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Human GPR174 protein NP_115942.1
(SEQ ID NO:1)

MPANYTCTRPDGDNTDFRYFIYAVTYTVILVPGGLIGNILALWVFYGYMKETKRAVIFMINLAIADLLQVL
SLPLRIFYVLNHDWPFGPGLCMFCFYLYKYNMYASTYFLVCISVRRFWFLMYPFRFHDCKQKYDLYISIA
GWLIIICLACVLFPLRLRTSDDTSGNRTKCFVDLPTRNVNLAQSVVMMTIGELIGFVTPLLIVLYCTWKTVL
SLQDKYPMAQDLGEKQKALKMILTCAGVFLICFAPYHFSFPLDFLVKSNEIKSCLARRVILIFHSVALCL
ASLNSCLDPVIYYFSTNEFRRLSRQDLHDSIQLHAKSFVSNHTASTMTPELC

FIG. 1A

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Human GPR174 cDNA (NM_032553.1) SEQ ID NO:2

CACCATTAGGCAAGATAGTTTCTCTAGAGAGAAATCATGCCTGCTAATTACACGTGTACCAGGCCAGATGG
AGACAAATACAGATTTTCGATACTTTATTTATGCAGTGACATACACTGTCAATTCTTGTGCCAGGTCTCATAG
GGAATATATTAGCCCTGTGGGTATCTATGTTATATGAAAGAAACAAACGAGCTGTGATATTTATGATA
AACTTAGCCATTGCTGACTTACTACAAGTTCTTTCCTTGCCACTGAGGATCTTCTACTACTTGAATCATGA
CTGGCCATTTGGGCTGGTCTCTGCAATGTTCTGTTCCTACCTGAAGTATGTCAACATGTATGCAAGCATCT
ACTTCTTGGTCTGCATCAGTGTGCAGCATTTTGGTTTCTCATGTACCCCTTTCGCTTCCATGACTGCAAA
CAGAAATATGACCTGTACATCAGCATTGCTGGCTGGCTGATCATCTGCCCTTGCCCTGTGTACTCTTCCACT
CCTCAGAACCAAGTATACCTCTGGCAATAGGACCACAAATGCTTTGTGGATCTTCCTACCAGGAATGTCA
ACCTGGCCCCAGTCCGTTGTTATGATGACCAATTGGCGAGTTGATTGGGTTTGTAACTCCGCTTCTGATTGTC
CTATATTGTACCTGGAAGACGGTTTATCACTGCAAGATAAATATCCCATGGCCCAAGATCTTGGAGAGAA
ACAGAAAGCCTTGAAGATGATTCTAACCTGTGCAGGGGTATTCCTAATTTGCTTTGCACCTTATCATTTCA
GTTTTCCTTTAGATTTCCCTGGTGAAGTCCAATGAAATTAAGAGCTGCCCTAGCCAGAAAGGTGATTCTAATA
TTTCATTCTGTGGCATTGTGCTTGTCTAGTCTGAATTCAATGCTTGAACCCAGTCATATACTACTTTTCCAC
TAATGAGTTCGGAAGACGGCTTCAAGACAAGATTTGCAATGACAGCATCCAACCTCCATGCAAAATCCTTTG
TGAGTAACCATACAGCTTCCACCATGACACCTGAATTATGCTAAACAAACCAAACTGAATGTGACCT
GAAATGCAAGTACATCAGAACATATCTGCAATACCCCAAGCCACAGGGAAGAACTTGCAAAACACACAGCT
TTTCAGTTCTGCTCTATCTTACTGCTATGGGGAATTCACTTCTTCAAGCAGGACCTATTTGGAGCATTAC
GATCCACGATTATTGATGTTGACATGTCCATGTAGTAATTTTCTTCAAGT

FIG. 1B

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Mouse GPR174 protein NP_001028423.1
(SEQ ID NO:3)

MTDNFTCNKTDGDNTRFRFYAVTYTVILVPGLIGNILALWVFYGYMKETKRAVVF
MINLAIADLLQILSLPLRIFYYLNHDWPFPGGLCMFCFYLYKYYNMYASIFYFLVCISV
RRFWFLMYPFRFNDCKQKYDLVISIIGWLIIICLACLLFPLLRNTDDTPGNRTKCFVD
LPIRNVNLAQSVAMITIGEVGVFTPLMIVLYCTWKTALSQNKYPISQHLGEKKKA
LKMILT CAGVFLVCFVPYHFSFPLDFLVKSNEIKSCFARRVILIFHSVALCLASLNS
CLDPVIYYFTTNEFRRLSRQDLPDNIQLHTKSYKIASNHATSTVAAELC

FIG. 1C

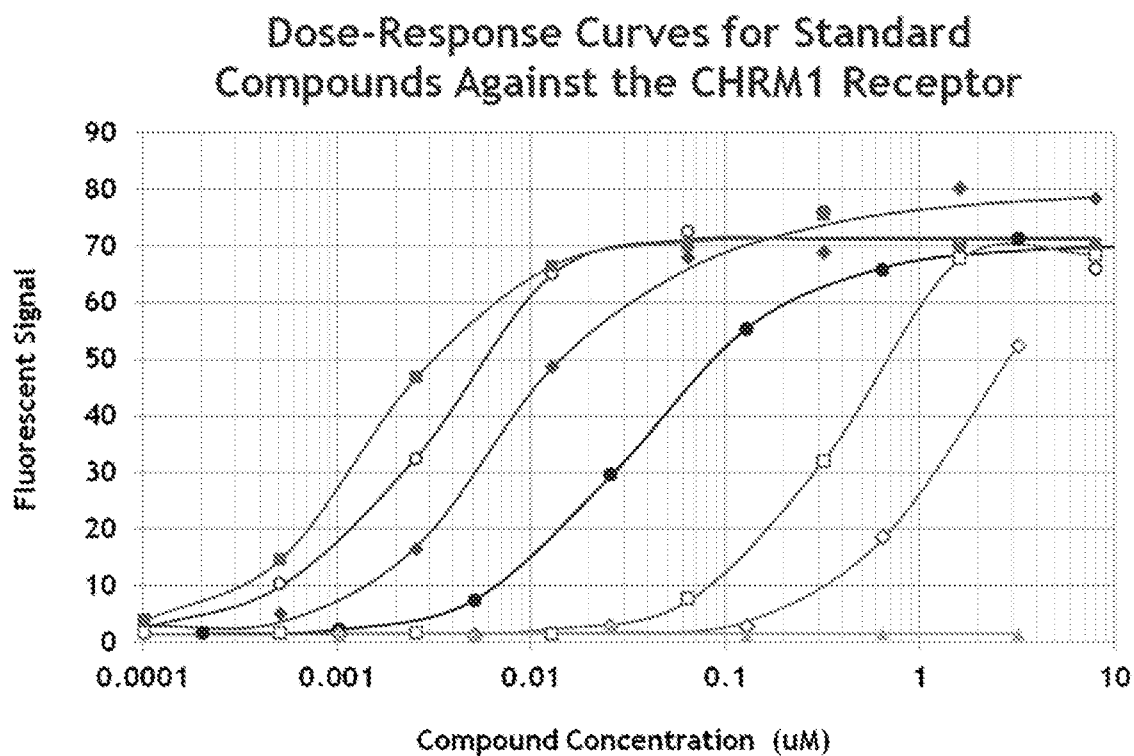
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Rat GPR174 protein NP_001100408.1
(SEQ ID NO:4)

