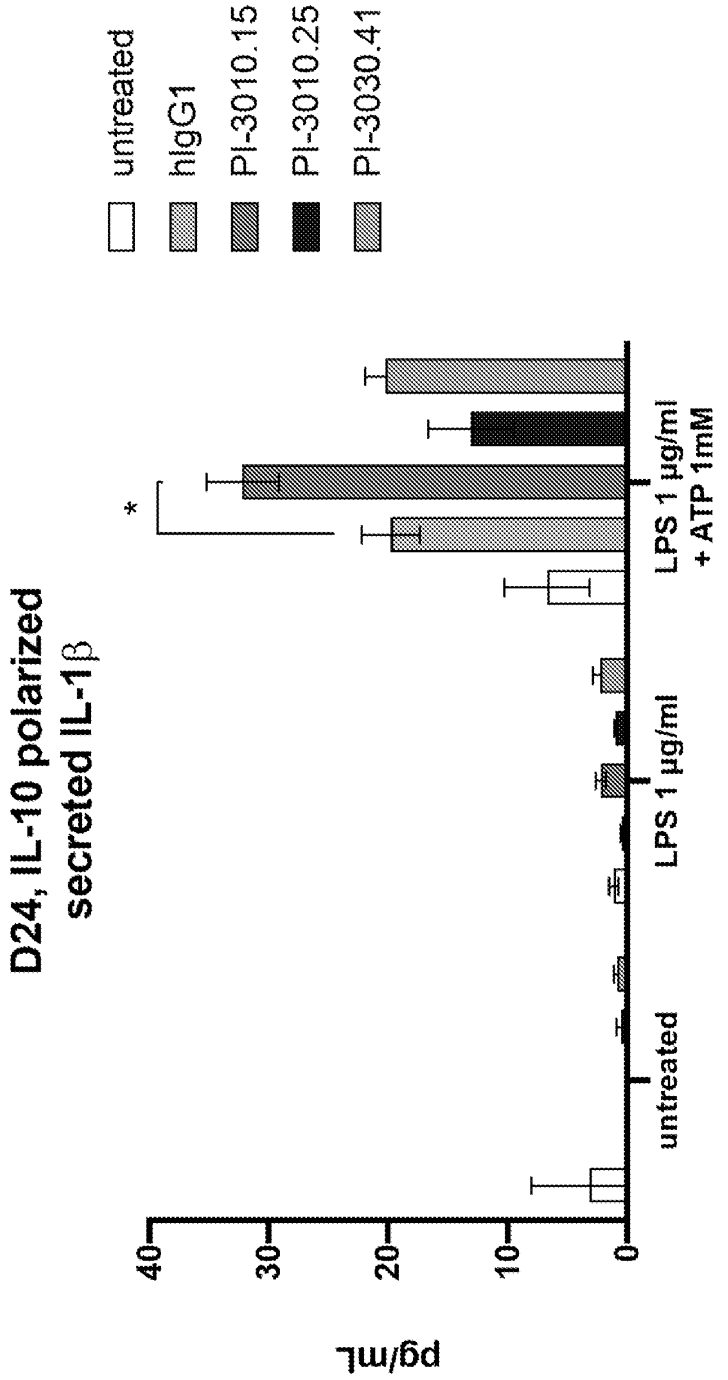
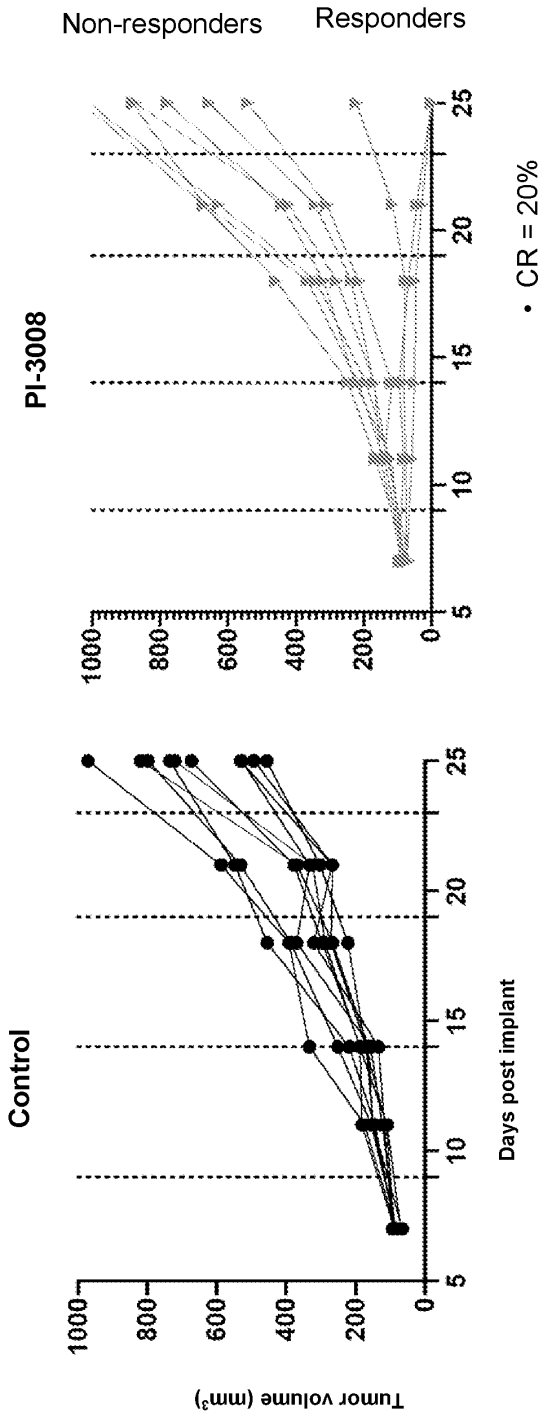

D24, IL-10 polarized
secreted IL-1β
untreated
hIgG1
PI-3010.15
PI-3010.25
PI-3030.41
*
pg/mL
40
30
20
10
0
untreated
LPS 1 µg/ml
LPS 1 µg/ml
+ ATP 1mM

FIG. 36


Non-responders
Responders
PI-3008
• CR = 20%
Control
Tumor volume (mm³)
Days post implant
0
200
400
600
800
1000
5
10
15
20
25

41

FIG. 37

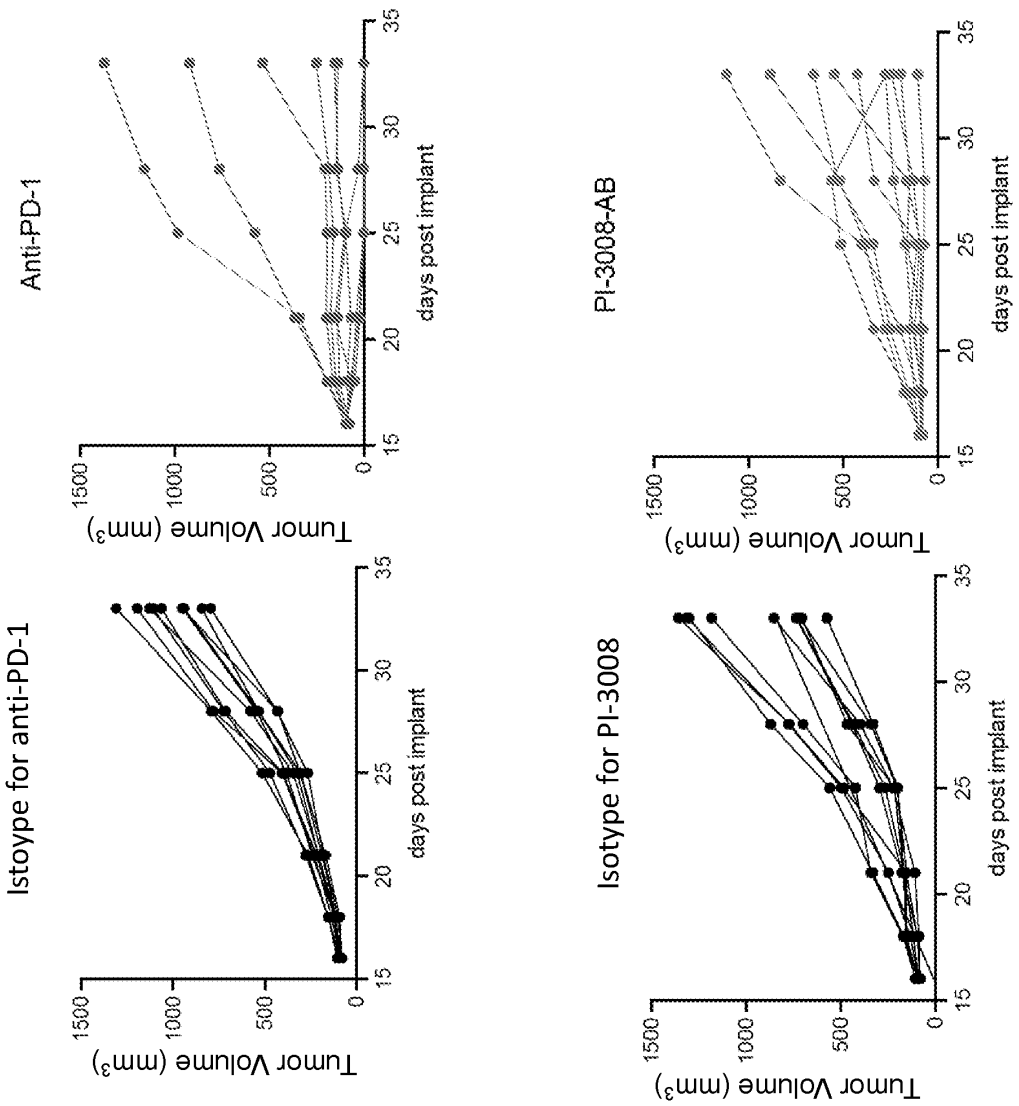

Anti-PD-1
Tumor Volume (mm3)
1500
1000
500
0
15
20
25
30
35
days post implant
Istoype for anti-PD-1
Tumor Volume (mm3)
1500
1000
500
0
15
20
25
30
35
days post implant
PI-3008-AB
Tumor Volume (mm3)
1500
1000
500
0
15
20
25
30
35
days post implant
Isotype for PI-3008
Tumor Volume (mm3)
1500
1000
500
0
15
20
25
30
35
days post implant

FIG. 38A

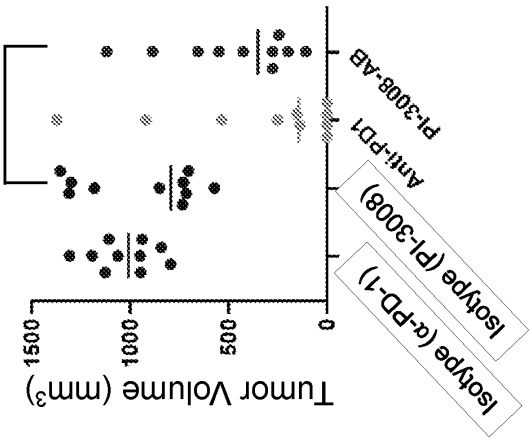


FIG. 38B

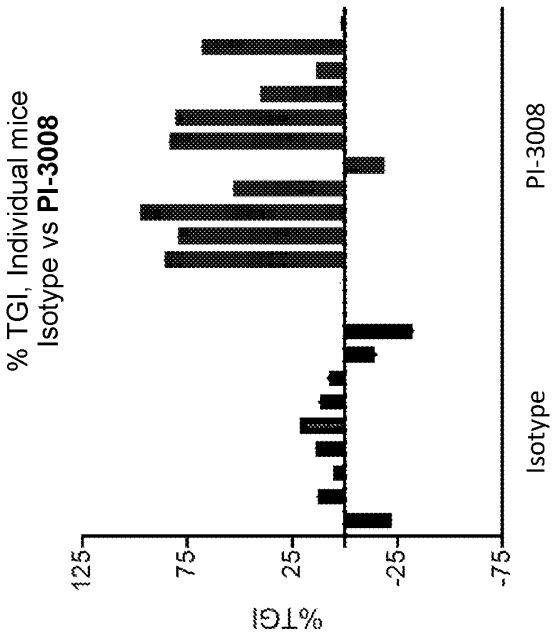


FIG. 38C

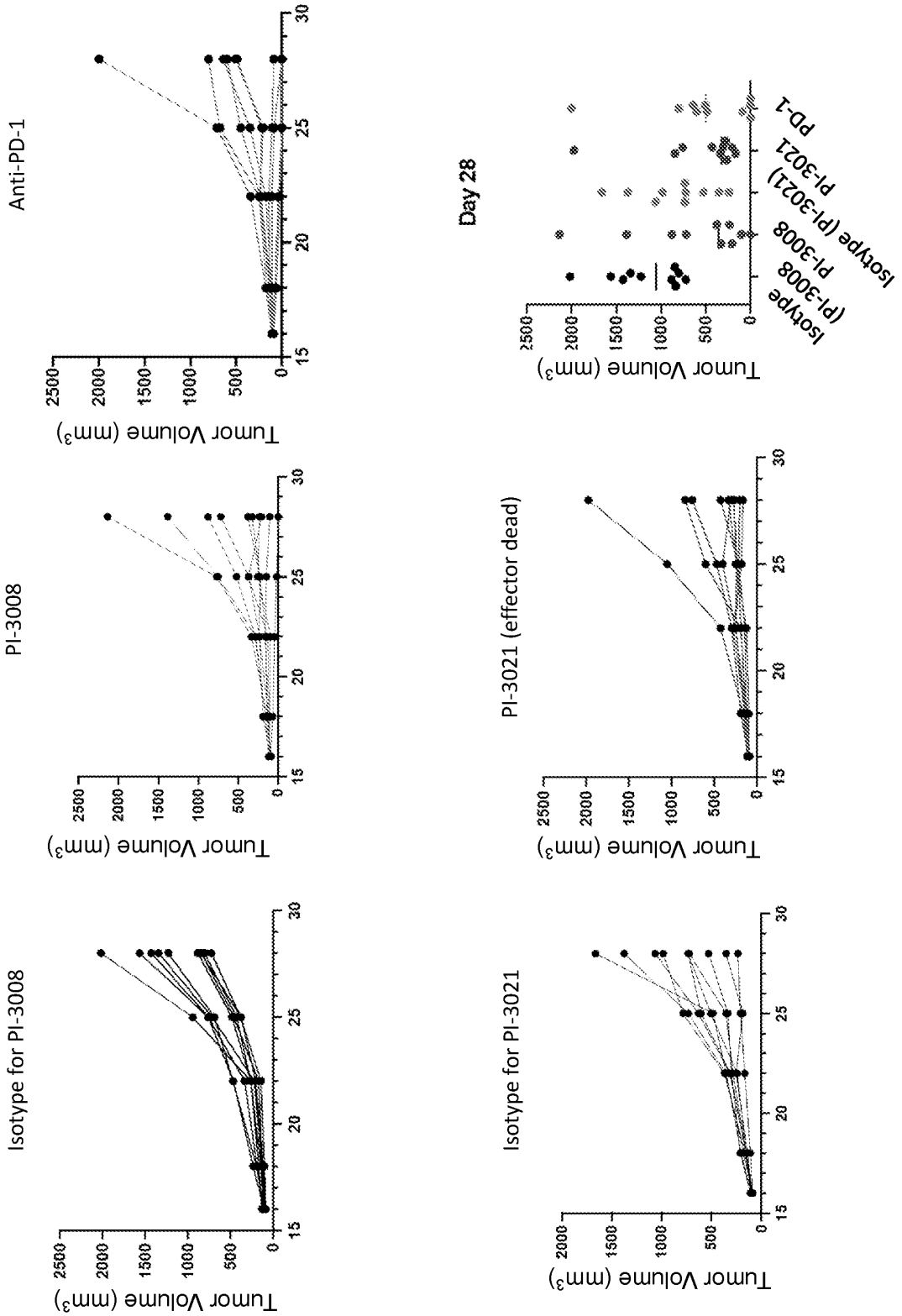

Isotype for PI-3008
PI-3008
Anti-PD-1
Isotype for PI-3021
PI-3021 (effector dead)
Day 28
Tumor Volume (mm3)
Isotype
PI-3008
PI-3021
Isotype (PI-3021)
PD-1