MTDNFTCNKTDGNDTDFRYFIYAVTYTVILVPGLIGNILALWIFYGYMKETKRAVVFMINLAIADLLQIL
SLPLRIFYYLNHDWPFPGGLCMFCFYLYVNMVYASIFYLCISVRRFWFLMYPFRFNDCKQKYDLYISIV
GWLIIICLACLLFPLLRTNDDTPGNRTKCFVDLPIRNVNLAQSVAMITIGEVVGFITPLMIVLYCTWKTAL
SLQNKYPISQHLGEKKKALRMILTCAAVFLICFAPYHFSFPLDFLVKSNEIKSCLARRVILIFHSVALCL
ASLNSCLDPVIYYFTTNEFRRLSRQELPDSIQLQTKSYKIVNNHGASPTAAELC

FIG. 1D

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Compound	Reported Potency (uM)
◆ Propantheline	0.2
○ Atropine	0.5
■ Scopolamine	1.0
● Pirenzepine	5.0
□ HHSID	16.0
◇ Himbacine	60 - 120
▲ Vehicle	

FIG. 2

GPCR Signaling Profile Algorithm

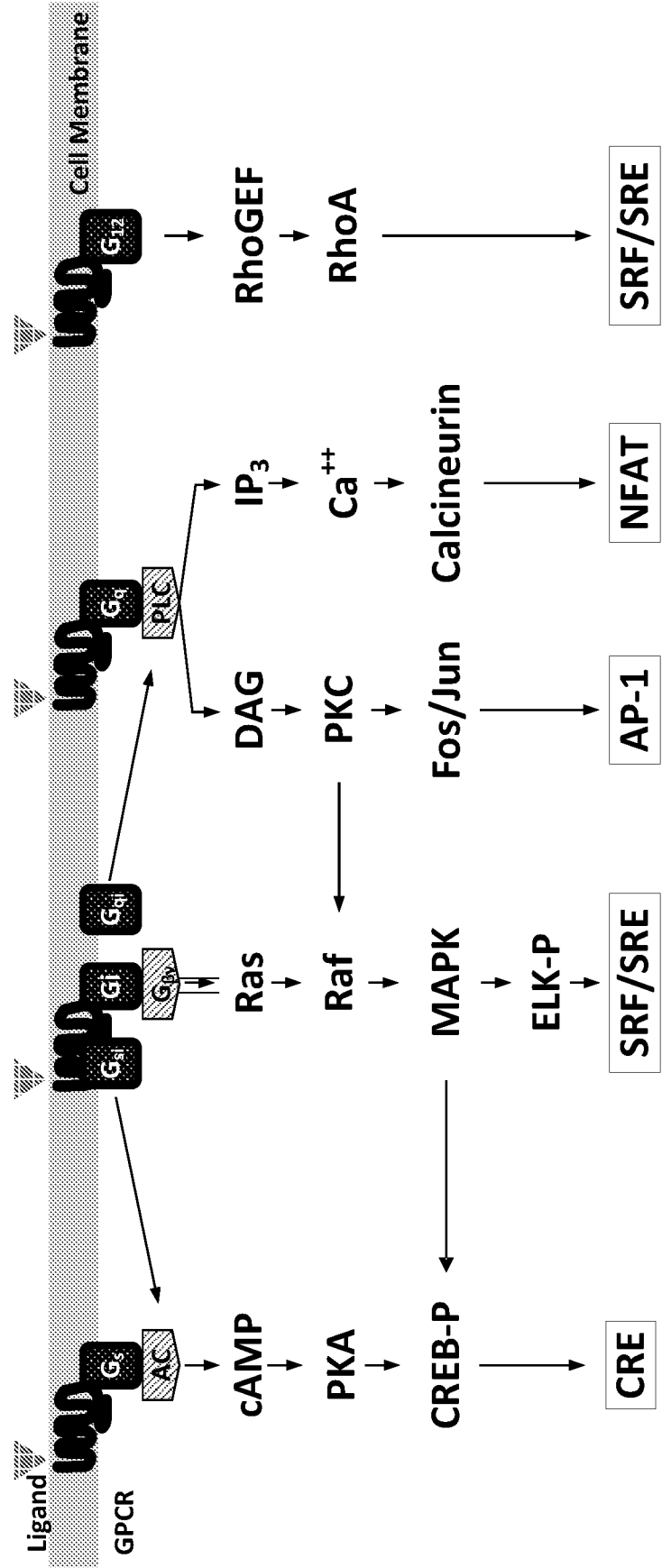


FIG. 3

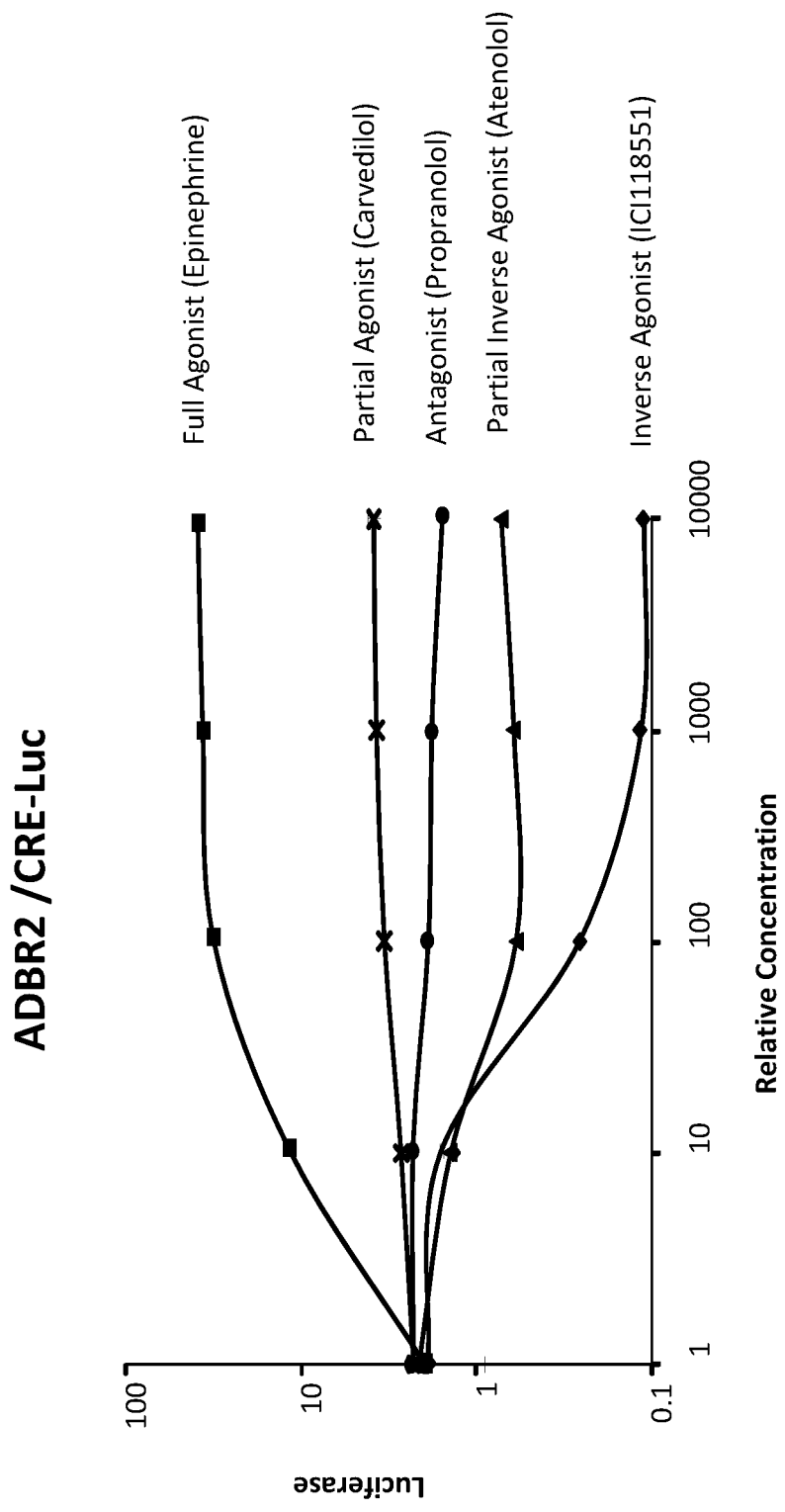


FIG. 4A

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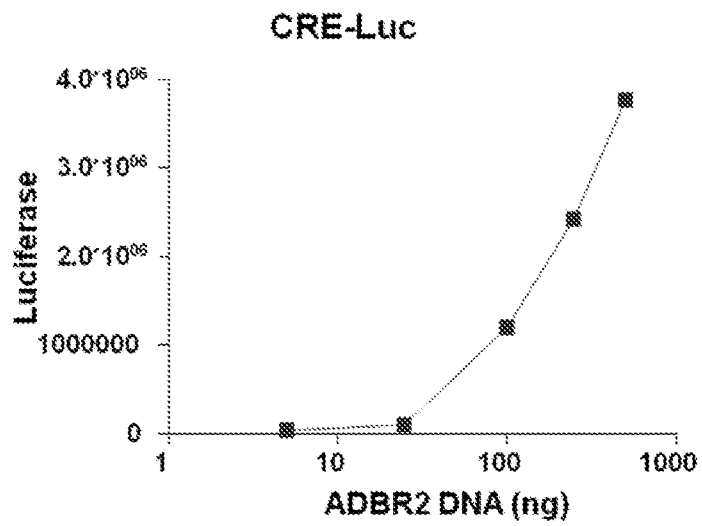


FIG. 4B

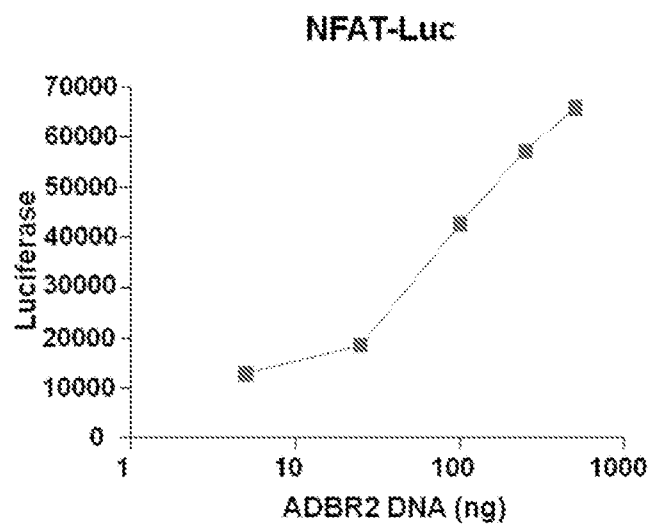


FIG. 4C

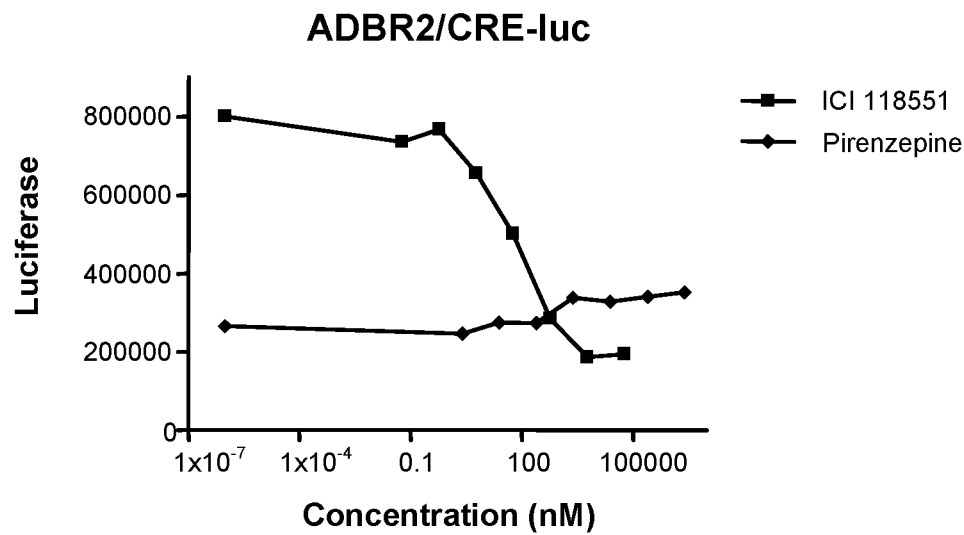


FIG. 4D

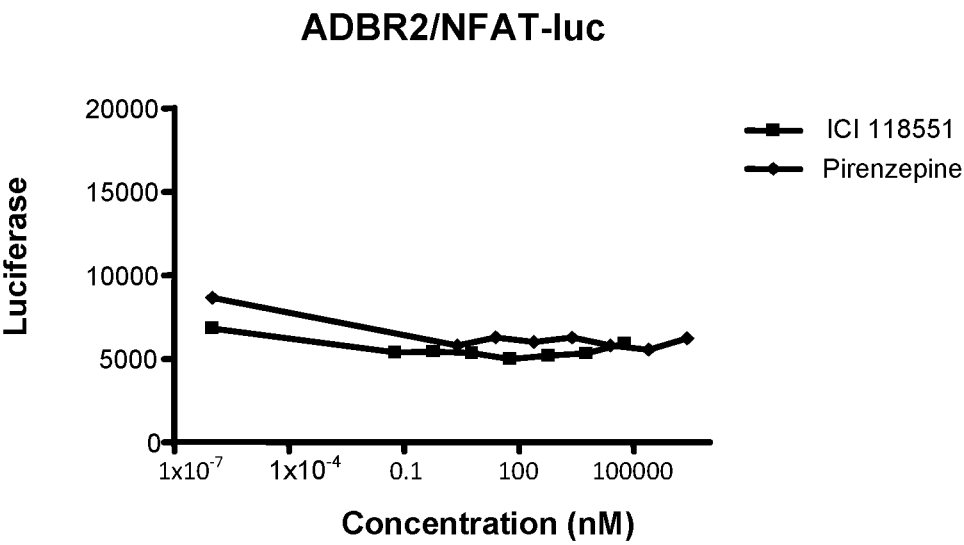


FIG. 4E

CRA Assay Results of Representative GPR174 interacting compounds

Compounds Against GPR174