FIG. 39A

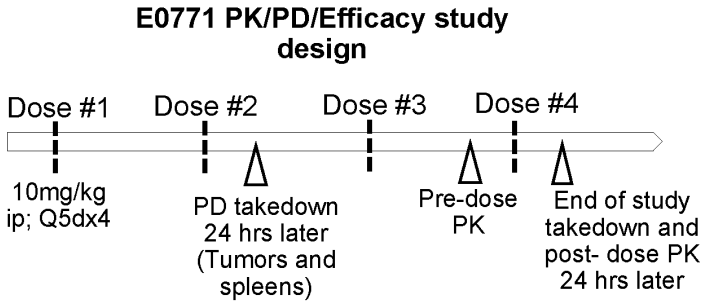


FIG. 39B

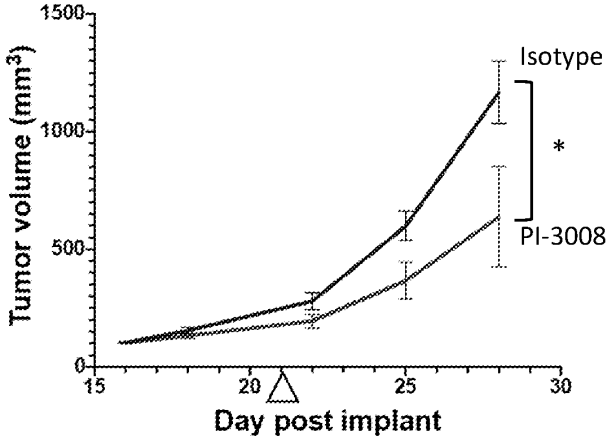


FIG. 39C

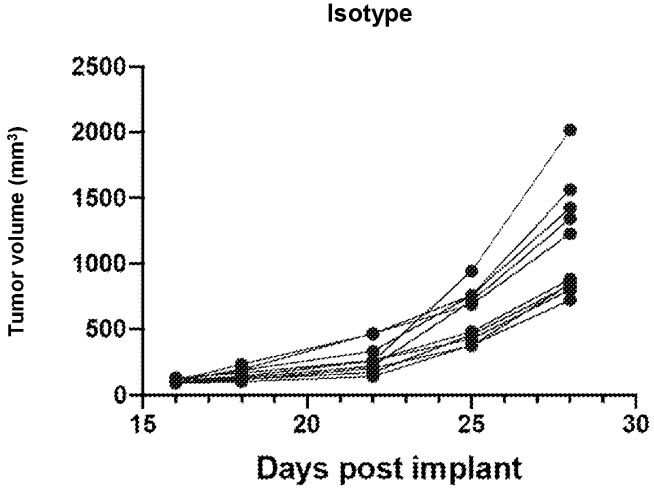


FIG. 39D

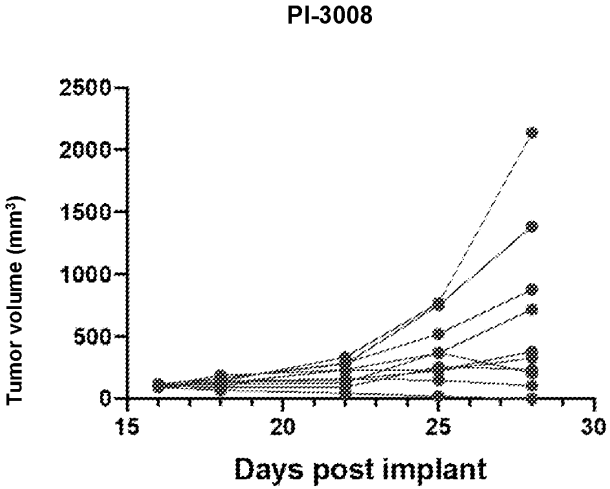


FIG. 39E

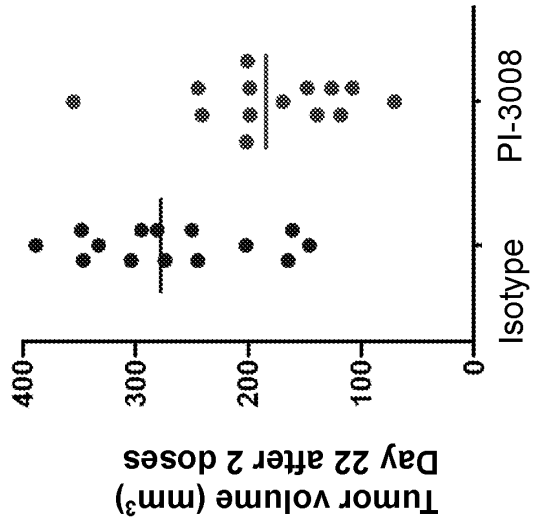


FIG. 39F

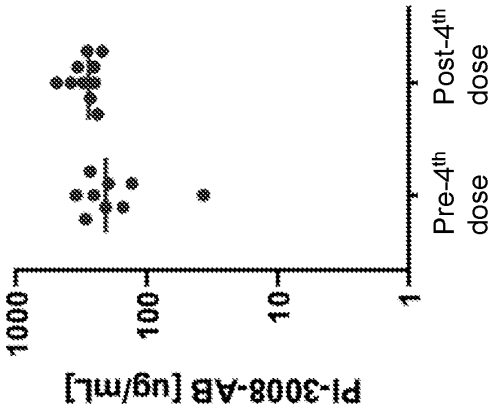


FIG. 40A

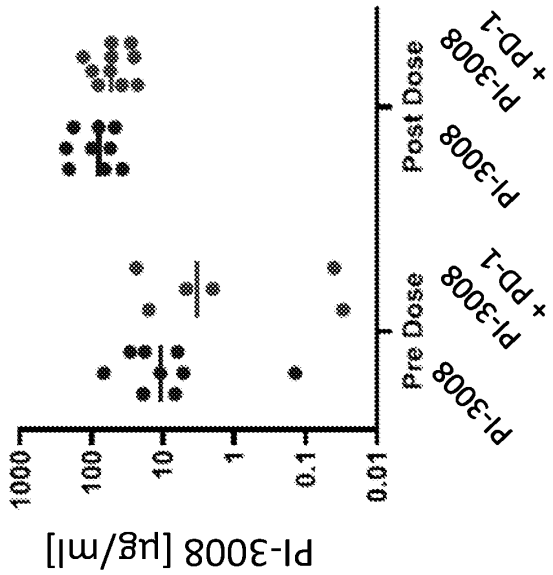


FIG. 40B

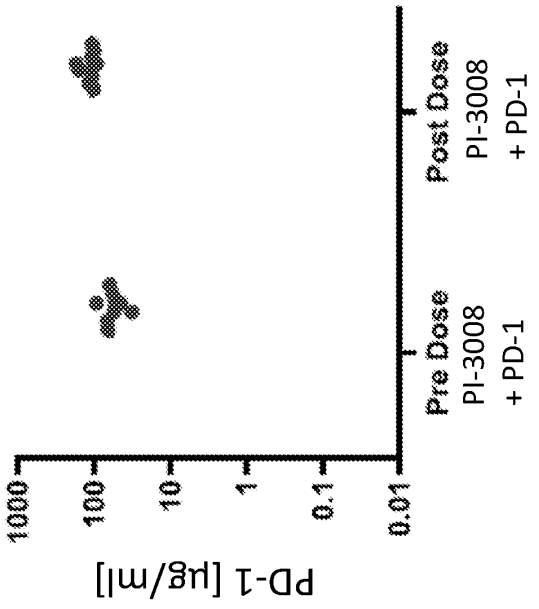


FIG. 41A

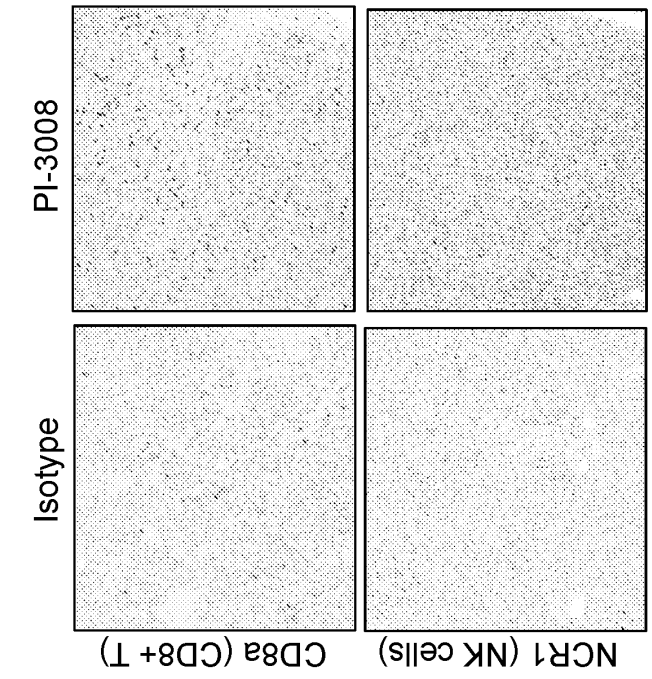


FIG. 41B

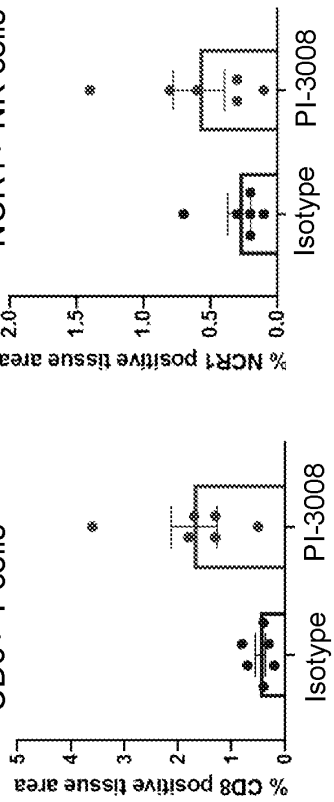


FIG. 41C

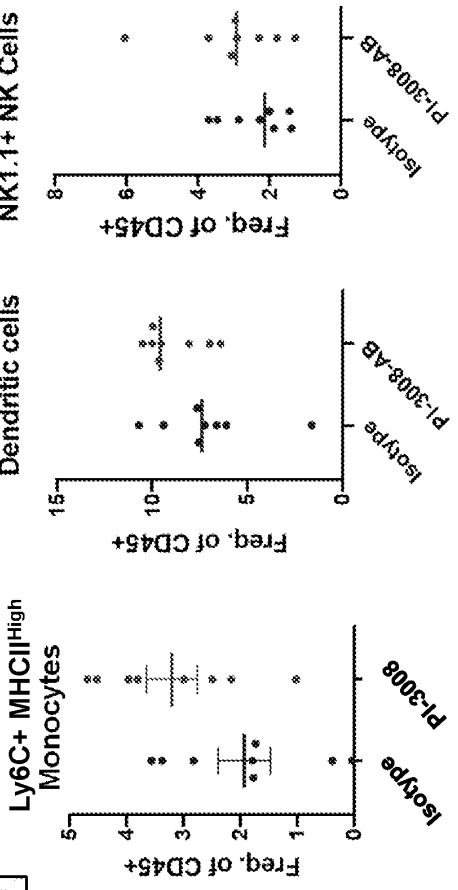


FIG. 41D

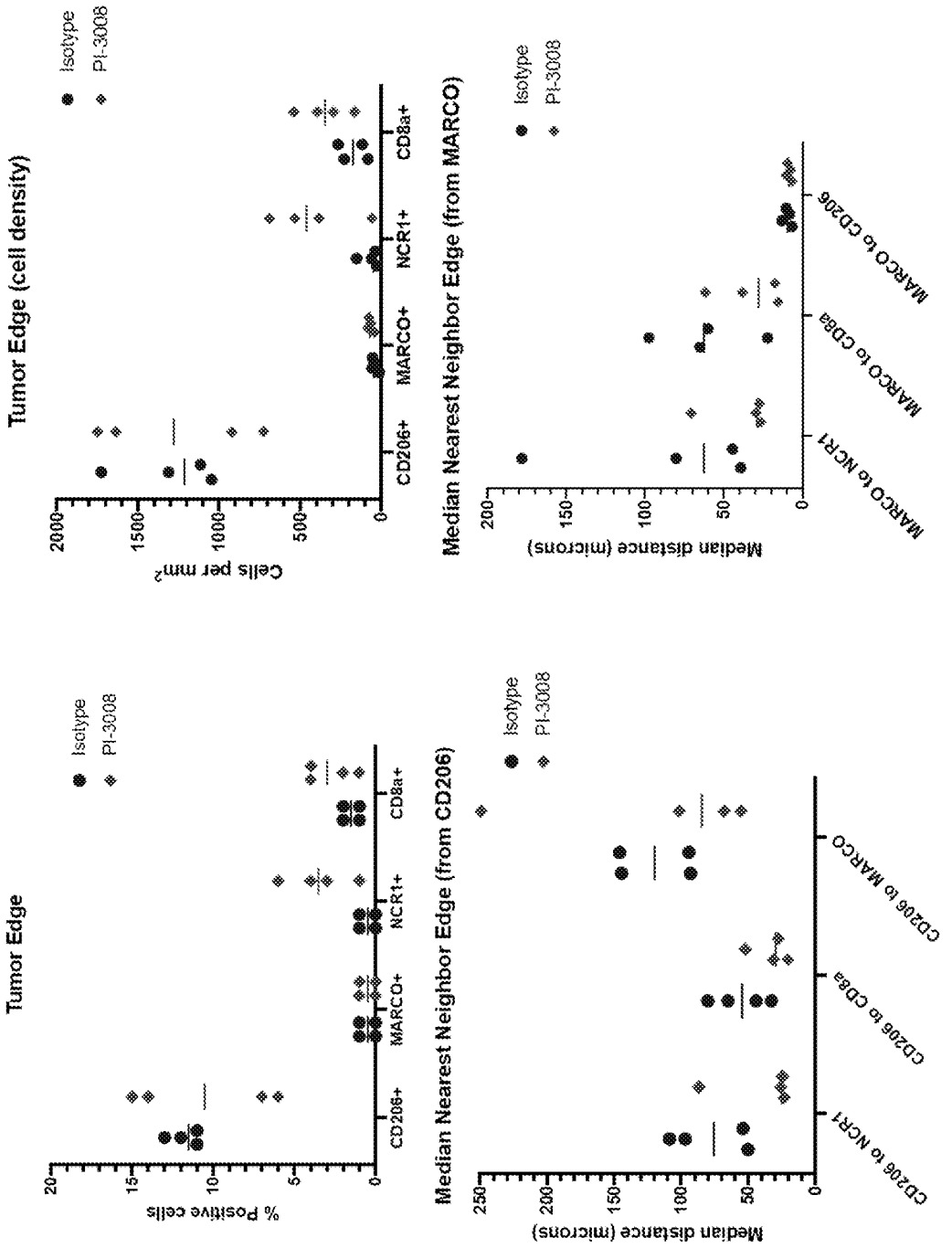

Tumor Edge
Isotype
PI-3008
% Positive cells
20
15
10
5
0
CD206+
MARCO+
NCR1+
CD8a+
Tumor Edge (cell density)
Isotype
PI-3008
Cells per mm²
2000
1500
1000
500
0
CD206+
MARCO+
NCR1+
CD8a+
Median Nearest Neighbor Edge (from CD206)
Isotype
PI-3008
Median distance (microns)
250
200
150
100
50
0
CD206 to NCR1
CD206 to CD8a
CD206 to MARCO
Median Nearest Neighbor Edge (from MARCO)
Isotype
PI-3008
Median distance (microns)
200
150
100
50
0
MARCO to NCR1
MARCO to CD8a
MARCO to CD206

FIG. 42A

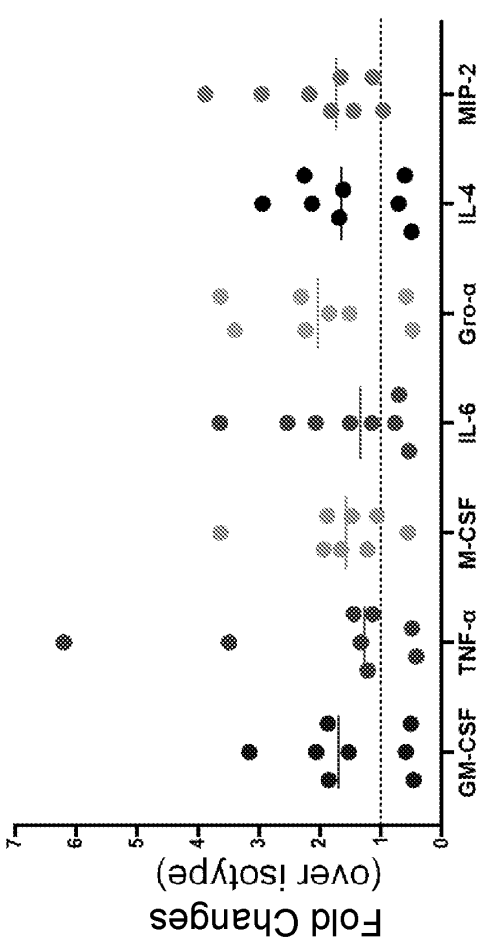


FIG. 42B

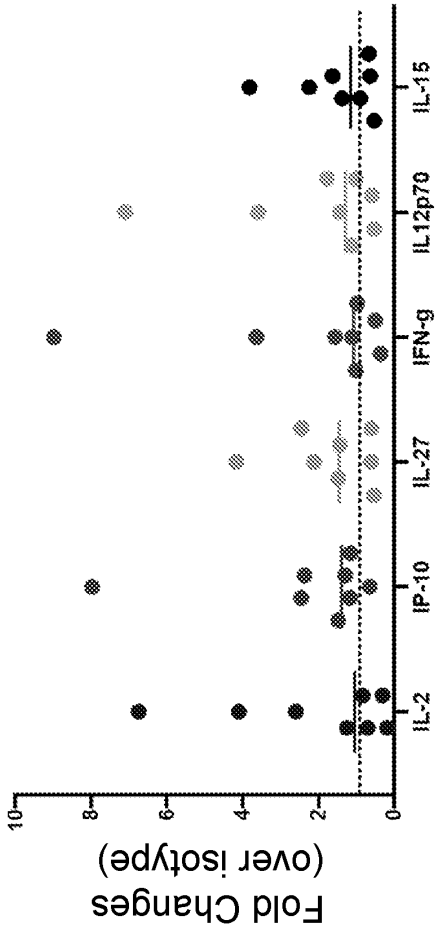


FIG. 43

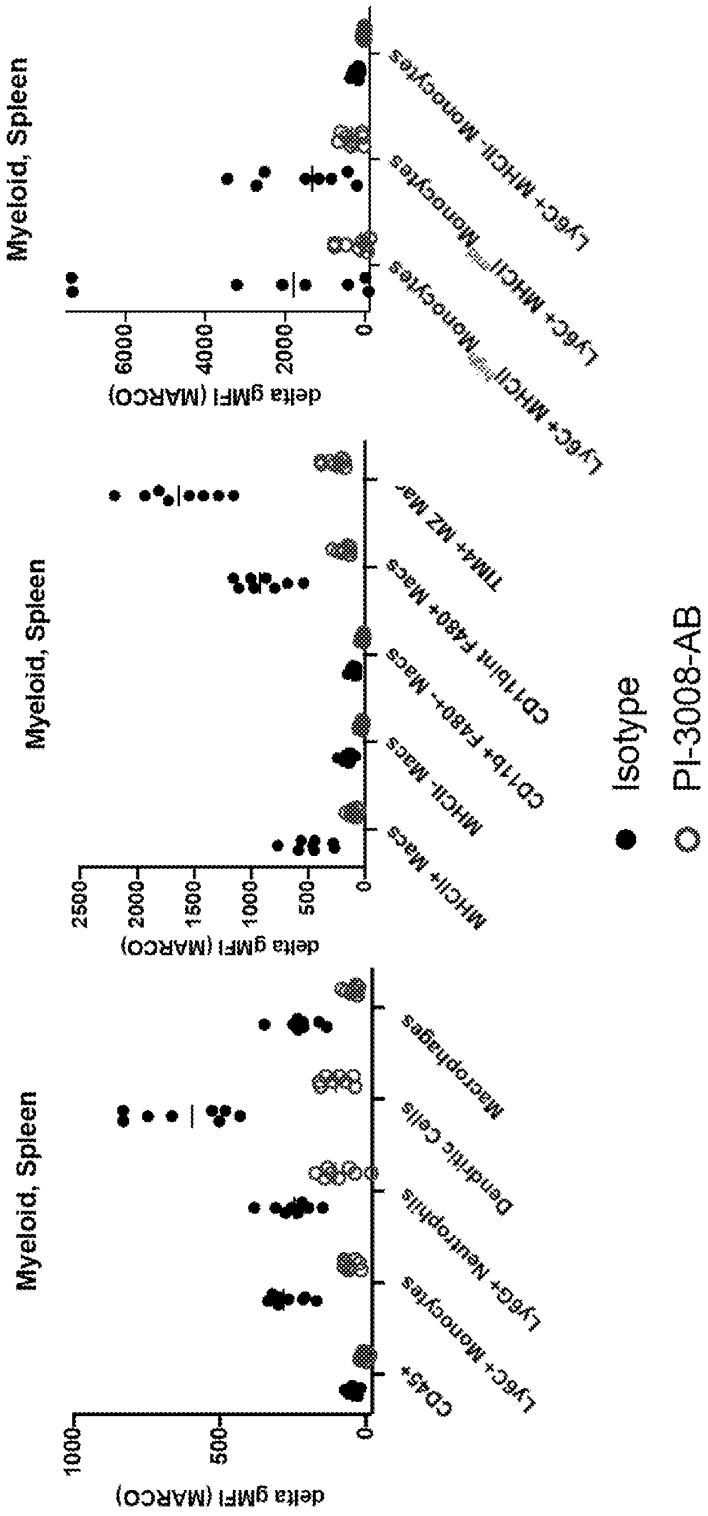

Myeloid, Spleen
delta gMFI (MARCO)
1000
500
0
CD45+
Ly6C+ Monocytes
Ly6G+ Neutrophils
Dendritic Cells
Macrophages
Myeloid, Spleen
delta gMFI (MARCO)
2500
2000
1500
1000
500
0
MHCII+ Macs
MHCII- Macs
CD11b+ F480+- Macs
CD11bInt F480+ Macs
TIM4+ MZ Mar
Myeloid, Spleen
delta gMFI (MARCO)
6000
4000
2000
0
Ly6C+ MHCII+ Monocytes
Ly6C+ MHCII++ Monocytes
Ly6C+ MHCII- Monocytes
Isotype
PI-3008-AB