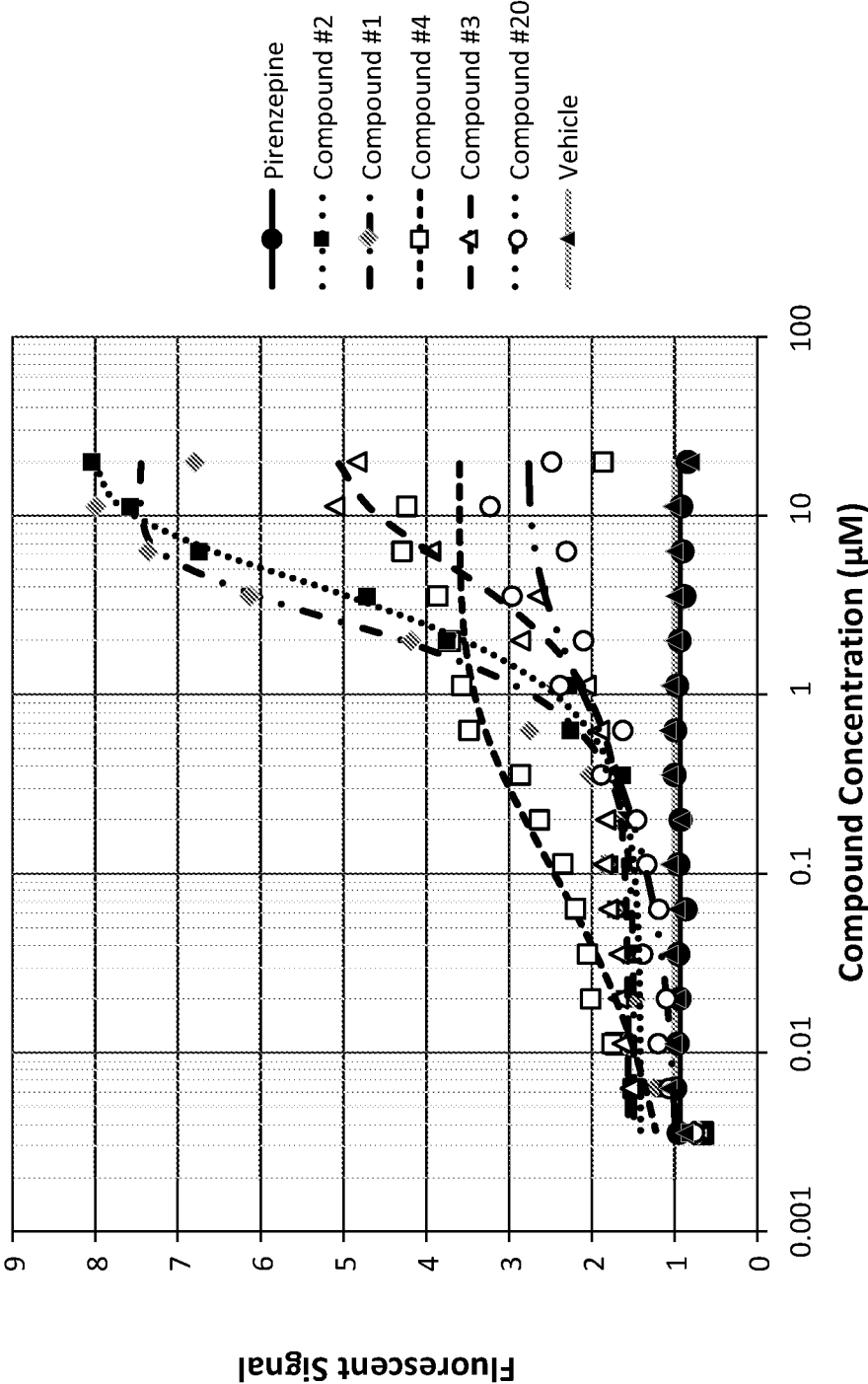


FIG. 5A

CRA Assay Results of Representative GPR174 interacting compounds

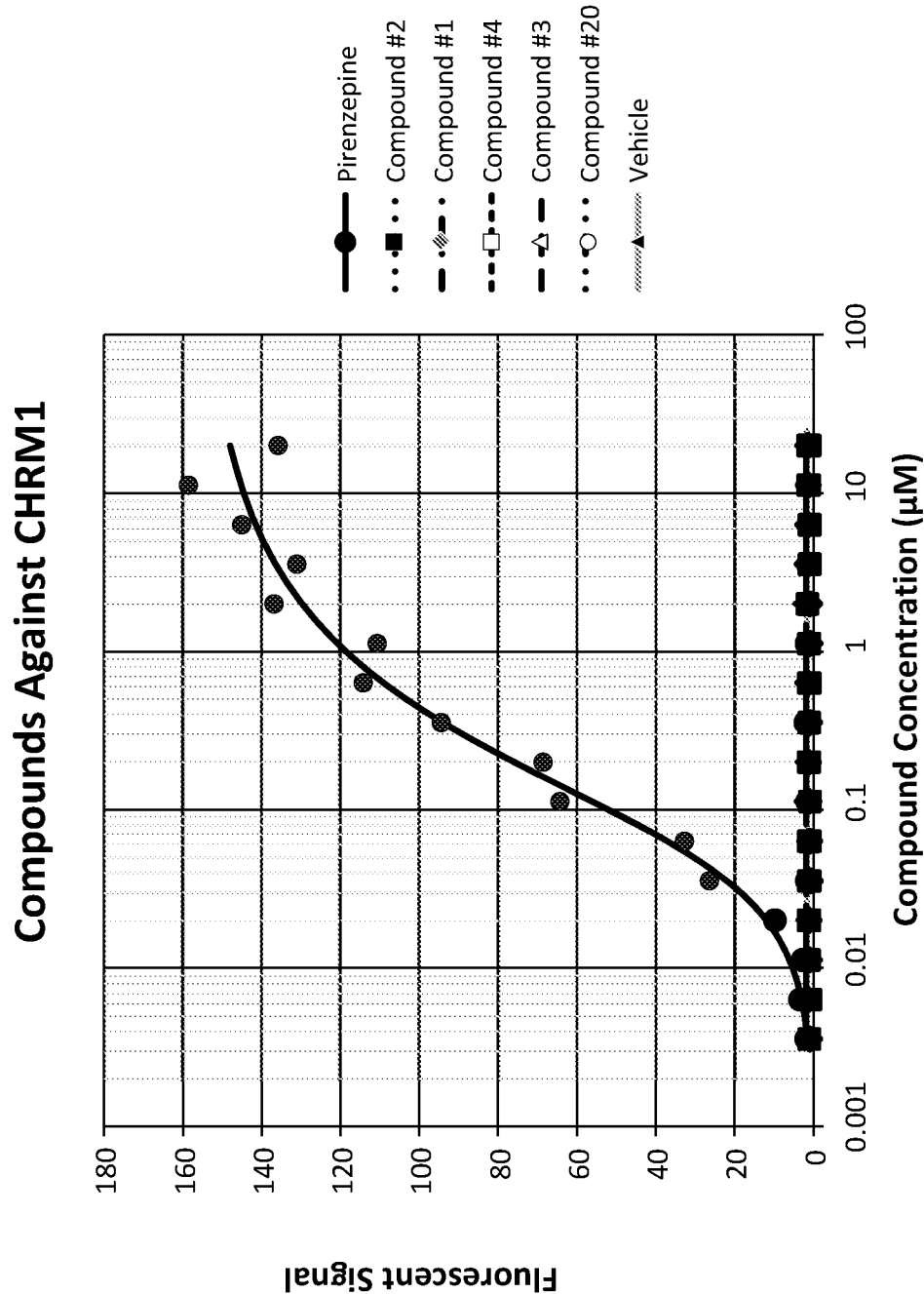


FIG. 5B

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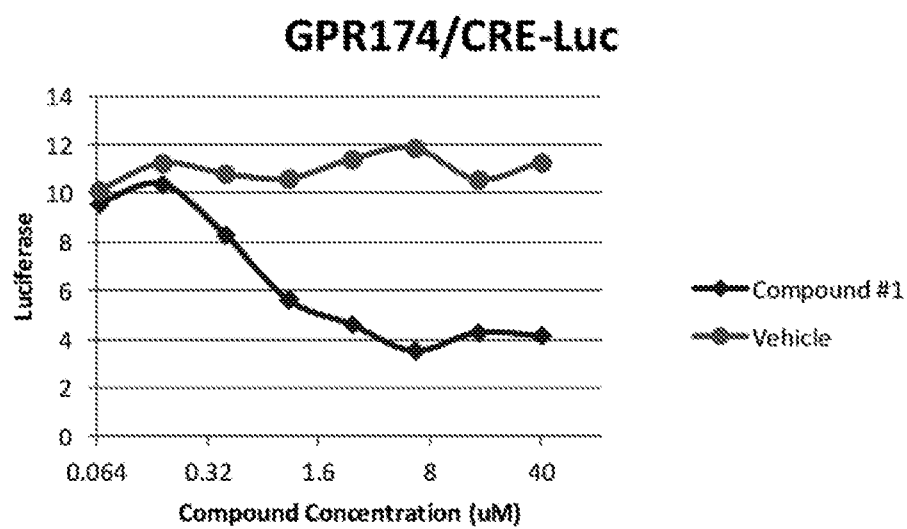


FIG. 6A

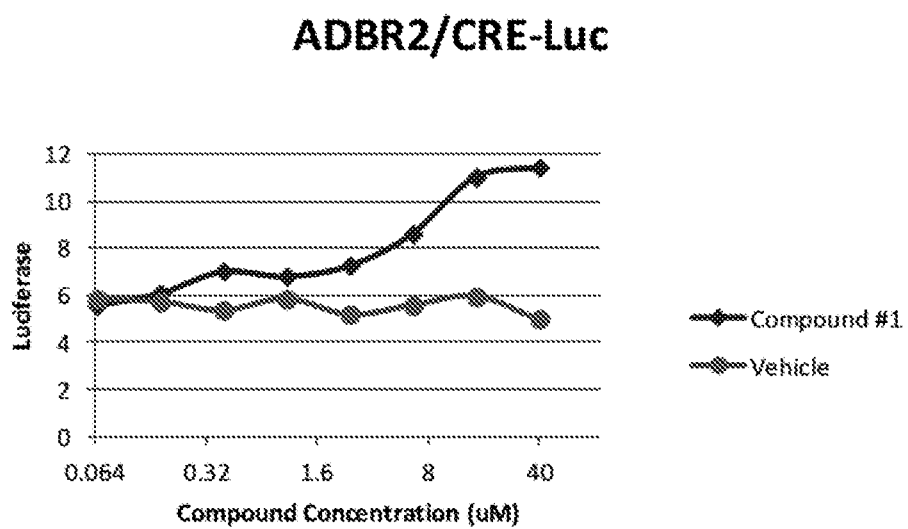


FIG. 6B

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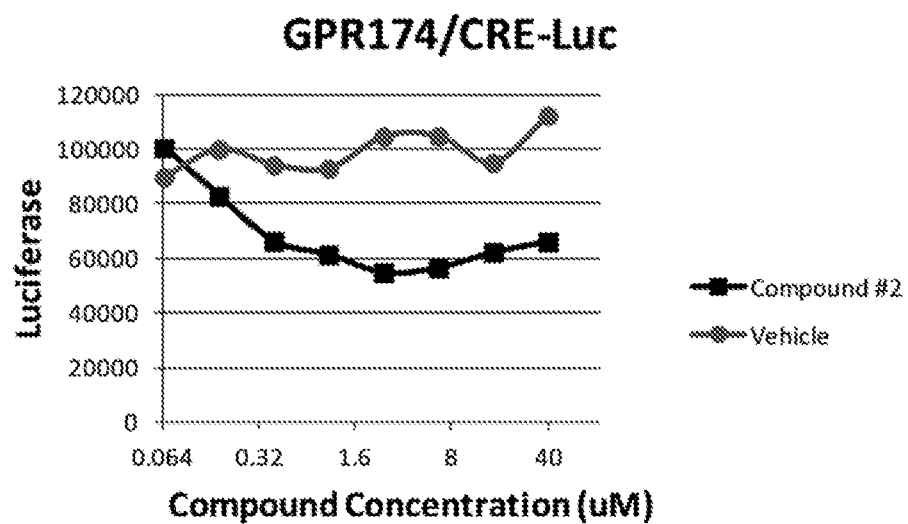


FIG. 7A

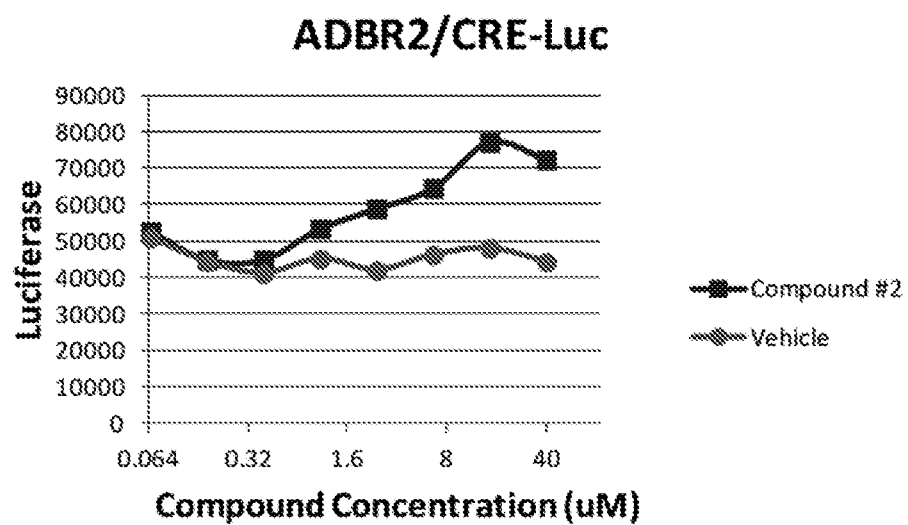


FIG. 7B

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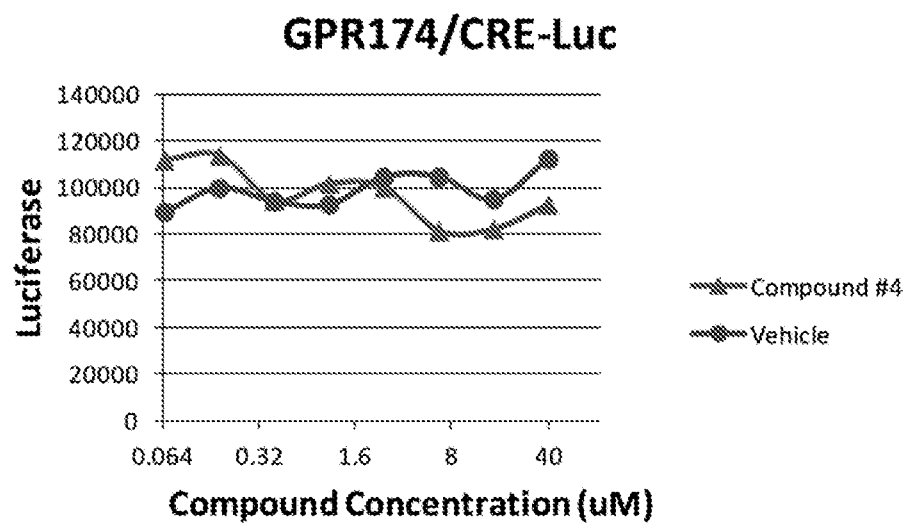