FIG. 44A

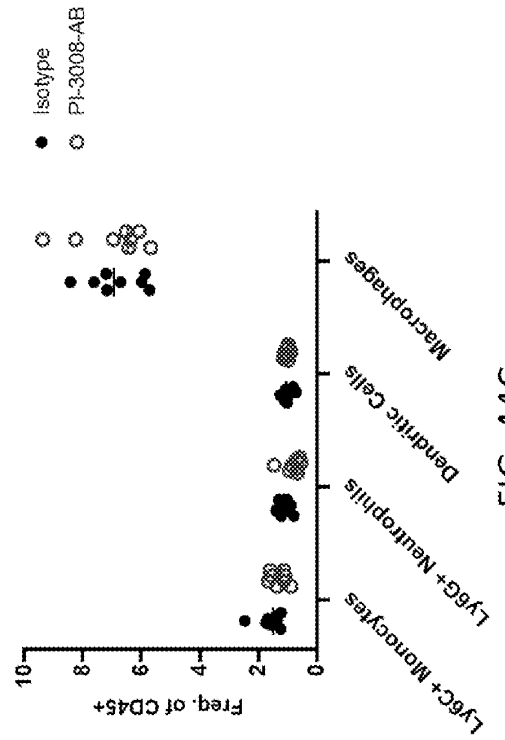


FIG. 44B

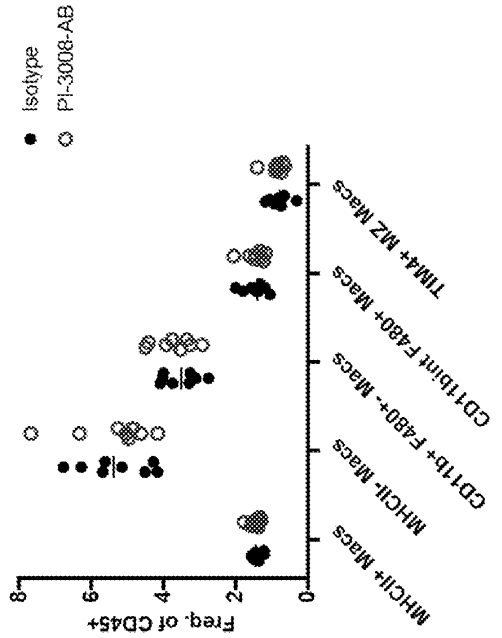


FIG. 44C

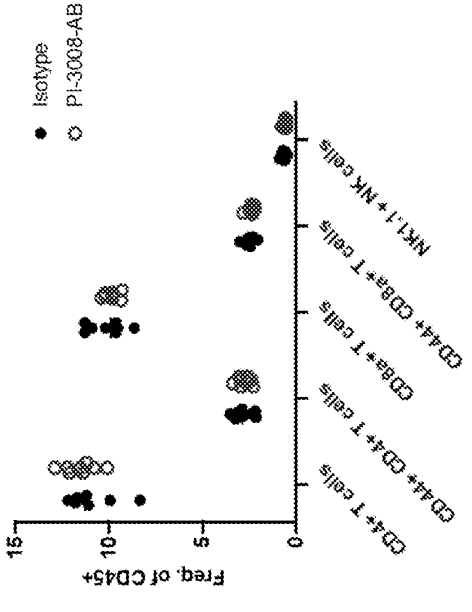


FIG. 44D

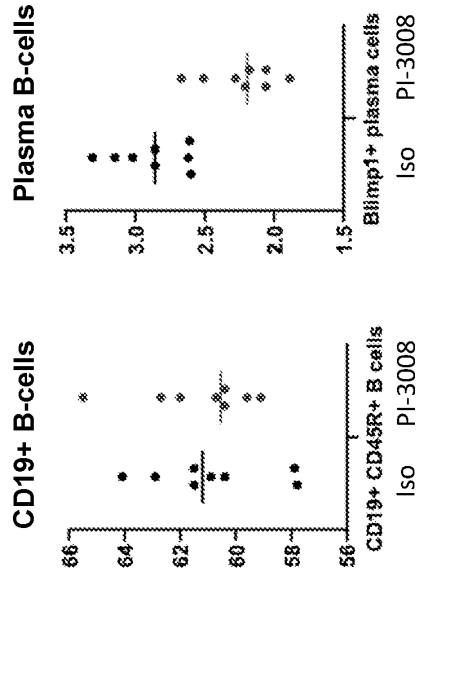


FIG. 45

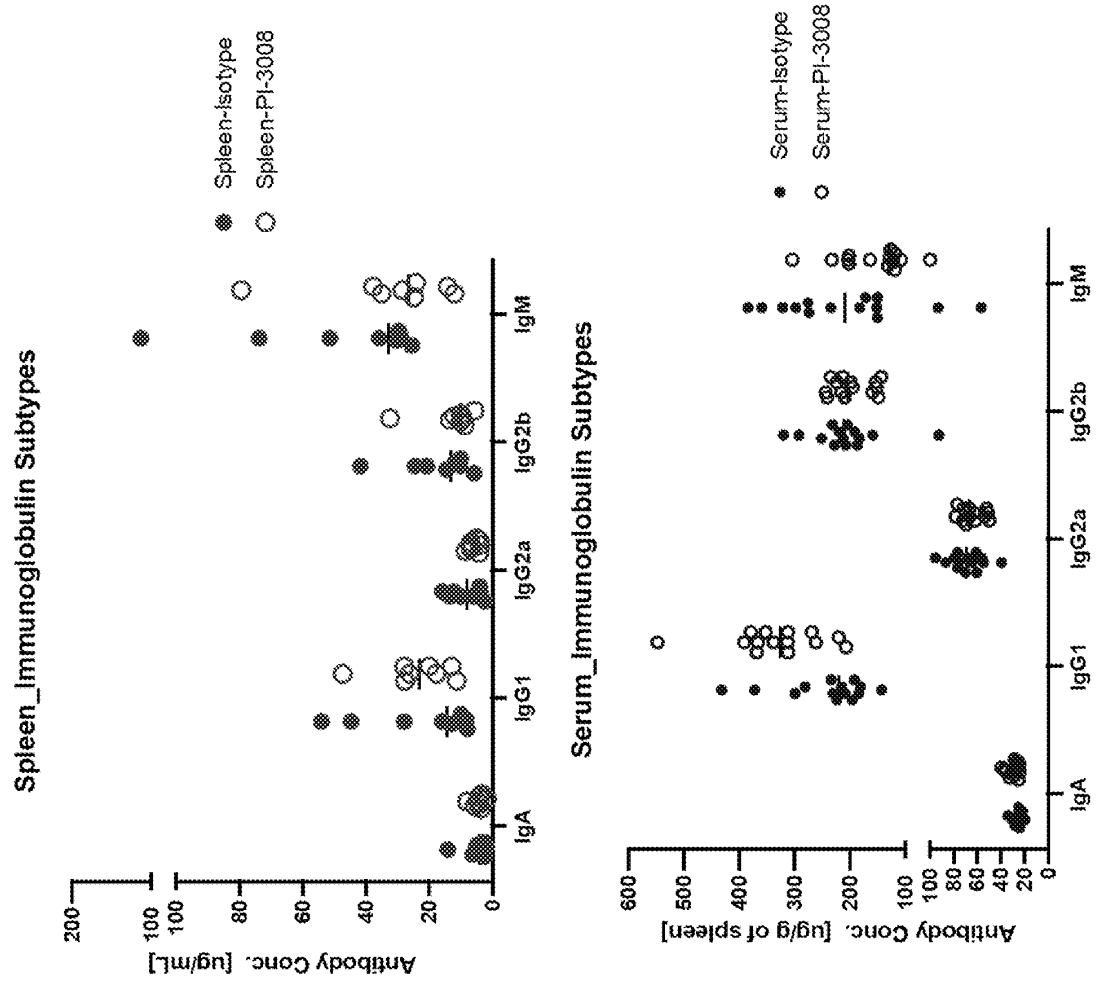

Spleen_Immunoglobulin Subtypes
Spleen-Isotype
Spleen-PI-3008
Antibody Conc. [ug/mL]
200
100
100
80
60
40
20
0
IgA
IgG1
IgG2a
IgG2b
IgM
Serum_Immunoglobulin Subtypes
Serum-Isotype
Serum-PI-3008
Antibody Conc. [ug/g of spleen]
600
500
400
300
200
100
100
80
60
40
20
0
IgA
IgG1
IgG2a
IgG2b
IgM

FIG. 46

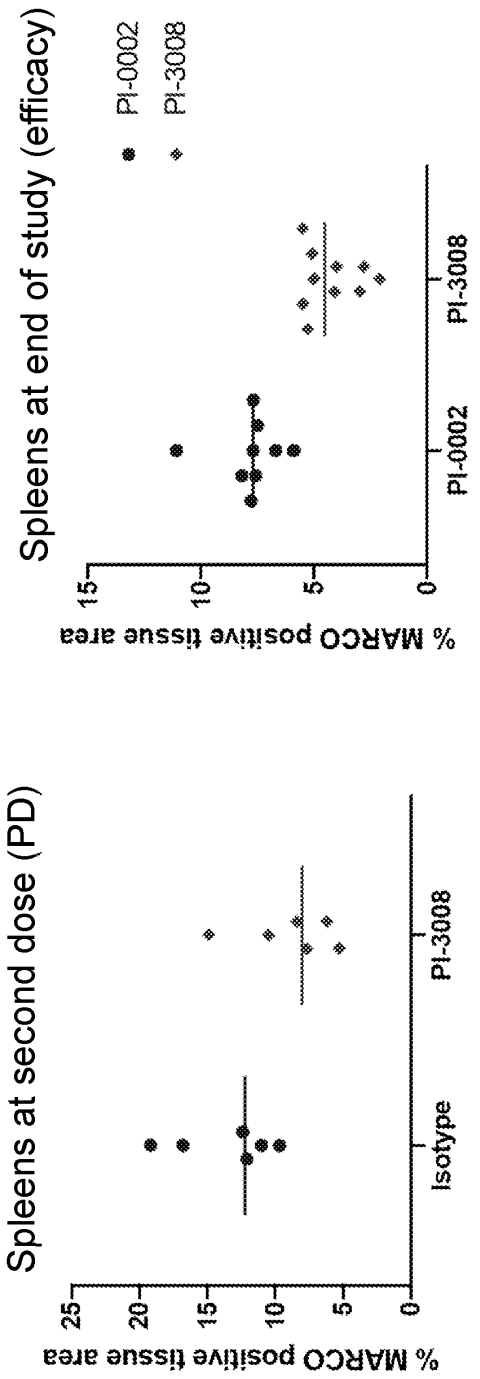

Spleens at second dose (PD)
% MARCO positive tissue area
25
20
15
10
5
0
Isotype
PI-3008
Spleens at end of study (efficacy)
% MARCO positive tissue area
15
10
5
0
PI-0002
PI-3008
PI-0002
PI-3008

FIG. 47A

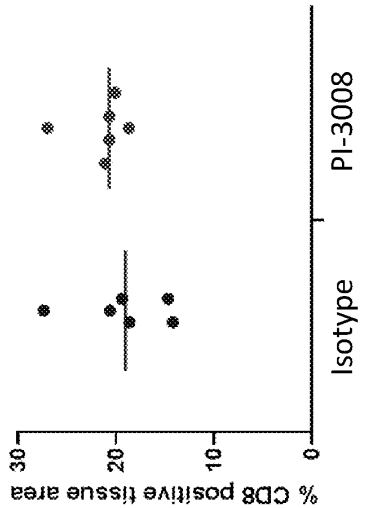


FIG. 47B

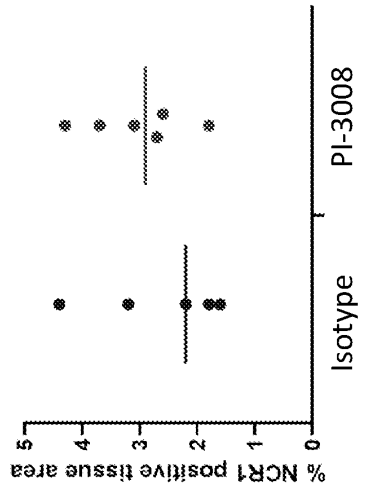


FIG. 47C

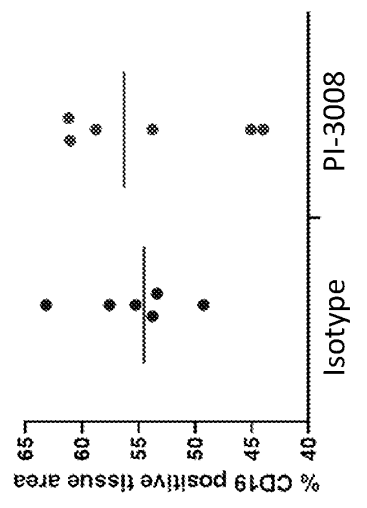


FIG. 47D

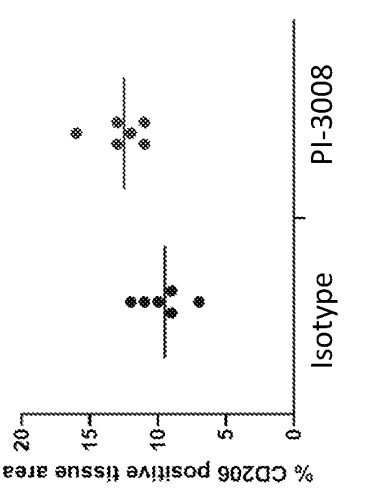


FIG. 48A
MARCO

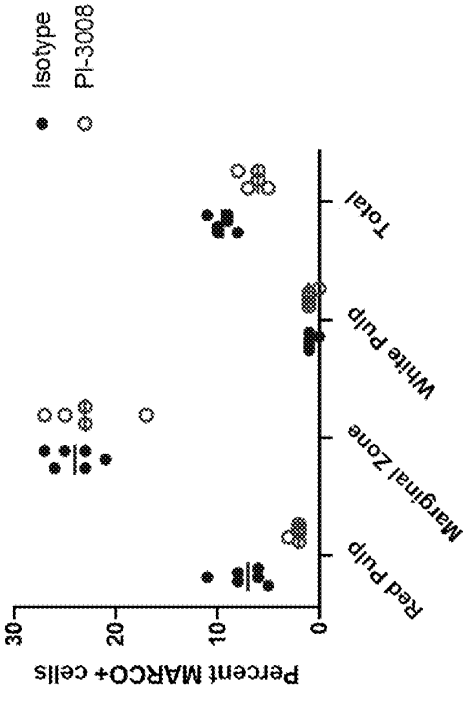


FIG. 48B
CD19

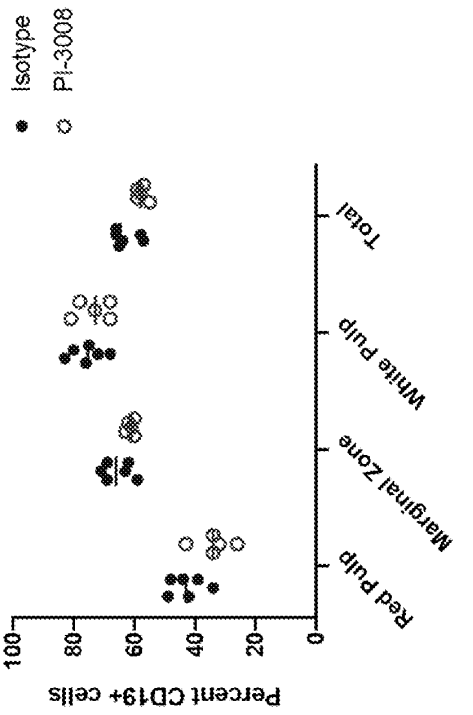


FIG. 48C
CD8

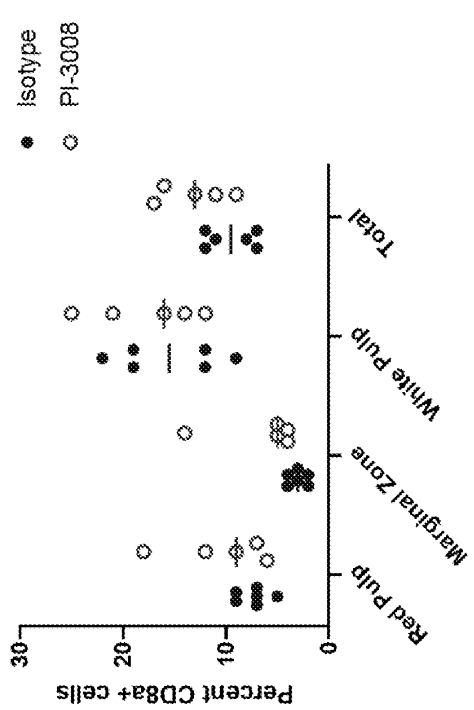


FIG. 48D
CD206

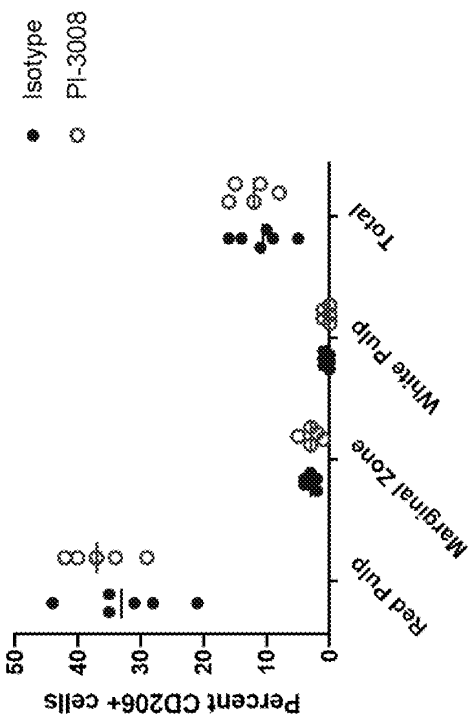


FIG. 49

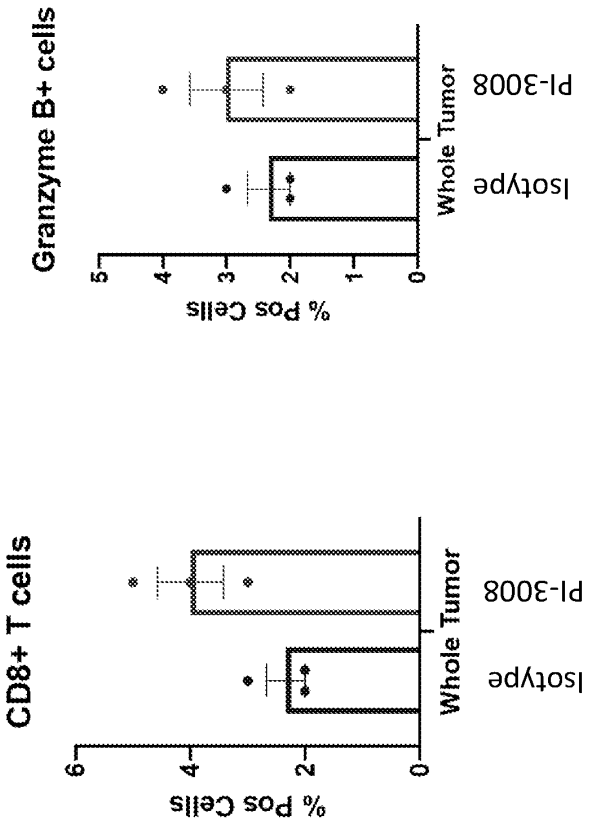
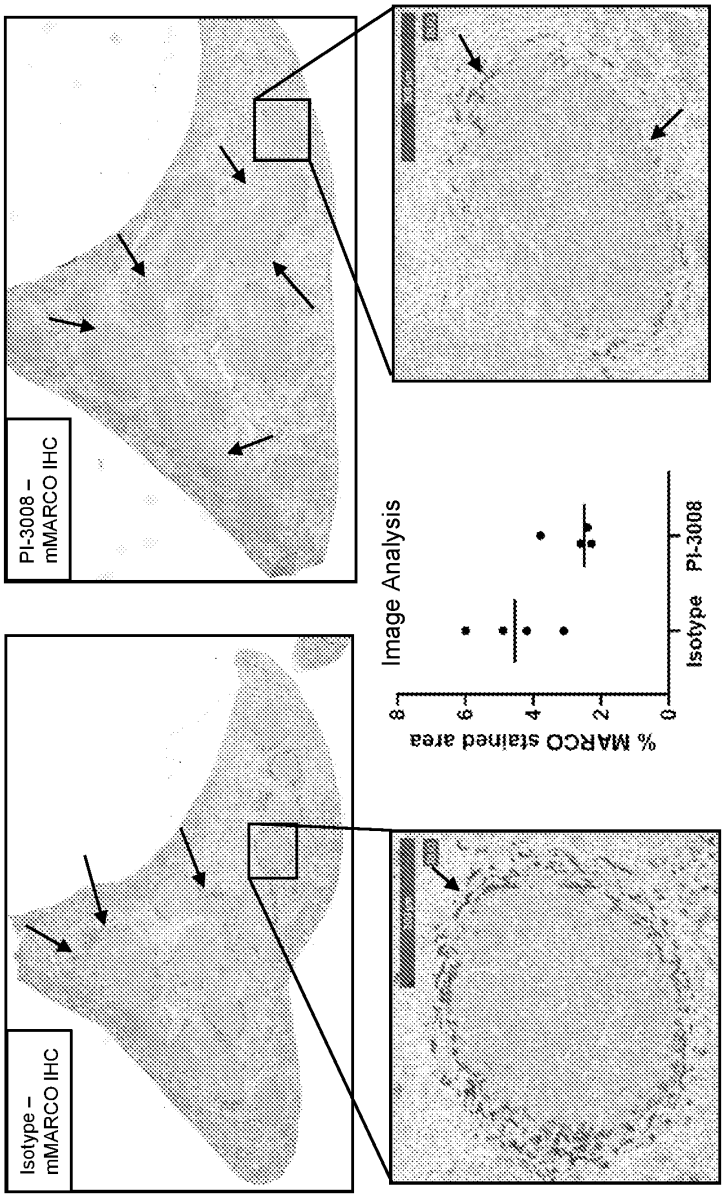

Granzyme B+ cells
% Pos Cells
0
1
2
3
4
5
Whole Tumor
Isotype
PI-3008
CD8+ T cells
% Pos Cells
0
2
4
6
Whole Tumor
Isotype
PI-3008

FIG. 50


Isotype – mMARCO IHC
PI-3008 – mMARCO IHC
Image Analysis
% MARCO stained area
8
6
4
2
0
Isotype
PI-3008

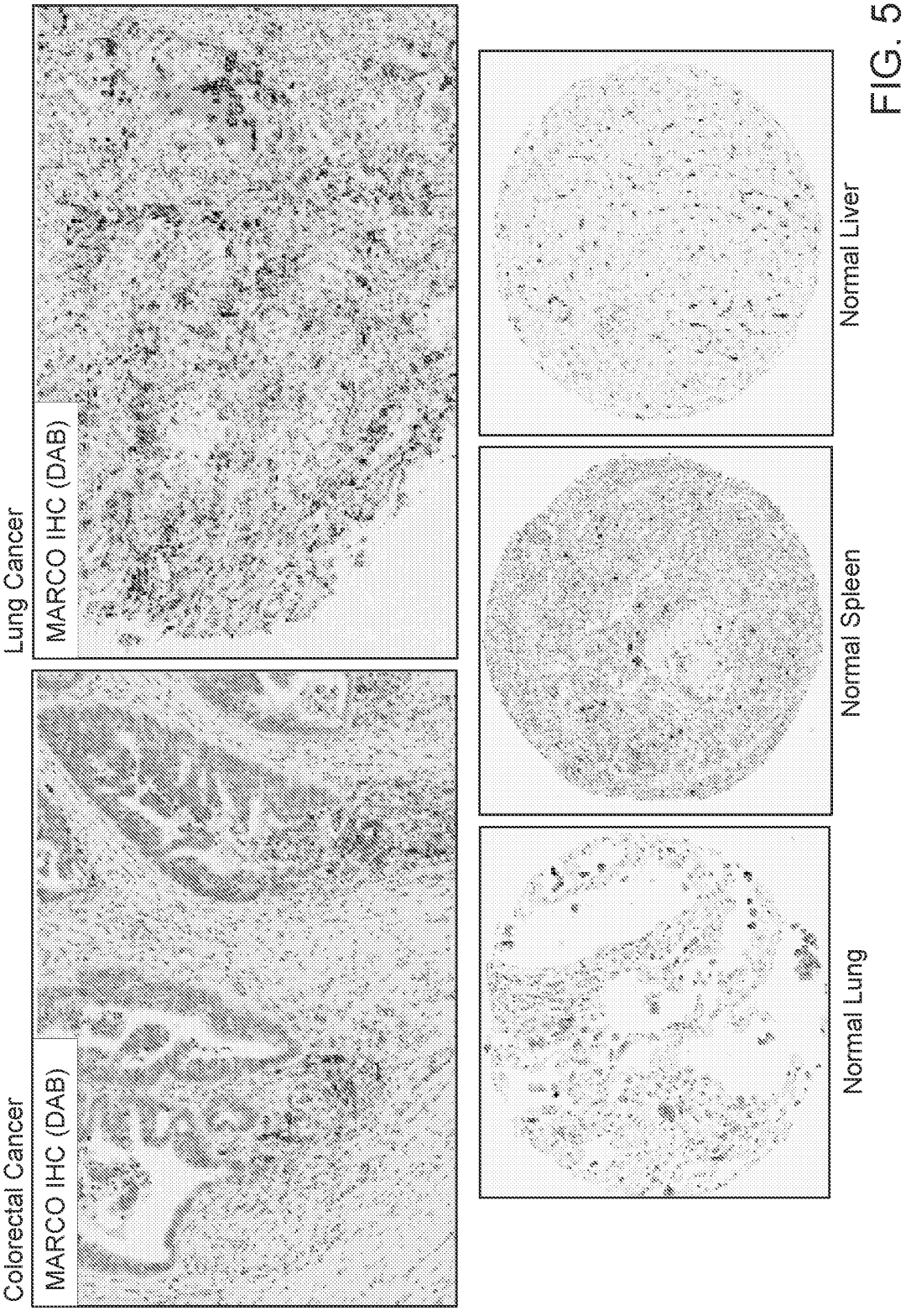

Colorectal Cancer
MARCO IHC (DAB)
Lung Cancer
MARCO IHC (DAB)
Normal Lung
Normal Spleen
Normal Liver

FIG. 51A

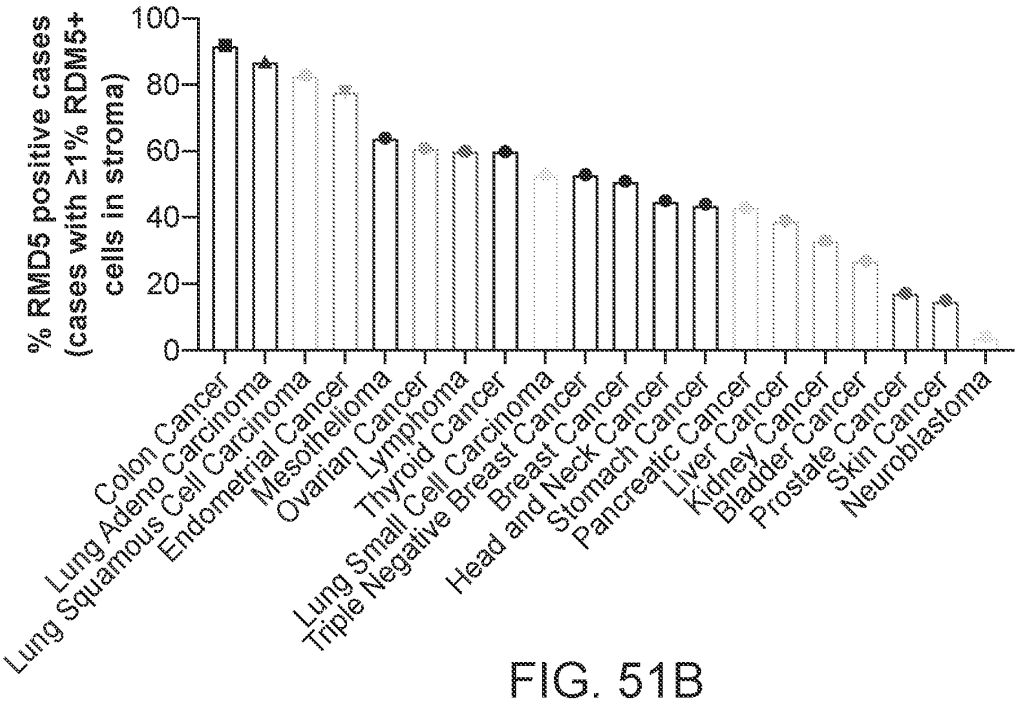


FIG. 51B

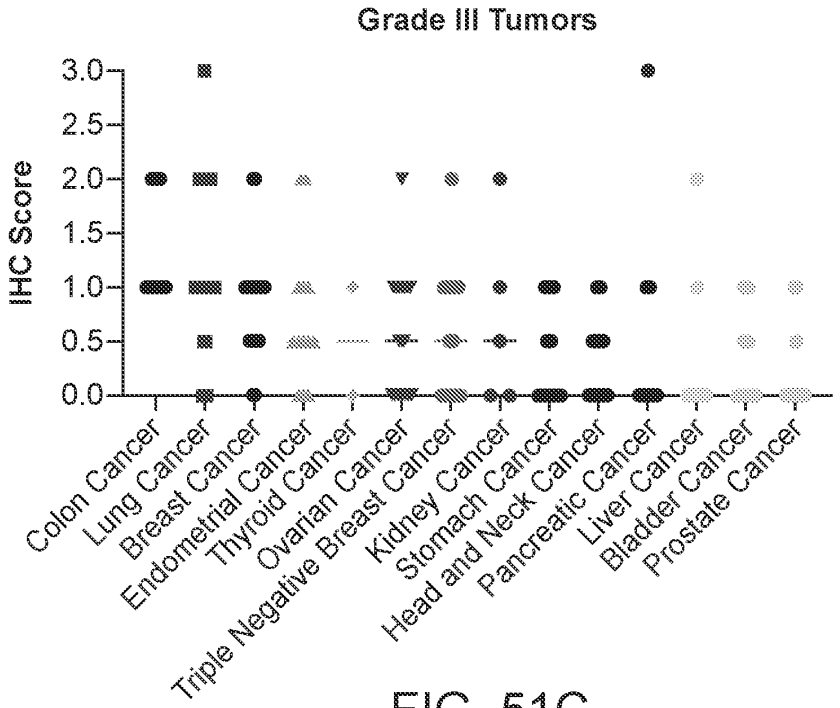


FIG. 51C

FIG. 52

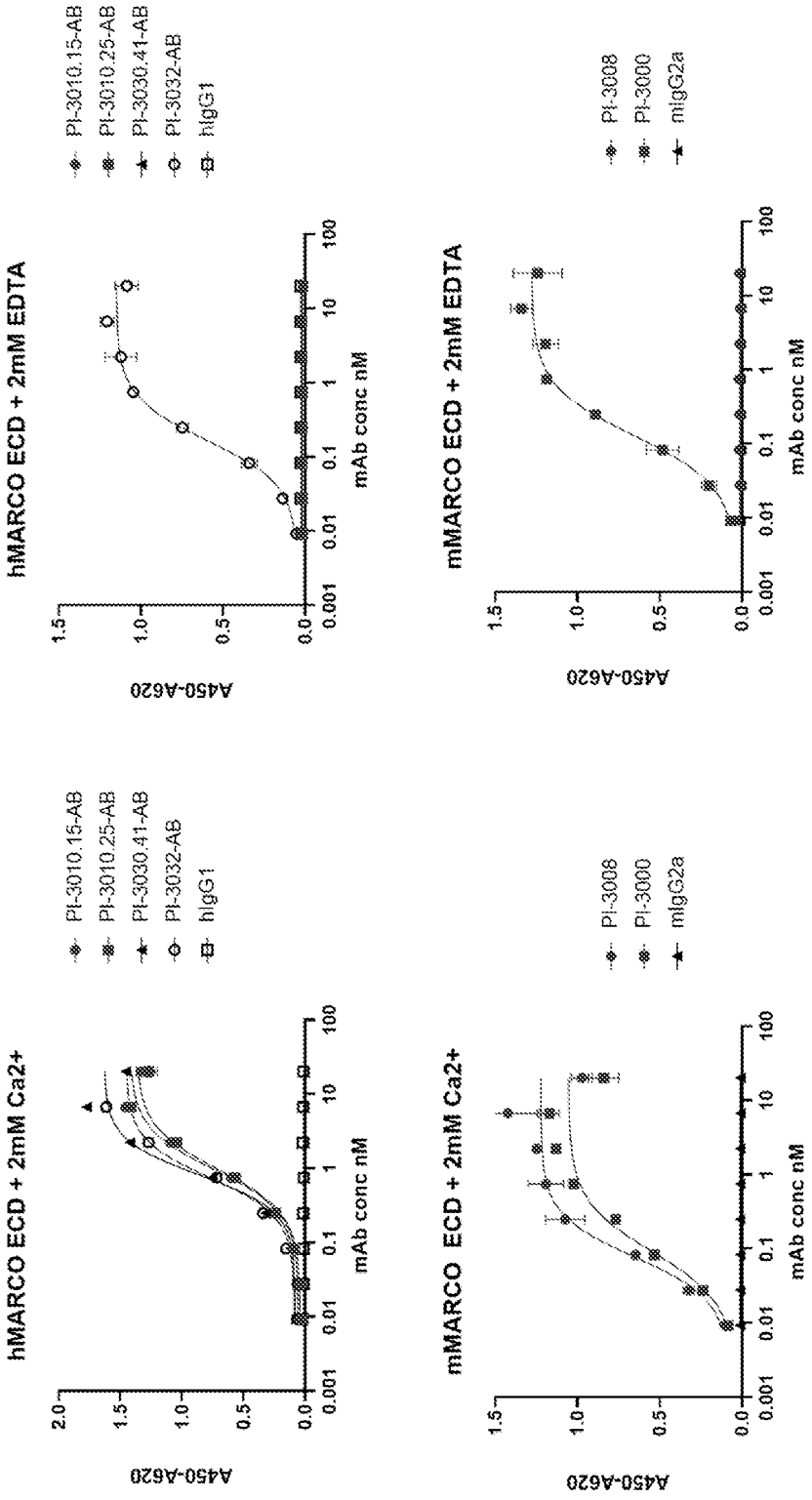

hMARCO ECD + 2mM Ca2+
mMARCO ECD + 2mM Ca2+
hMARCO ECD + 2mM EDTA
mMARCO ECD + 2mM EDTA
A450-A620
mAb conc nM
PI-3010.15-AB
PI-3010.25-AB
PI-3030.41-AB
PI-3032-AB
hIgG1
PI-3008
PI-3000
mIgG2a

FIG. 53

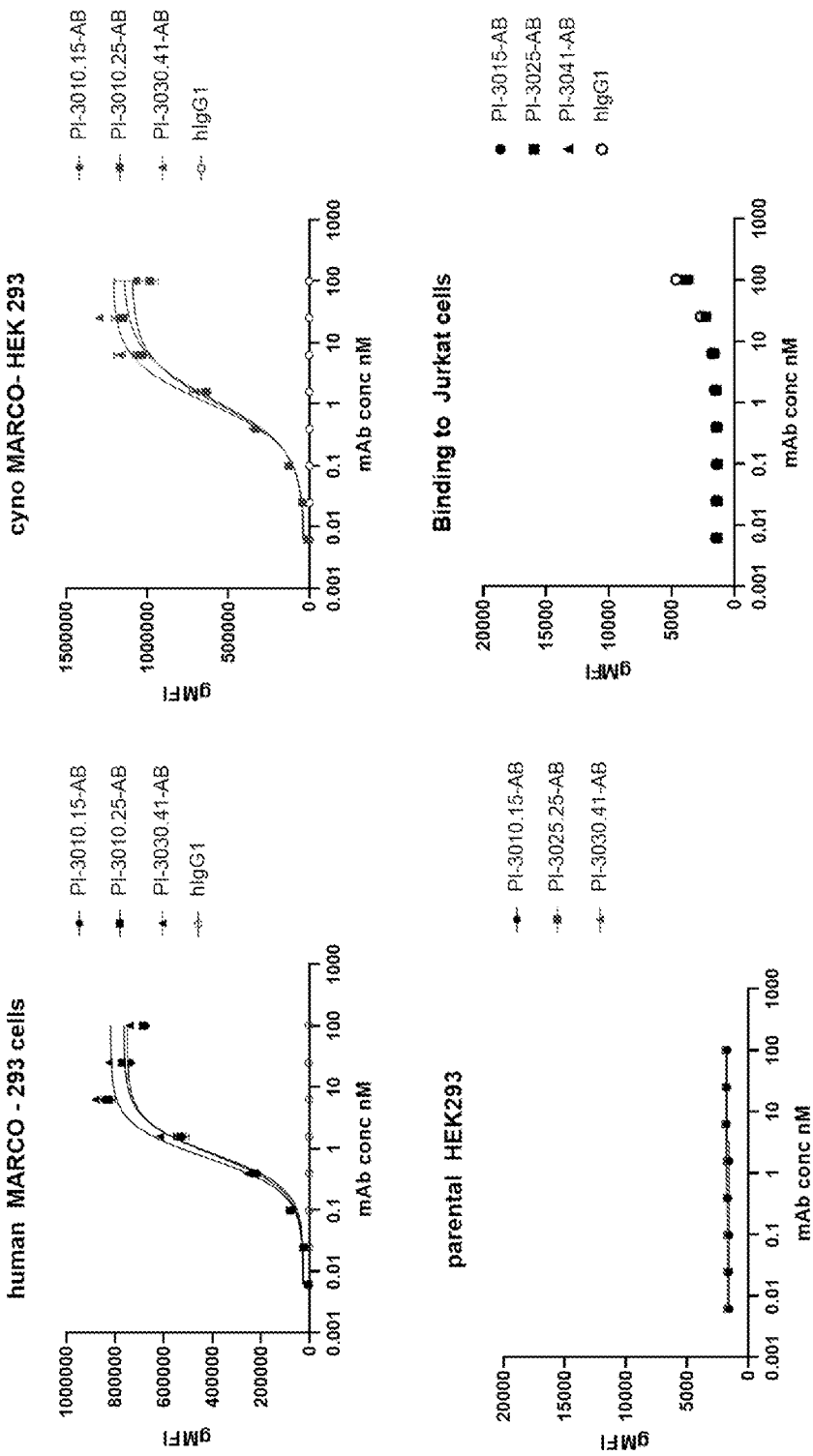
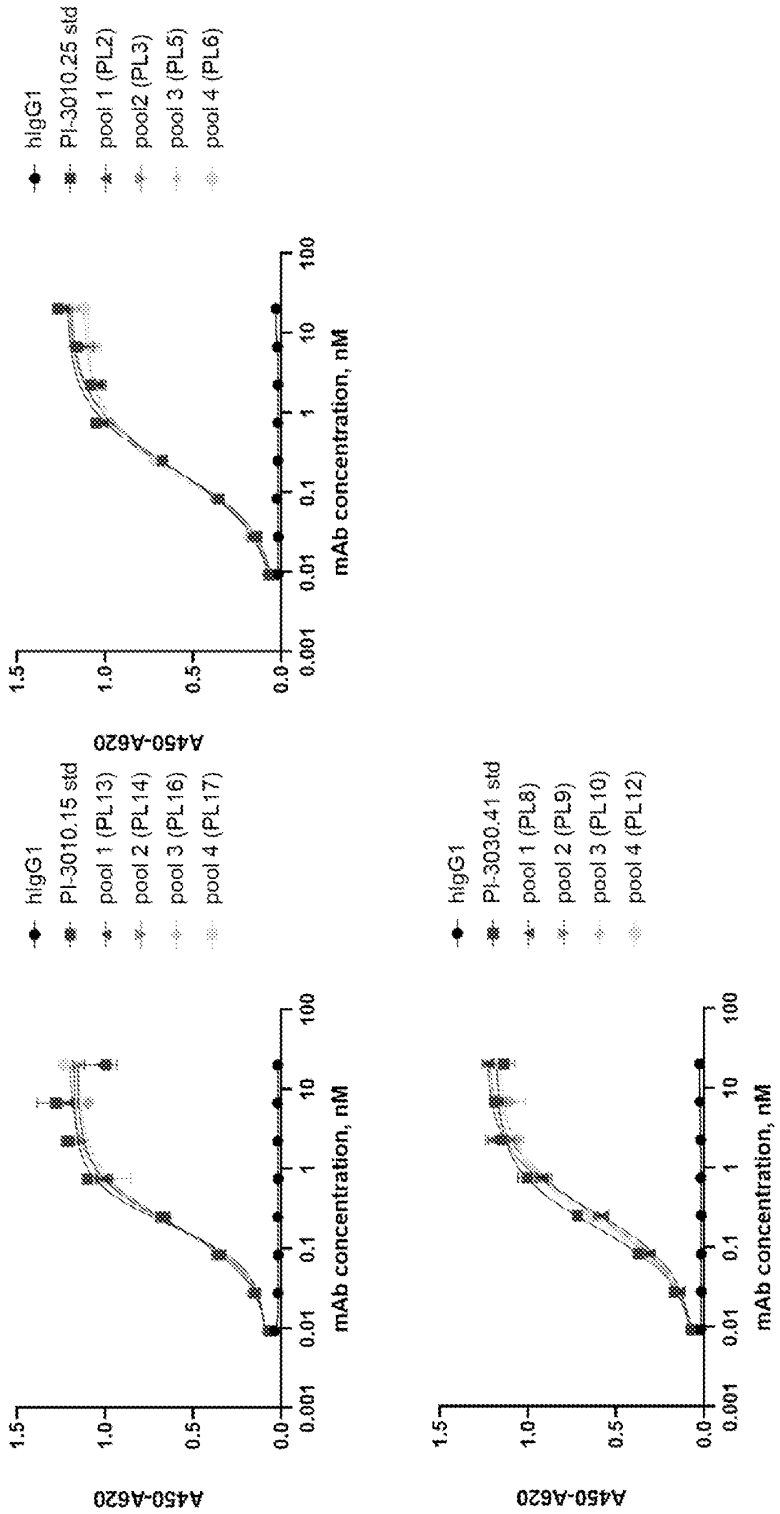