FIG. 8A

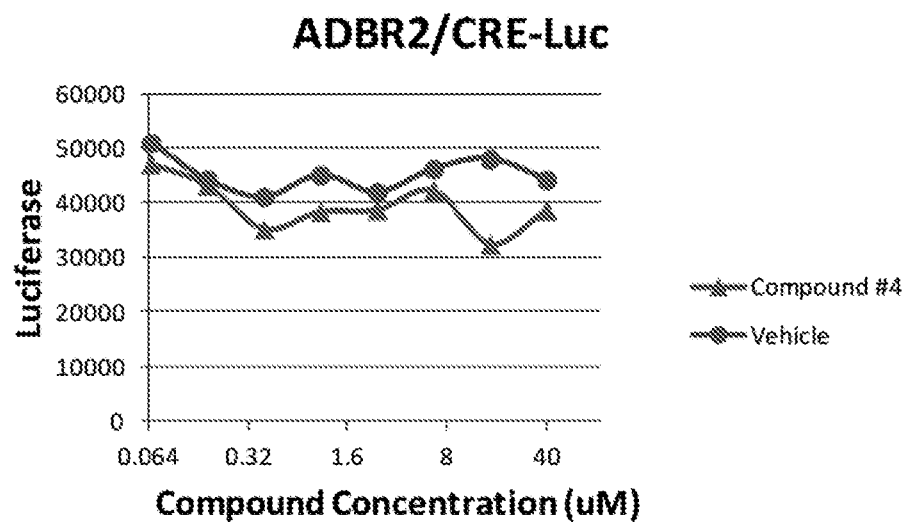


FIG. 8B

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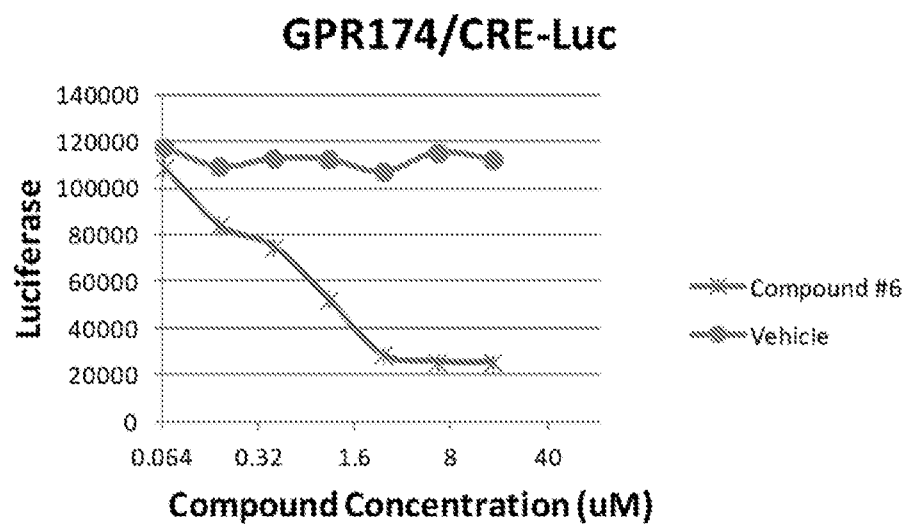


FIG. 9A

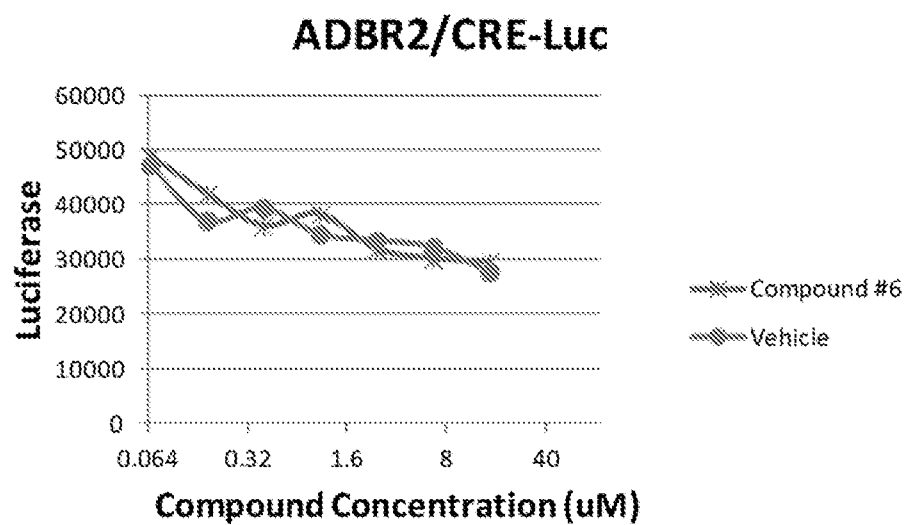


FIG. 9B

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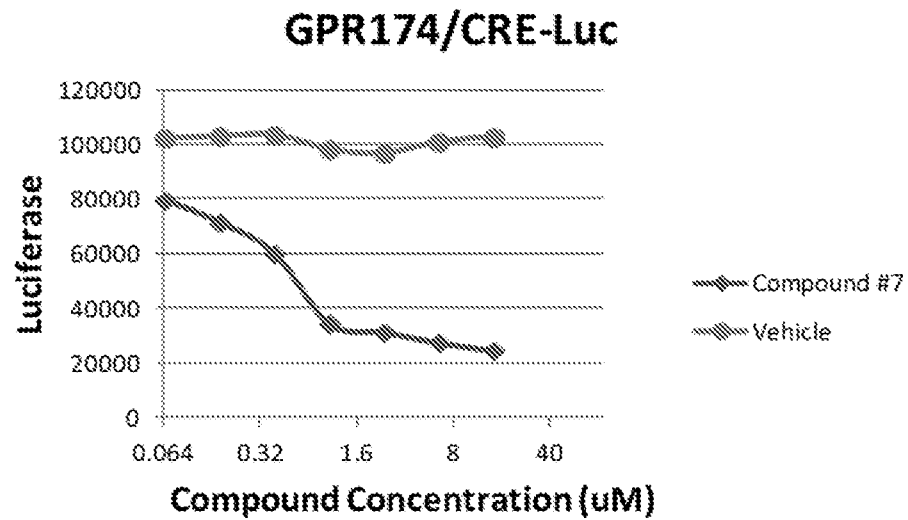