cyno MARCO- HEK 293
PI-3010.15-AB
PI-3010.25-AB
PI-3030.41-AB
hIgG1
gMFI
mAb conc nM
Binding to Jurkat cells
PI-3015-AB
PI-3025-AB
PI-3041-AB
hIgG1
gMFI
mAb conc nM
human MARCO - 293 cells
PI-3010.15-AB
PI-3010.25-AB
PI-3030.41-AB
hIgG1
gMFI
mAb conc nM
parental HEK293
PI-3010.15-AB
PI-3025.25-AB
PI-3030.41-AB
gMFI
mAb conc nM

FIG. 54


hIgG1
PI-3010.25 std
pool 1 (PL2)
pool2 (PL3)
pool 3 (PL5)
pool 4 (PL6)
A450-A620
mAb concentration, nM
hIgG1
PI-3010.15 std
pool 1 (PL13)
pool 2 (PL14)
pool 3 (PL16)
pool 4 (PL17)
A450-A620
mAb concentration, nM
hIgG1
PI-3030.41 std
pool 1 (PL8)
pool 2 (PL9)
pool 3 (PL10)
pool 4 (PL12)
A450-A620
mAb concentration, nM

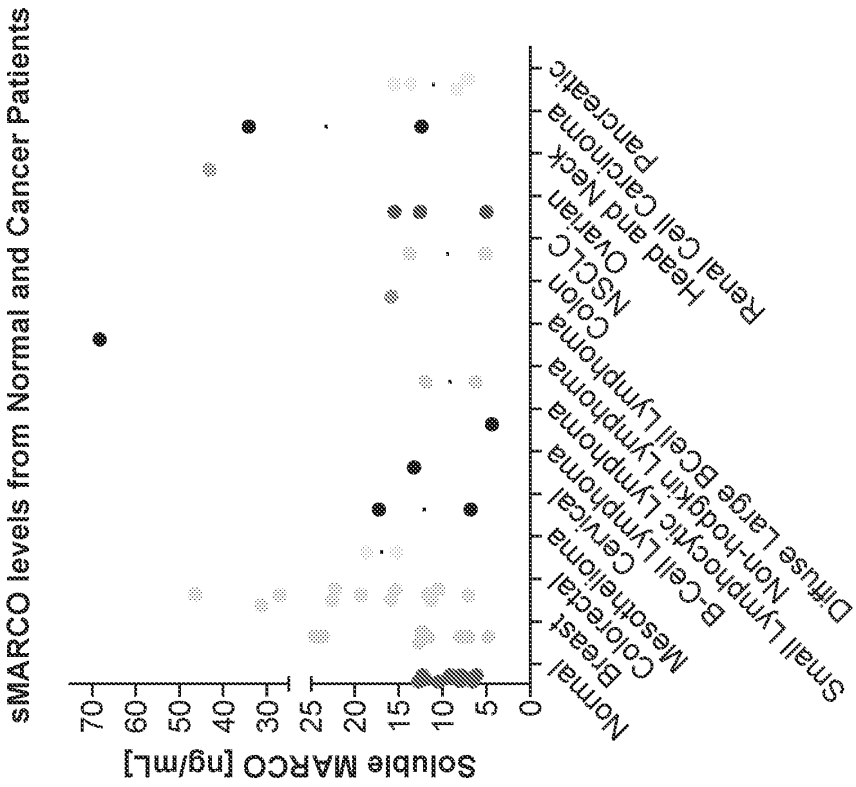


FIG. 55B

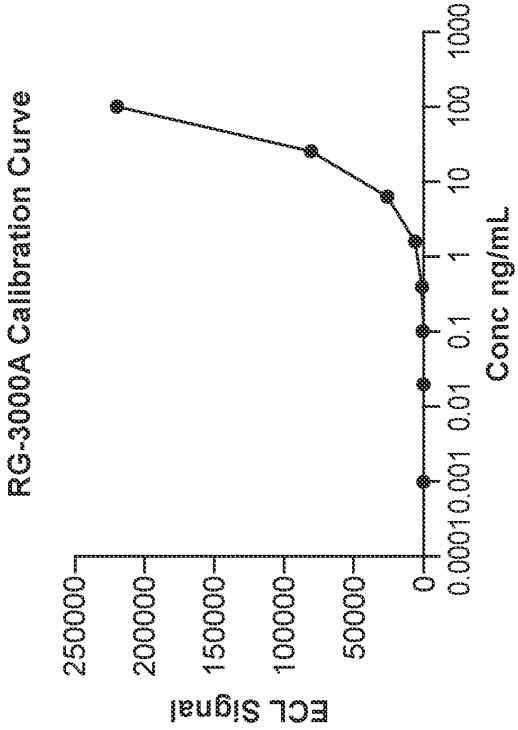


FIG. 55A

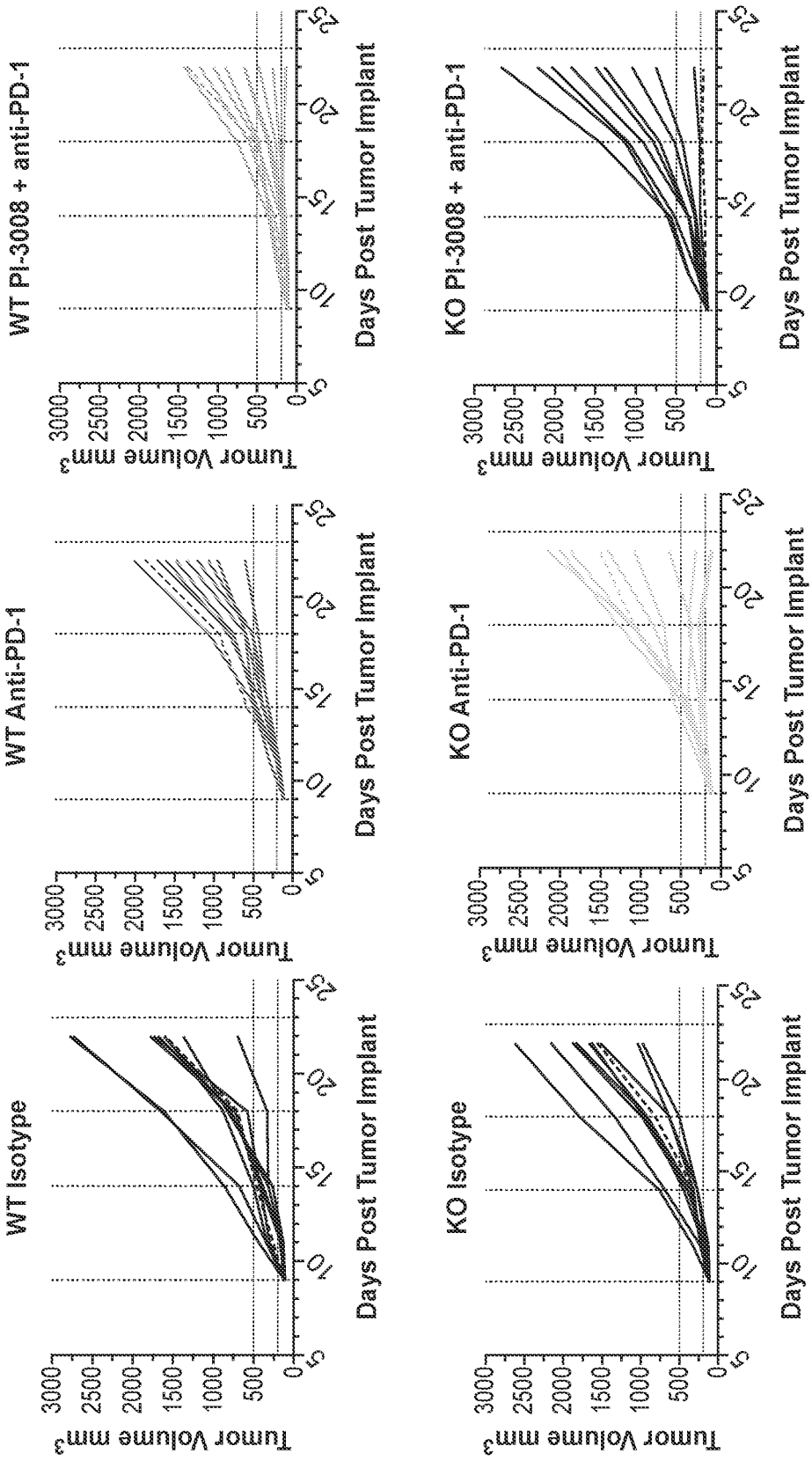

WT Isotype
WT Anti-PD-1
WT PI-3008 + anti-PD-1
KO Isotype
KO Anti-PD-1
KO PI-3008 + anti-PD-1
Tumor Volume mm3
Days Post Tumor Implant
0
500
1000
1500
2000
2500
3000
5
10
15
20
25

FIG. 56

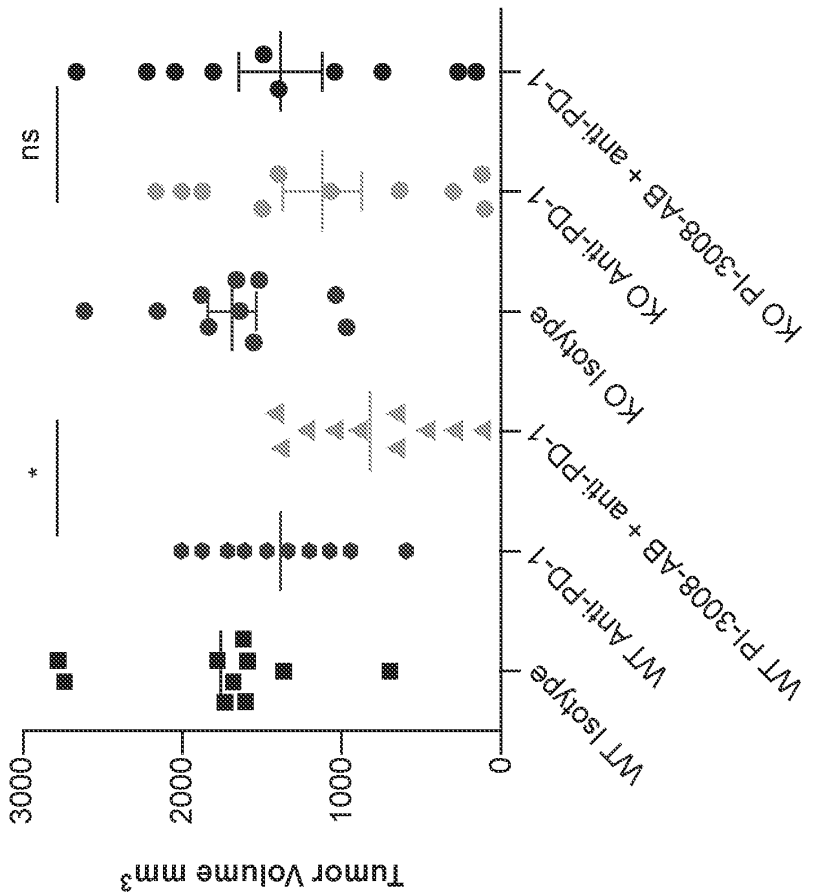

Tumor Volume mm3
3000
2000
1000
0
WT Isotype
WT Anti-PD-1
WT PI-3008-AB + anti-PD-1
KO Isotype
KO Anti-PD-1
KO PI-3008-AB + anti-PD-1
*
ns

FIG. 56 (Cont.)

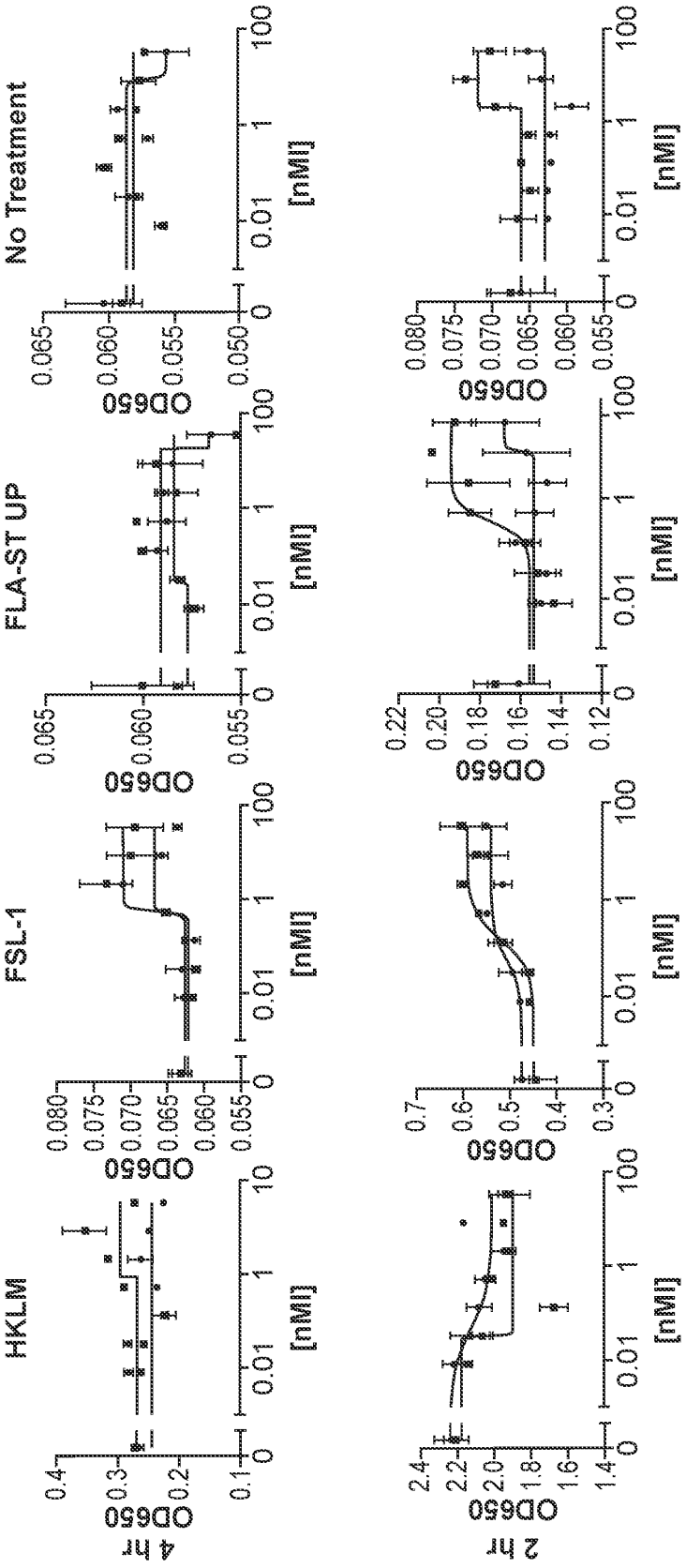

No Treatment
FLA-ST UP
FSL-1
HKLM
4 hr
2 hr
OD650
[nM]
Isotype
PI-3015

FIG. 57

FIG. 58

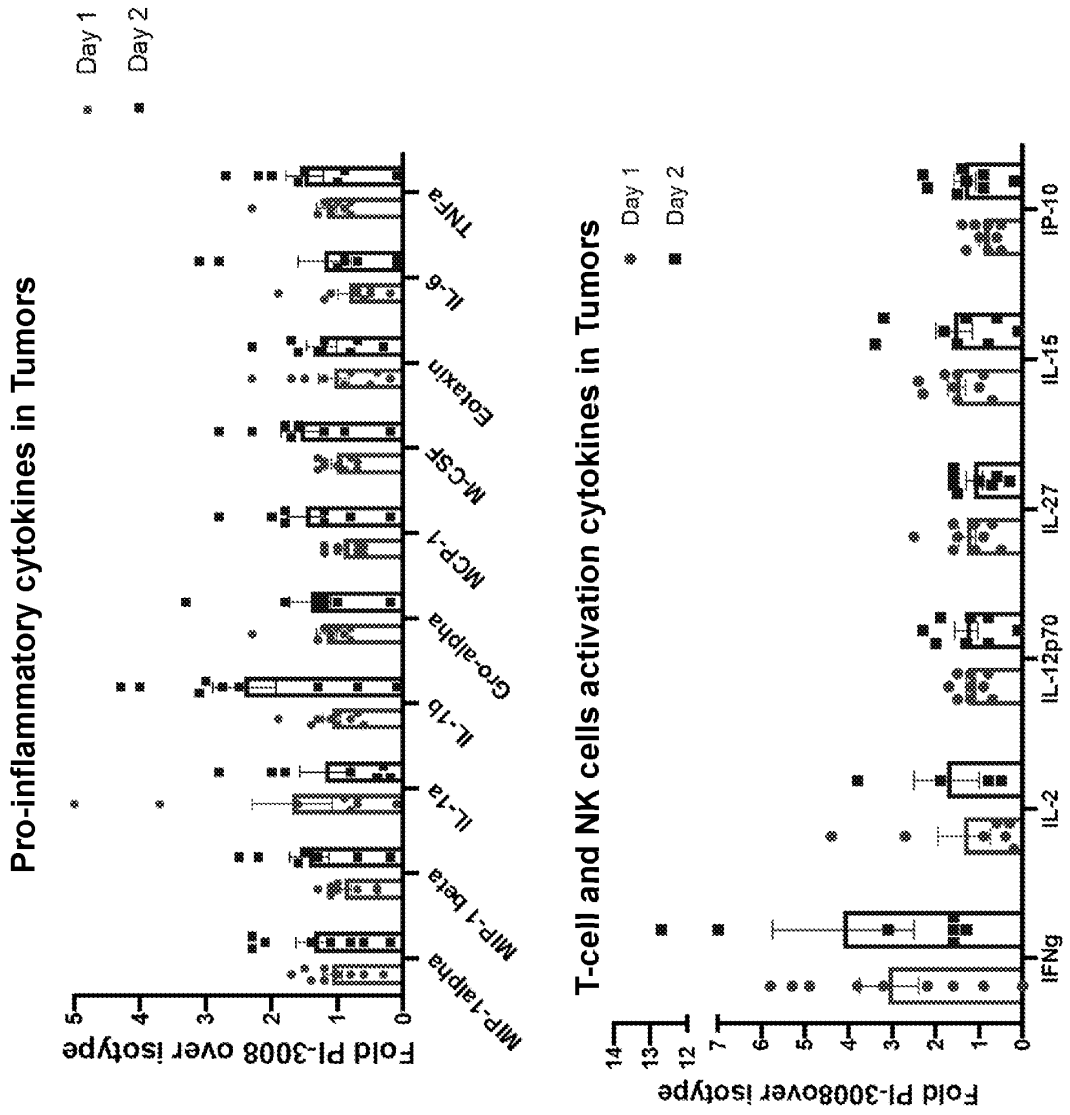

Pro-inflammatory cytokines in Tumors
Day 1
Day 2
Fold PI-3008 over isotype
0
1
2
3
4
5
MIP-1alpha
MIP-1 beta
IL-1a
IL-1b
Gro-alpha
MCP-1
M-CSF
Eotaxin
IL-6
TNFa
T-cell and NK cells activation cytokines in Tumors
Day 1
Day 2
Fold PI-3008over isotype
0
1
2
3
4
5
6
7
12
13
14
IFNg
IL-2
IL-12p70
IL-27
IL-15
IP-10

FIG. 59

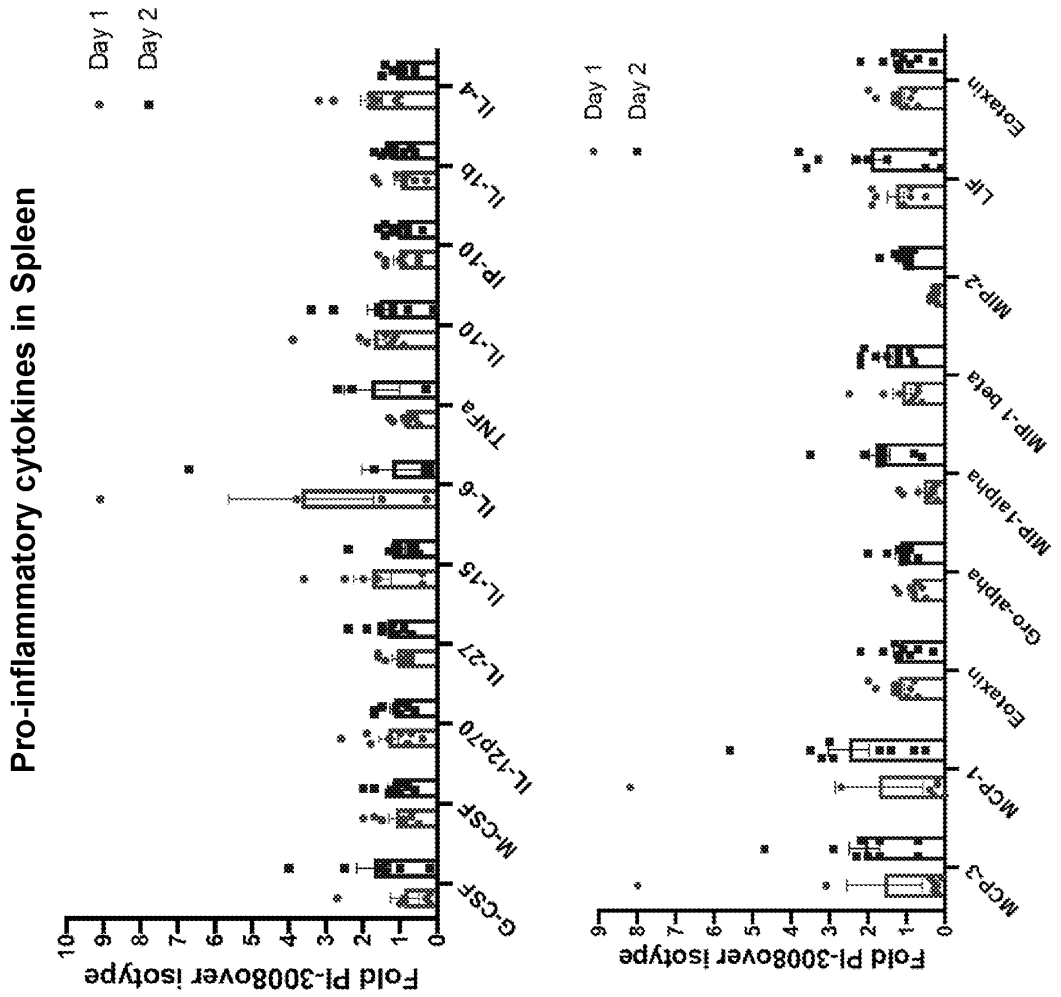

Pro-inflammatory cytokines in Spleen
Day 1
Day 2
Fold PI-3008over isotype
0
1
2
3
4
5
6
7
8
9
10
G-CSF
M-CSF
IL-12P70
IL-27
IL-15
IL-6
TNFa
IL-10
IP-10
IL-1b
IL-4
MCP-3
MCP-1
Eotaxin
Gro-alpha
MIP-1alpha
MIP-1 beta
MIP-2
LIF
Eotaxin

FIG. 60

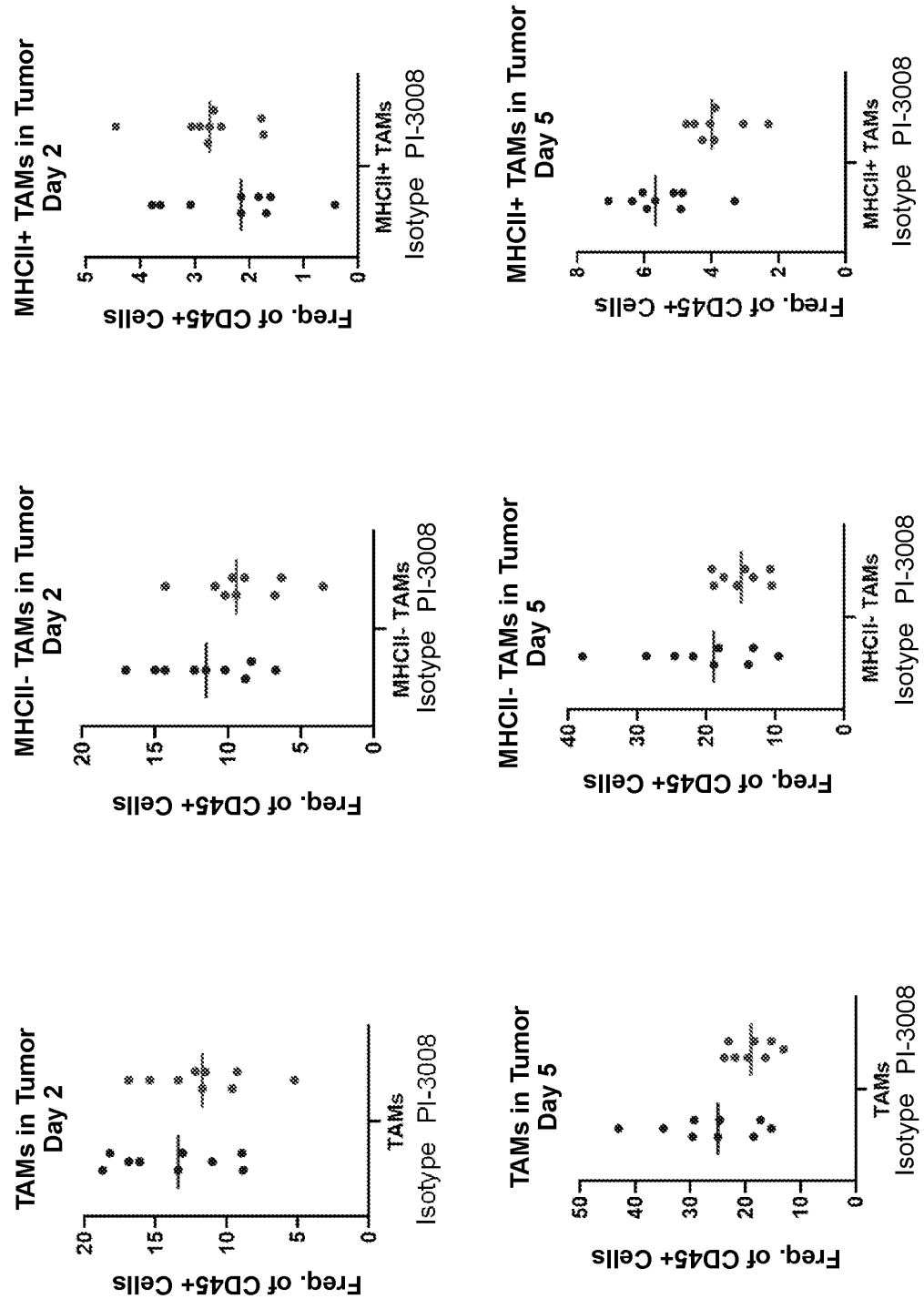

TAMs in Tumor
Day 2
Freq. of CD45+ Cells
TAMs
Isotype PI-3008
MHCII- TAMs in Tumor
Day 2
Freq. of CD45+ Cells
MHCII- TAMs
Isotype PI-3008
MHCII+ TAMs in Tumor
Day 2
Freq. of CD45+ Cells
MHCII+ TAMs
Isotype PI-3008
TAMs in Tumor
Day 5
Freq. of CD45+ Cells
TAMs
Isotype PI-3008
MHCII- TAMs in Tumor
Day 5
Freq. of CD45+ Cells
MHCII- TAMs
Isotype PI-3008
MHCII+ TAMs in Tumor
Day 5
Freq. of CD45+ Cells
MHCII+ TAMs
Isotype PI-3008

FIG. 61

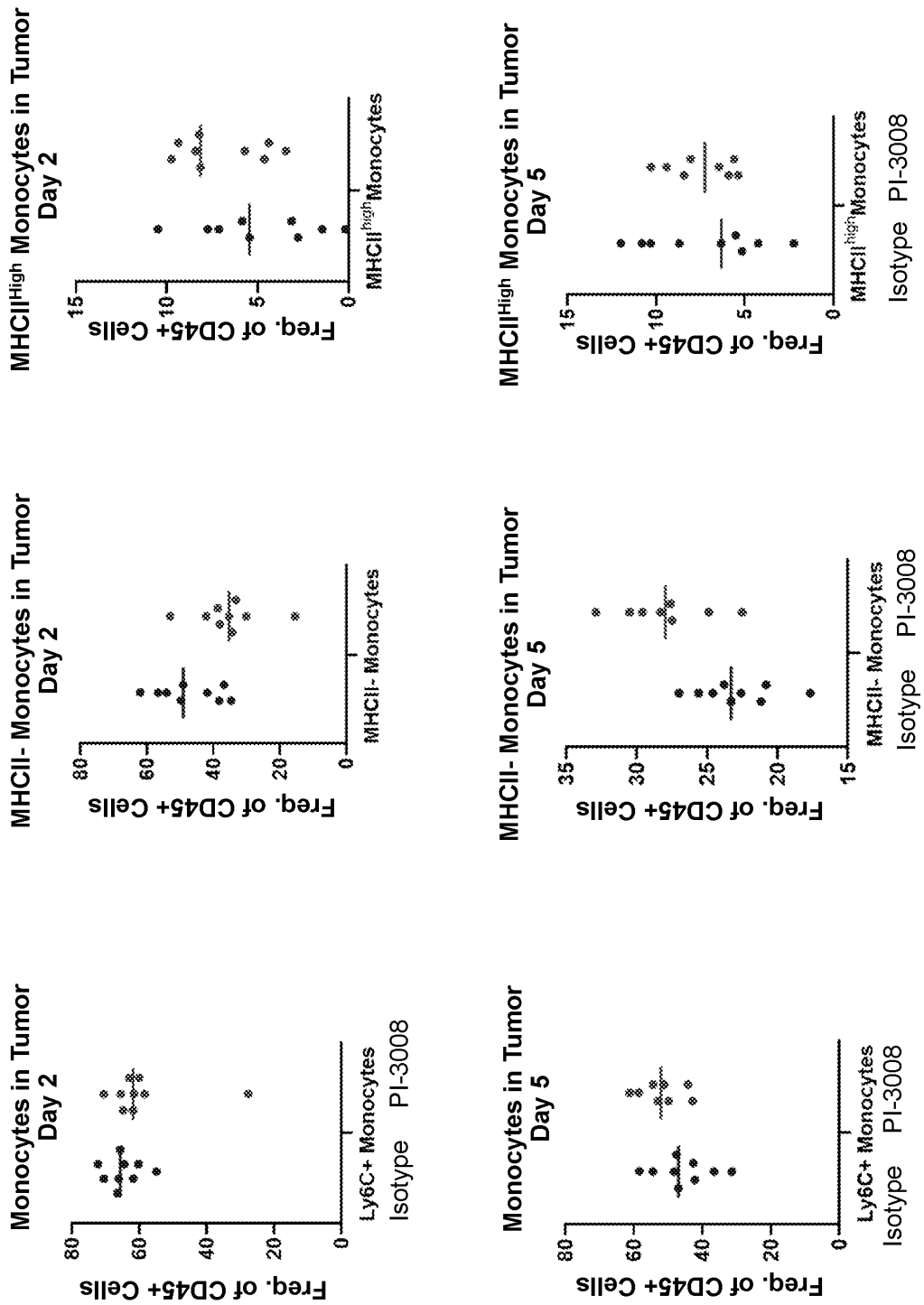

Monocytes in Tumor Day 2
Freq. of CD45+ Cells
Ly6C+ Monocytes
Isotype PI-3008
MHCII- Monocytes in Tumor Day 2
MHCII- Monocytes
MHCII^{High} Monocytes in Tumor Day 2
MHCII^{high}Monocytes
Monocytes in Tumor Day 5
MHCII- Monocytes in Tumor Day 5
MHCII^{High} Monocytes in Tumor Day 5

FIG. 62

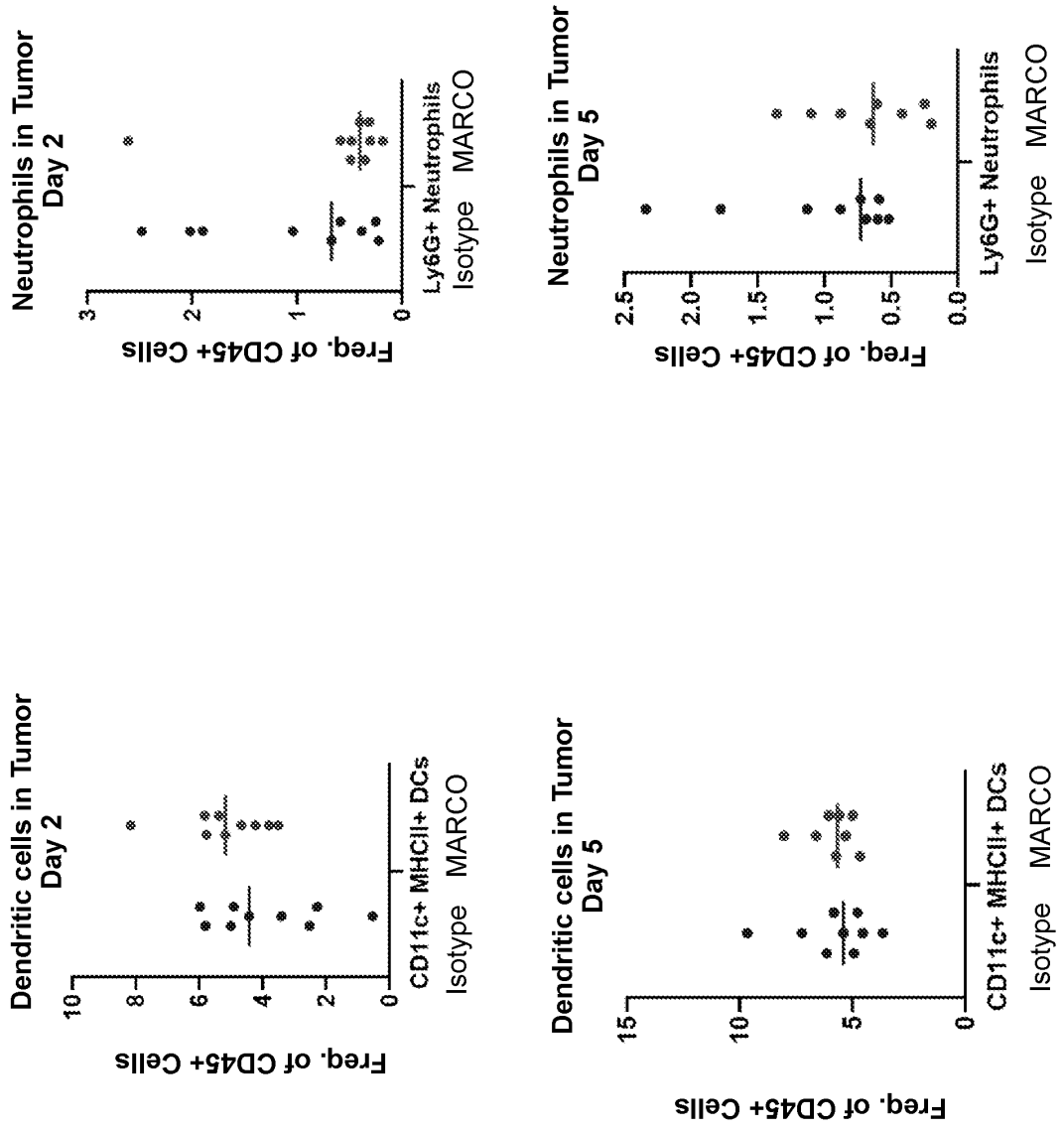

Neutrophils in Tumor
Day 2
Freq. of CD45+ Cells
0
1
2
3
Ly6G+ Neutrophils
Isotype
MARCO
Neutrophils in Tumor
Day 5
Freq. of CD45+ Cells
0.0
0.5
1.0
1.5
2.0
2.5
Ly6G+ Neutrophils
Isotype
MARCO
Dendritic cells in Tumor
Day 2
Freq. of CD45+ Cells
0
2
4
6
8
10
CD11c+ MHCII+ DCs
Isotype
MARCO
Dendritic cells in Tumor
Day 5
Freq. of CD45+ Cells
0
5
10
15
CD11c+ MHCII+ DCs
Isotype
MARCO

FIG. 63

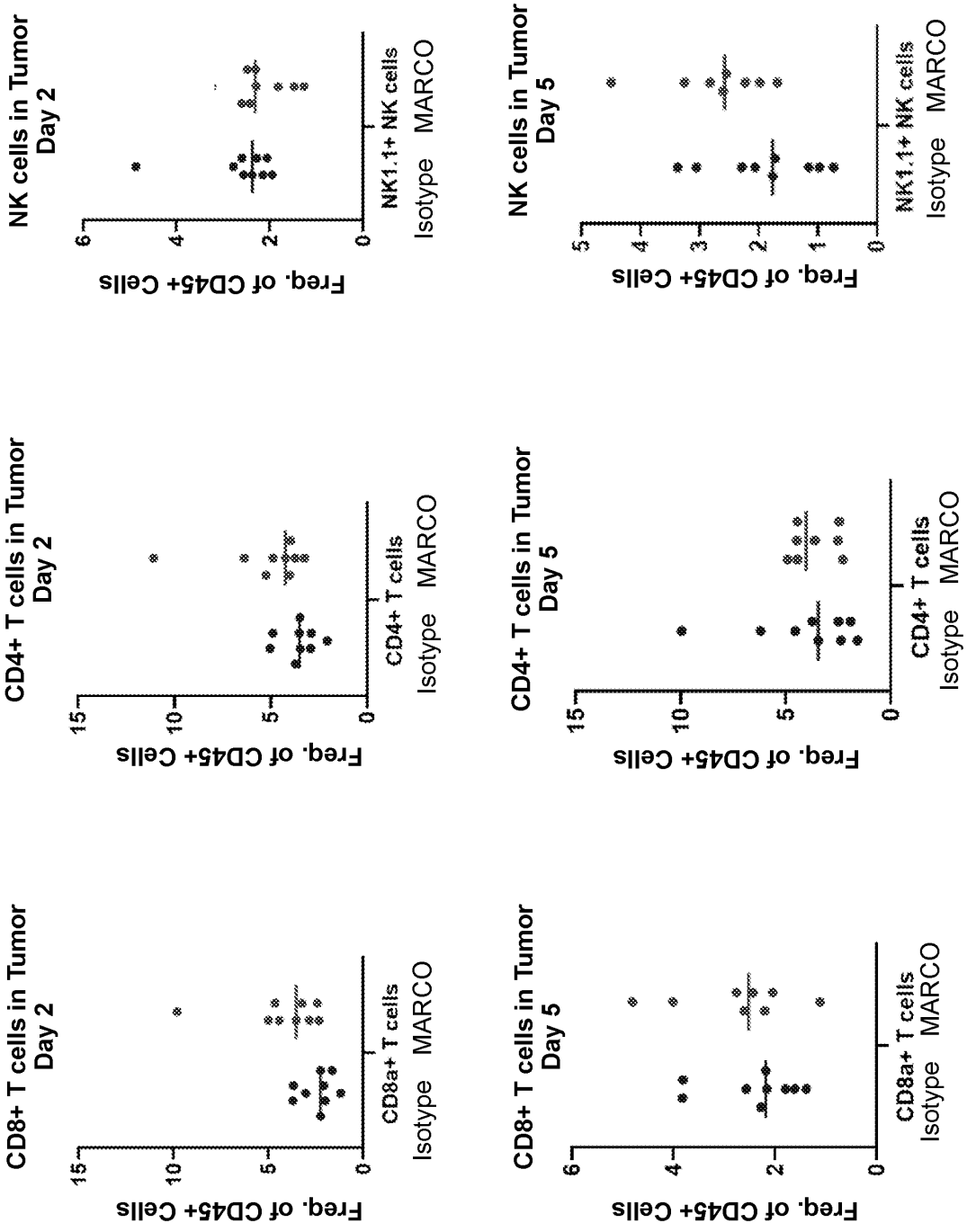

CD8+ T cells in Tumor Day 2
Freq. of CD45+ Cells
15
10
5
0
CD8a+ T cells
Isotype MARCO
CD4+ T cells in Tumor Day 2
Freq. of CD45+ Cells
15
10
5
0
CD4+ T cells
Isotype MARCO
NK cells in Tumor Day 2
Freq. of CD45+ Cells
6
4
2
0
NK1.1+ NK cells
Isotype MARCO
CD8+ T cells in Tumor Day 5
Freq. of CD45+ Cells
6
4
2
0
CD8a+ T cells
Isotype MARCO
CD4+ T cells in Tumor Day 5
Freq. of CD45+ Cells
15
10
5
0
CD4+ T cells
Isotype MARCO
NK cells in Tumor Day 5
Freq. of CD45+ Cells
5
4
3
2
1
0
NK1.1+ NK cells
Isotype MARCO

FIG. 64

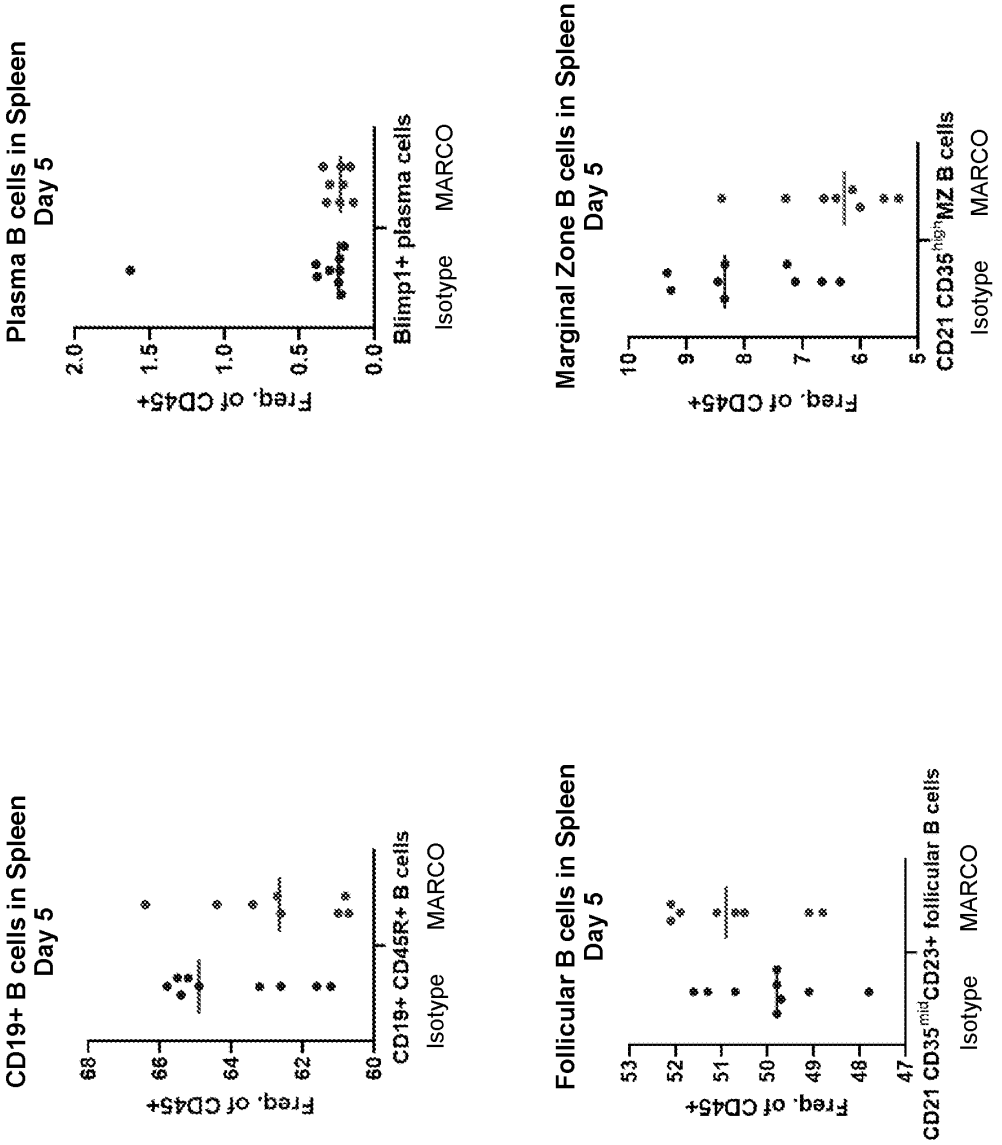

Plasma B cells in Spleen
Day 5
Freq. of CD45+
2.0
1.5
1.0
0.5
0.0
Blimp1+ plasma cells
Isotype
MARCO
Marginal Zone B cells in Spleen
Day 5
Freq. of CD45+
10
9
8
7
6
5
CD21 CD35high MZ B cells
Isotype
MARCO
CD19+ B cells in Spleen
Day 5
Freq. of CD45+
68
66
64
62
60
CD19+ CD45R+ B cells
Isotype
MARCO
Follicular B cells in Spleen
Day 5
Freq. of CD45+
53
52
51
50
49
48
47
CD21 CD35mid CD23+ follicular B cells
Isotype
MARCO

FIG. 65

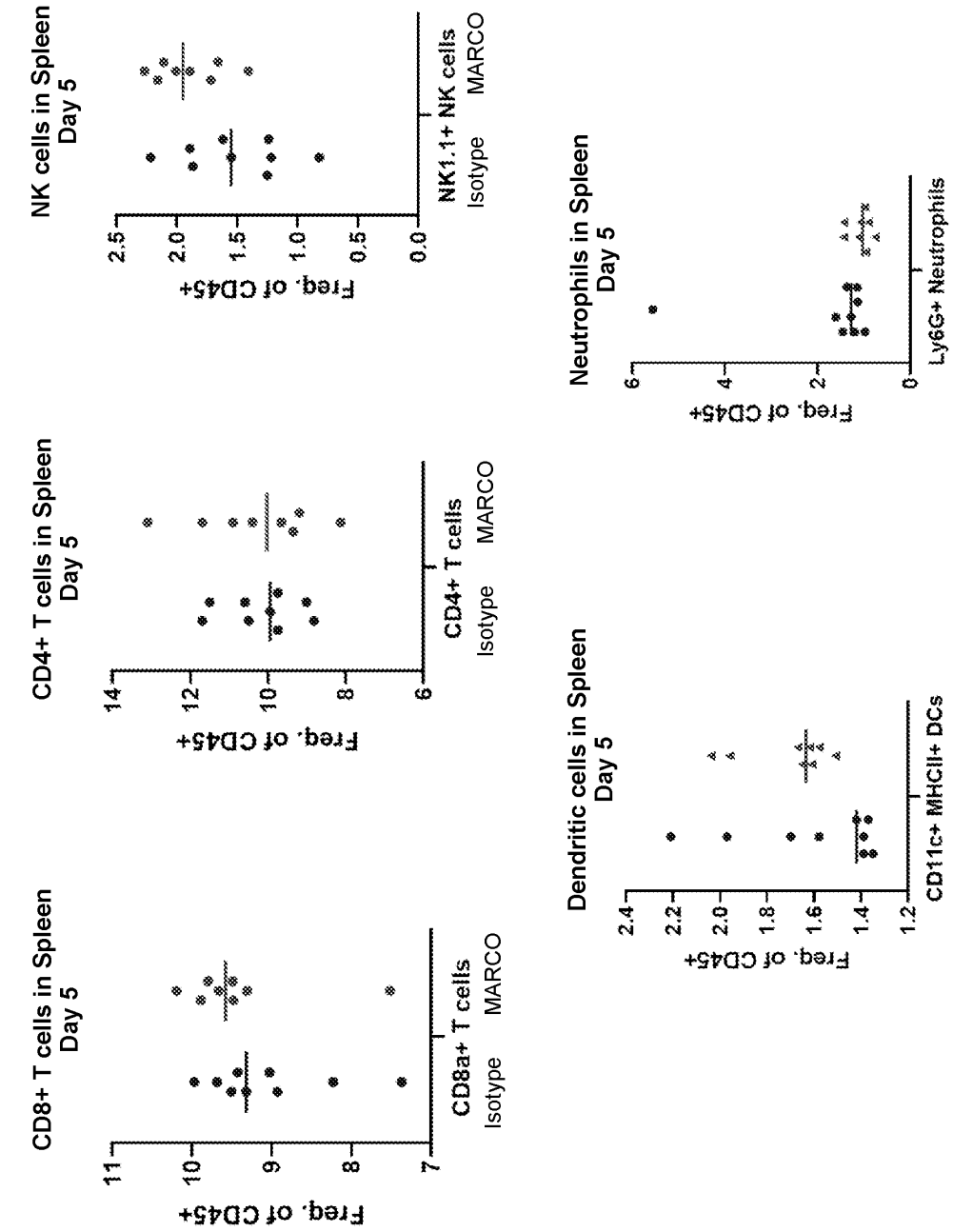

CD8+ T cells in Spleen
Day 5
Freq. of CD45+
CD8a+ T cells
Isotype
MARCO
CD4+ T cells in Spleen
Day 5
Freq. of CD45+
CD4+ T cells
Isotype
MARCO
NK cells in Spleen
Day 5
Freq. of CD45+
NK1.1+ NK cells
Isotype
MARCO
Dendritic cells in Spleen
Day 5
Freq. of CD45+
CD11c+ MHCII+ DCs
Neutrophils in Spleen
Day 5
Freq. of CD45+
Ly6G+ Neutrophils

FIG. 66

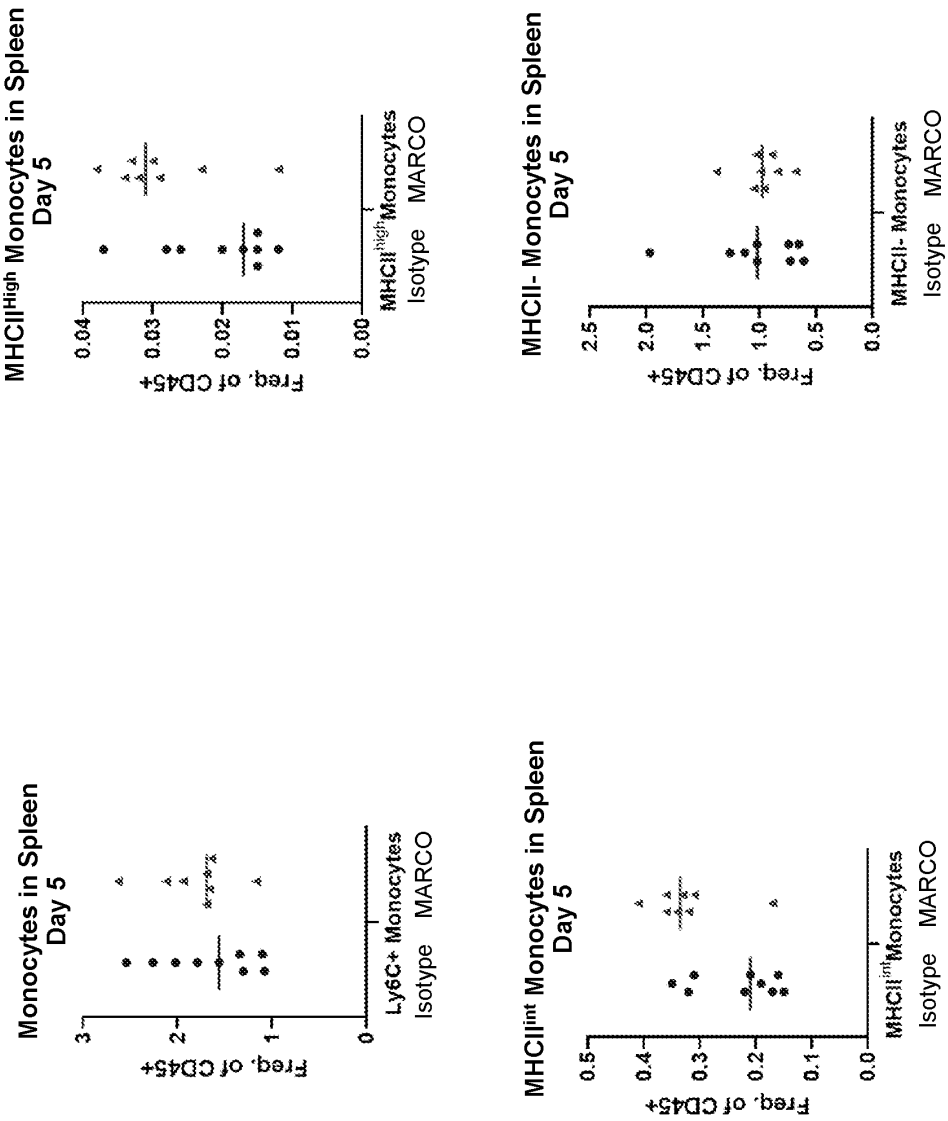

Monocytes in Spleen
Day 5
Freq. of CD45+
Ly6C+ Monocytes
Isotype MARCO
MHCII^High Monocytes in Spleen
Day 5
Freq. of CD45+
MHCII^high Monocytes
Isotype MARCO
MHCII^int Monocytes in Spleen
Day 5
Freq. of CD45+
MHCII^int Monocytes
Isotype MARCO
MHCII- Monocytes in Spleen
Day 5
Freq. of CD45+
MHCII- Monocytes
Isotype MARCO

FIG. 67

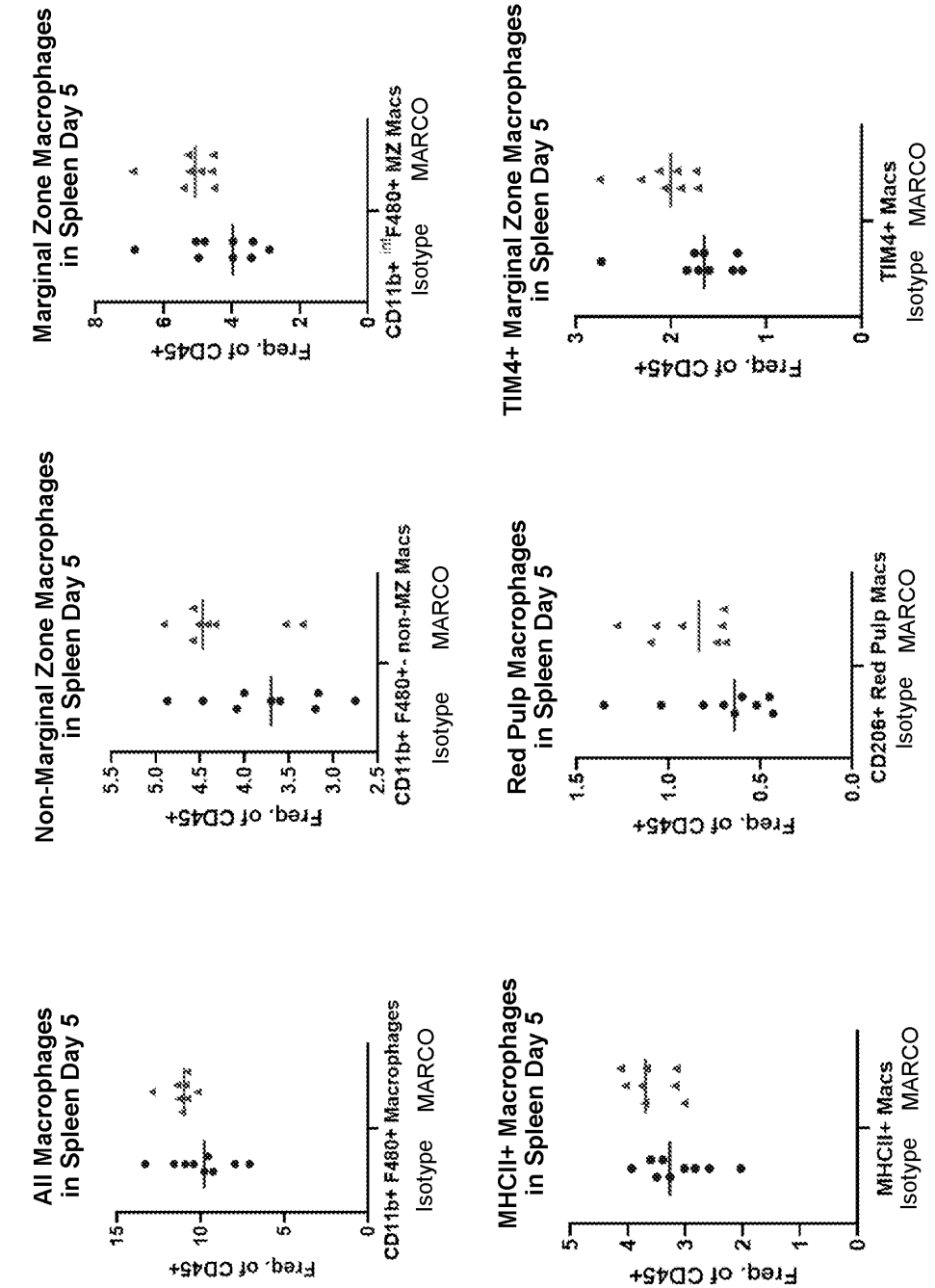

All Macrophages in Spleen Day 5
Freq. of CD45+
CD11b+ F480+ Macrophages
Isotype MARCO
Non-Marginal Zone Macrophages in Spleen Day 5
Freq. of CD45+
CD11b+ F480+ non-MZ Macs
Isotype MARCO
Marginal Zone Macrophages in Spleen Day 5
Freq. of CD45+
CD11b+ F480+ MZ Macs
Isotype MARCO
MHCII+ Macrophages in Spleen Day 5
Freq. of CD45+
MHCII+ Macs
Isotype MARCO
Red Pulp Macrophages in Spleen Day 5
Freq. of CD45+
CD206+ Red Pulp Macs
Isotype MARCO
TIM4+ Marginal Zone Macrophages in Spleen Day 5
Freq. of CD45+
TIM4+ Macs
Isotype MARCO

FIG. 68

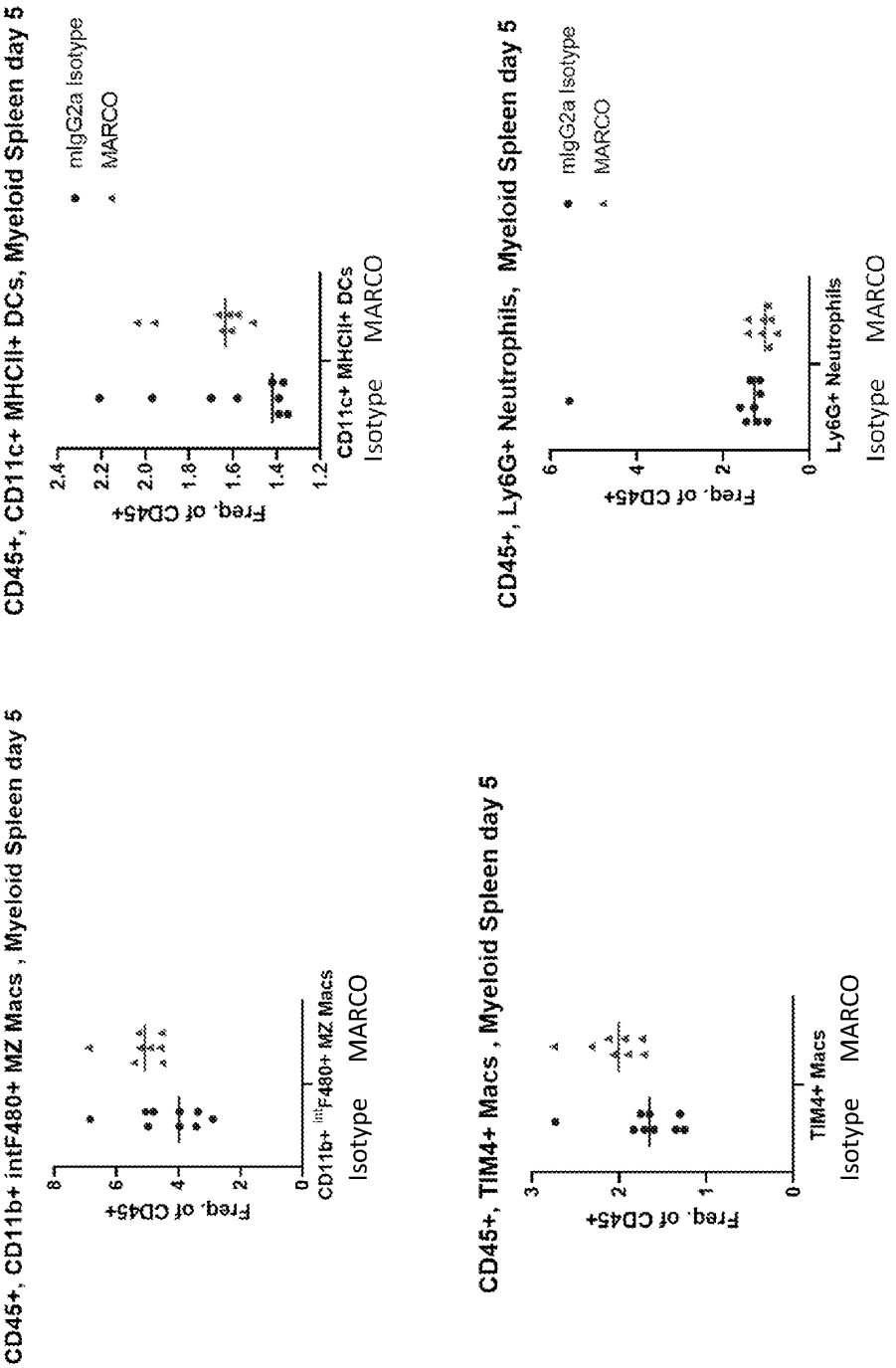

CD45+, CD11b+ intF480+ MZ Macs , Myeloid Spleen day 5
Freq. of CD45+
CD11b+ intF480+ MZ Macs
Isotype MARCO
CD45+, CD11c+ MHCII+ DCs, Myeloid Spleen day 5
mIgG2a Isotype
MARCO
Freq. of CD45+
CD11c+ MHCII+ DCs
Isotype MARCO
CD45+, TIM4+ Macs , Myeloid Spleen day 5
Freq. of CD45+
TIM4+ Macs
Isotype MARCO
CD45+, Ly6G+ Neutrophils, Myeloid Spleen day 5
mIgG2a Isotype
MARCO
Freq. of CD45+
Ly6G+ Neutrophils
Isotype MARCO

FIG. 69

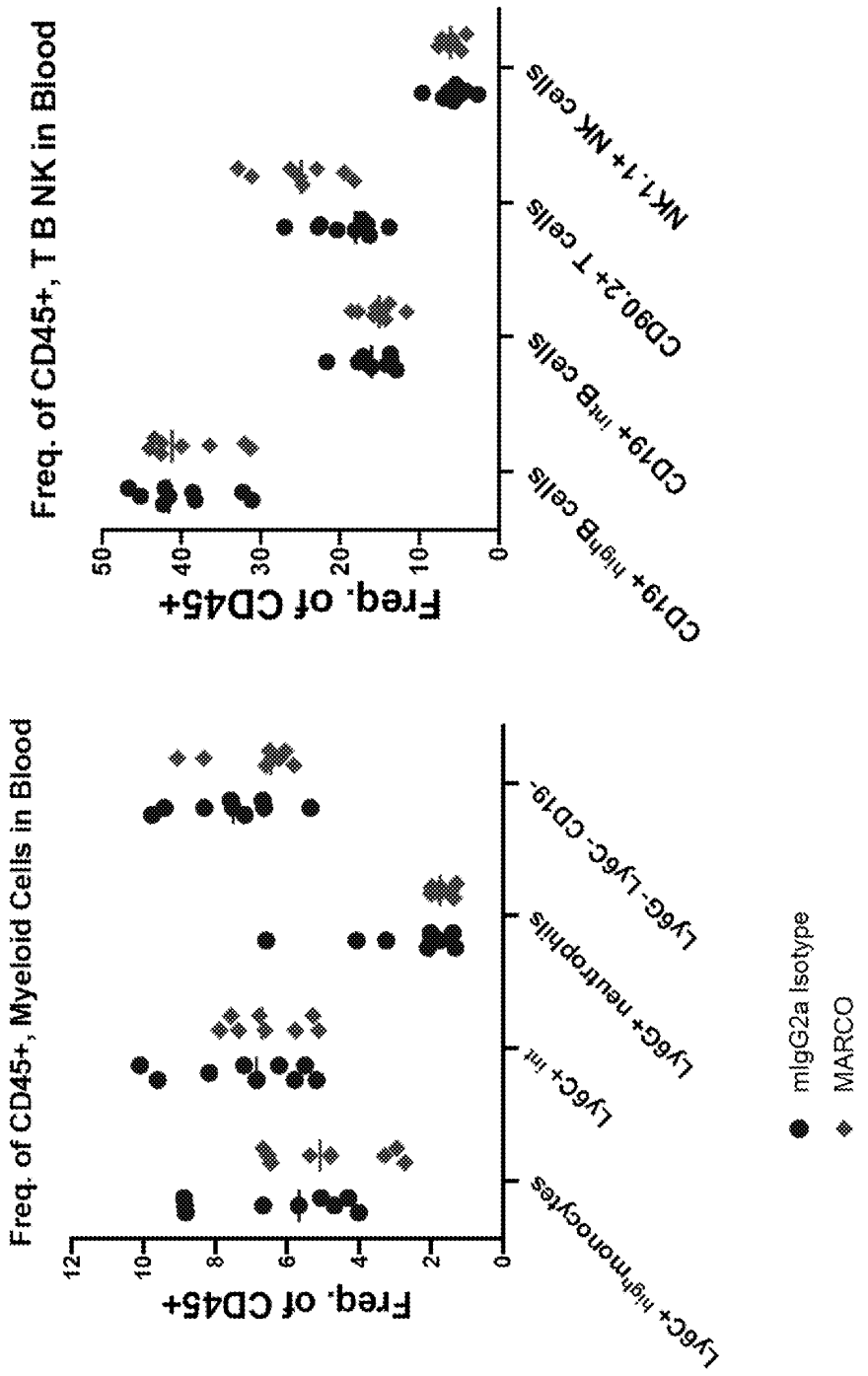

Freq. of CD45+, Myeloid Cells in Blood
Freq. of CD45+
0
2
4
6
8
10
12
Ly6C+ highmonocytes
Ly6C+ int
Ly6G+ neutrophils
Ly6G- Ly6C- CD19-
Freq. of CD45+, T B NK in Blood
Freq. of CD45+
0
10
20
30
40
50
CD19+ highB cells
CD19+ intB cells
CD90.2+ T cells
NK1.1+ NK cells
mIgG2a Isotype
MARCO

FIG. 70

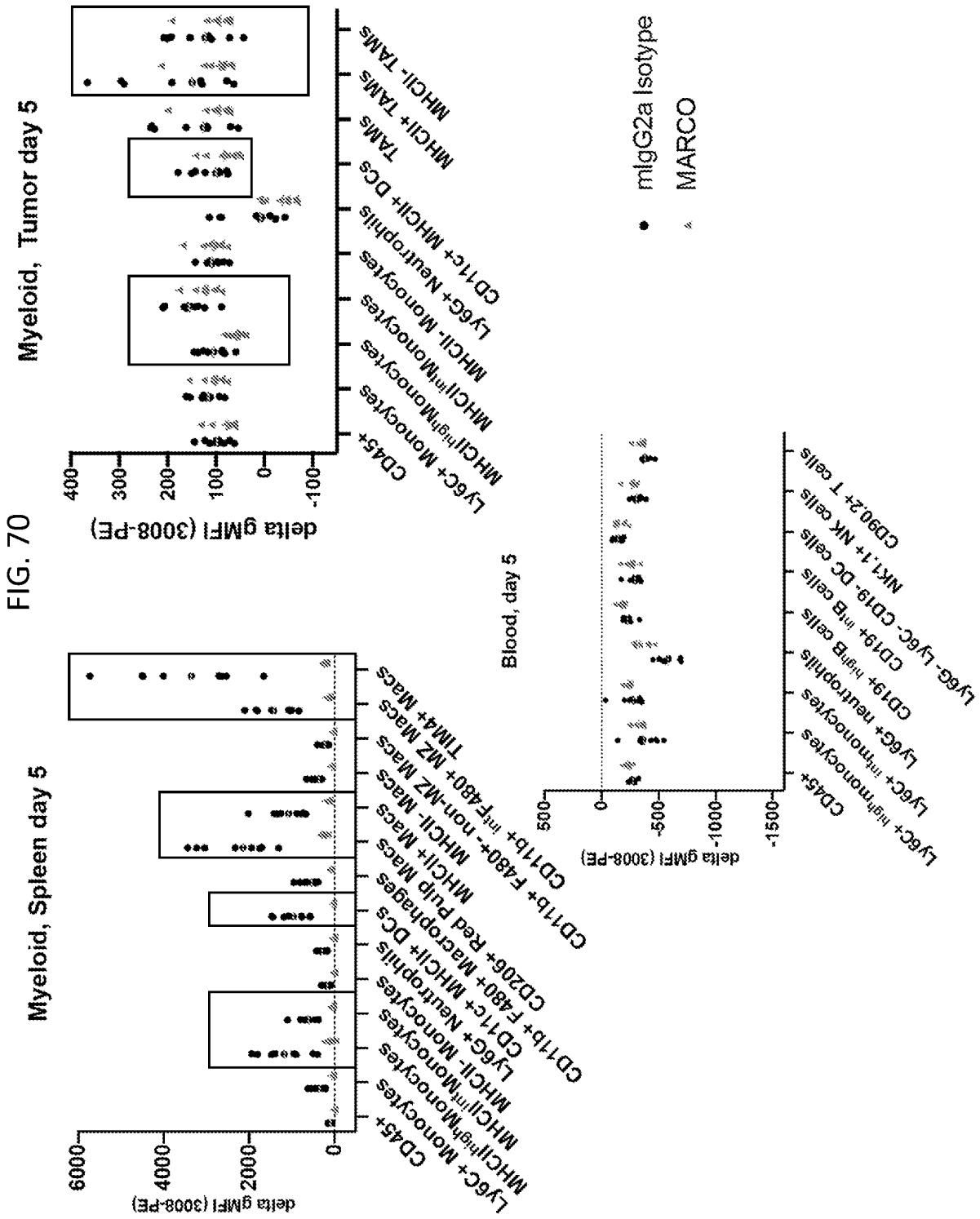
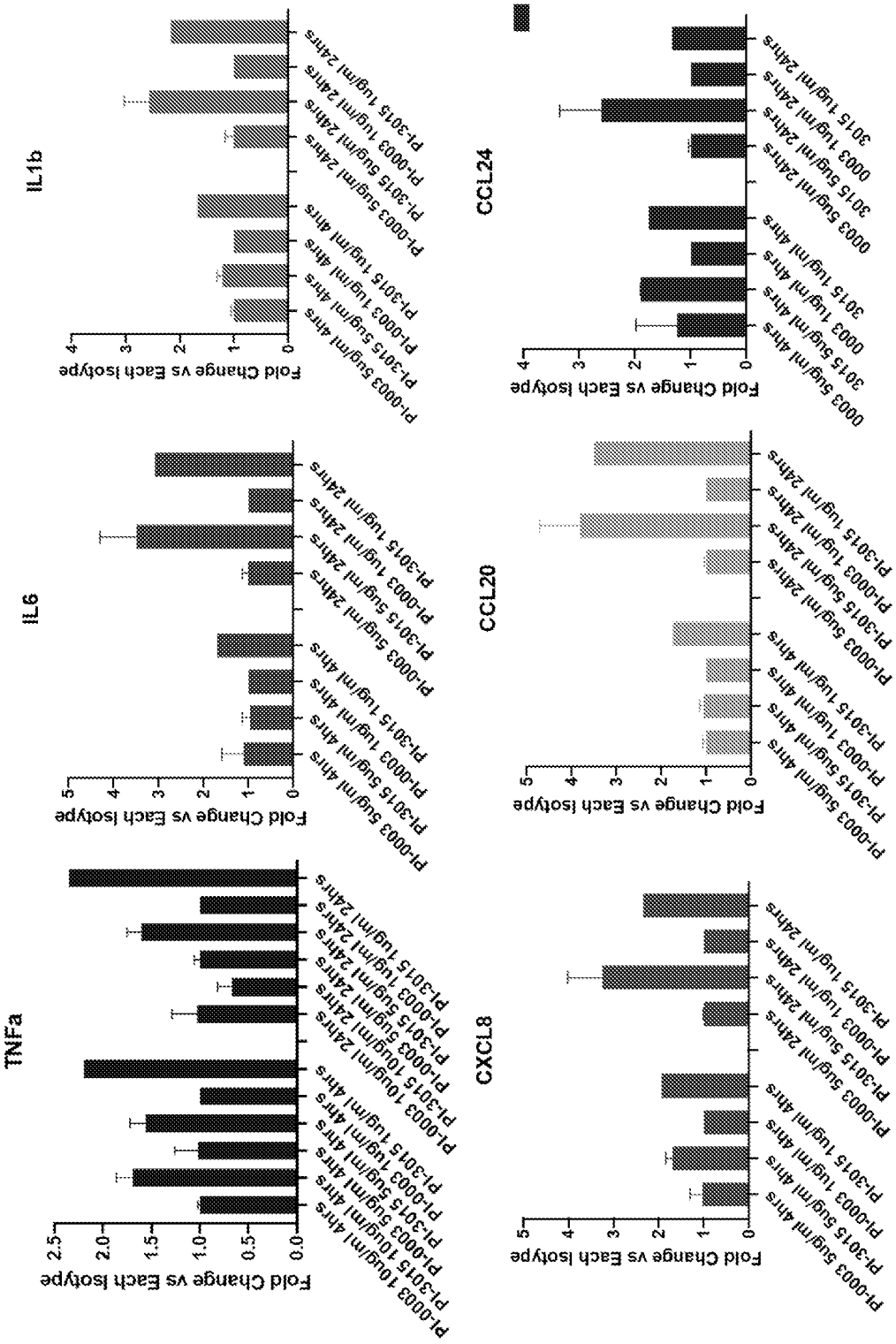

Myeloid, Tumor day 5
delta gMFI (3008-PE)
400
300
200
100
0
-100
CD45+
Ly6C+ Monocytes
MHCIIhighMonocytes
MHCIIintMonocytes
MHCII- Monocytes
Ly6G+ Neutrophils
CD11c+ MHCII+ DCs
TAMs
MHCII+ TAMs
MHCII- TAMs
Myeloid, Spleen day 5
delta gMFI (3008-PE)
6000
4000
2000
0
CD45+
Ly6C+ Monocytes
MHCIIhighMonocytes
MHCIIintMonocytes
MHCII- Monocytes
Ly6G+ Neutrophils
CD11c+ MHCII+ DCs
CD11b+ F480+ Macrophages
CD206+ Red Pulp Macs
MHCII+ Macs
MHCII- Macs
CD11b+ F480+ non-MZ Macs
CD11b+ intF480+ MZ Macs
TIM4+ Macs
Blood, day 5
mIgG2a Isotype
MARCO
delta gMFI (3008-PE)
500
0
-500
-1000
-1500
CD45+
Ly6C+ highmonocytes
Ly6C+ intmonocytes
Ly6G+ neutrophils
CD19+ highB cells
CD19+ intB cells
Ly6G- Ly6C- CD19- DC cells
NK1.1+ NK cells
CD90.2+ T cells

FIG. 71


TNFa
IL6
IL1b
CXCL8
CCL20
CCL24
Fold Change vs Each Isotype
Pt-0003 5ug/ml 4hrs
Pt-0003 1ug/ml 4hrs
Pt-3015 5ug/ml 4hrs
Pt-3015 1ug/ml 4hrs
Pt-0003 10ug/ml 24hrs
Pt-0003 5ug/ml 24hrs
Pt-0003 1ug/ml 24hrs
Pt-3015 10ug/ml 24hrs
Pt-3015 5ug/ml 24hrs
Pt-3015 1ug/ml 24hrs