FIG. 10A

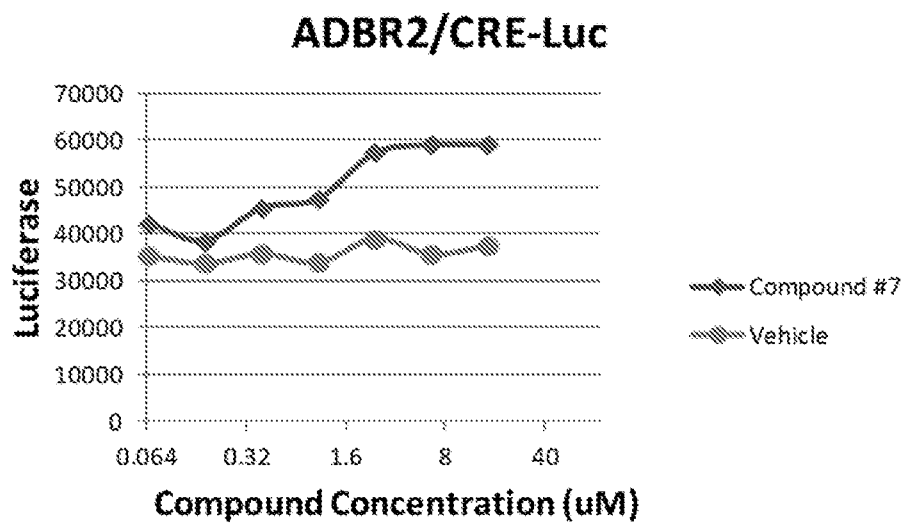


FIG. 10B

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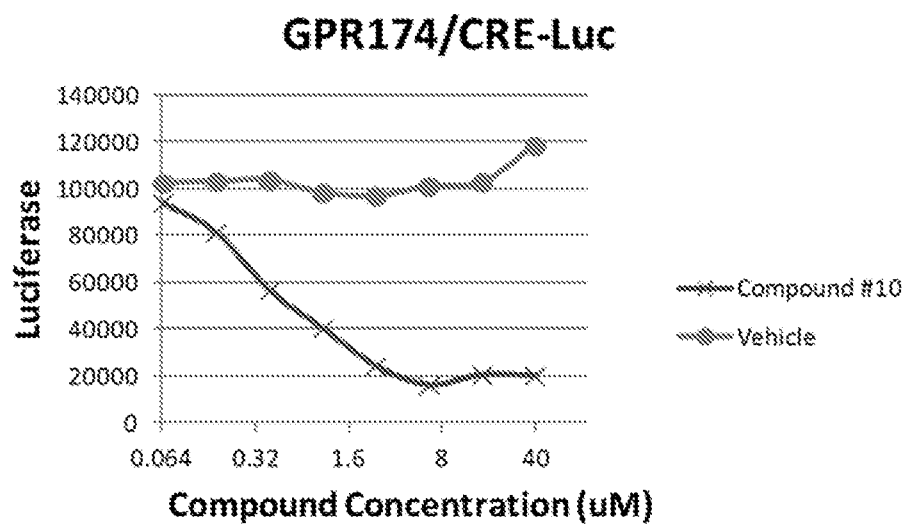


FIG. 11A

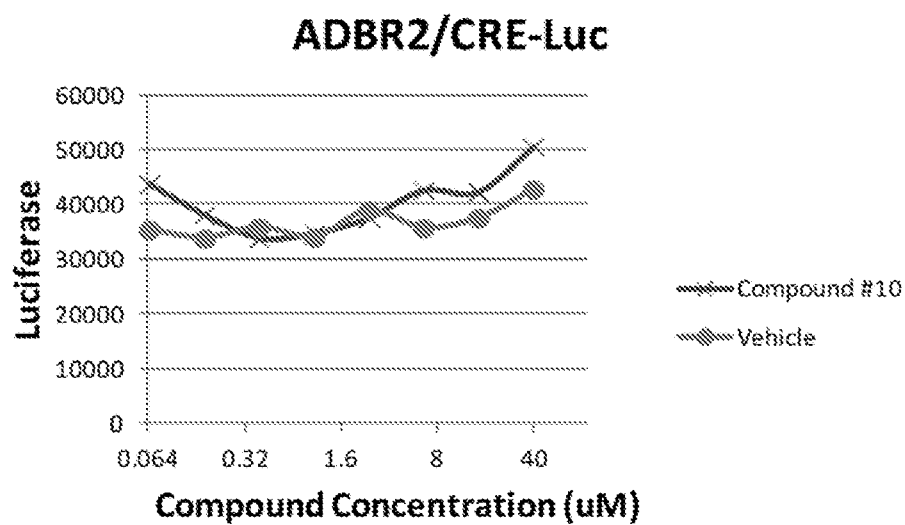


FIG. 11B

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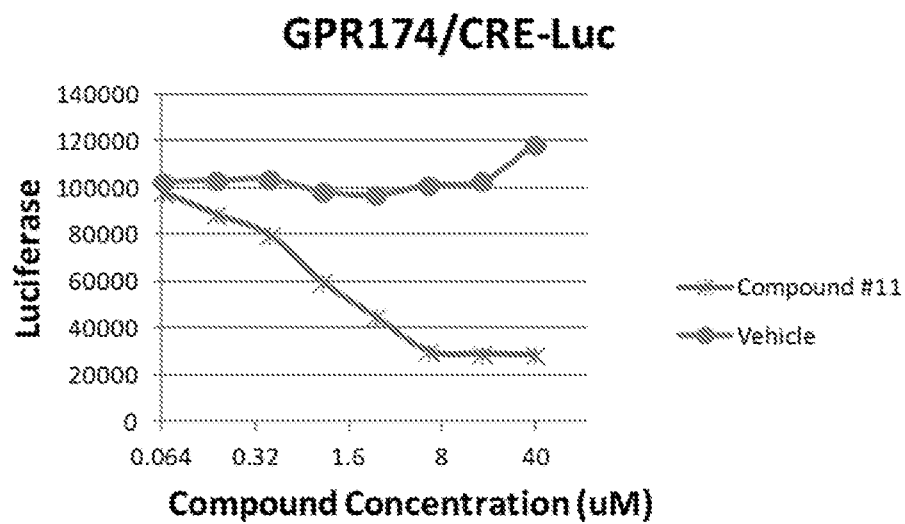


FIG. 12A

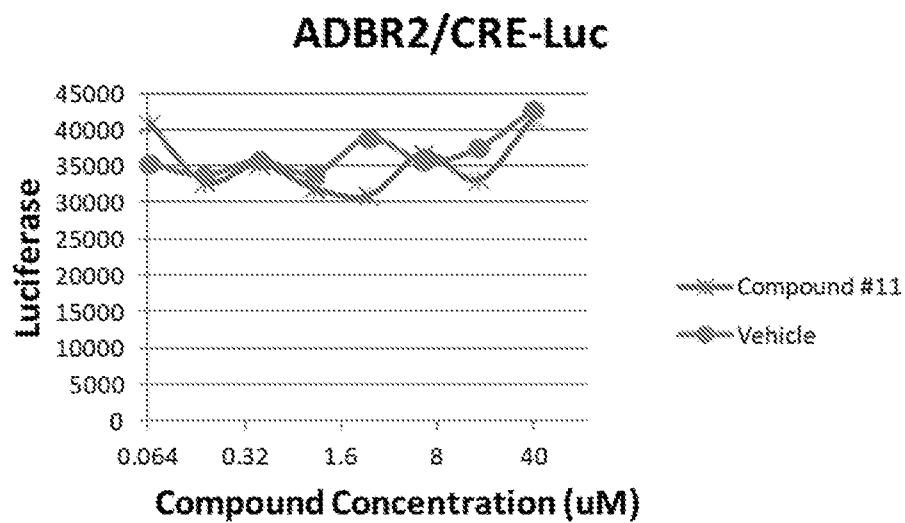


FIG. 12B

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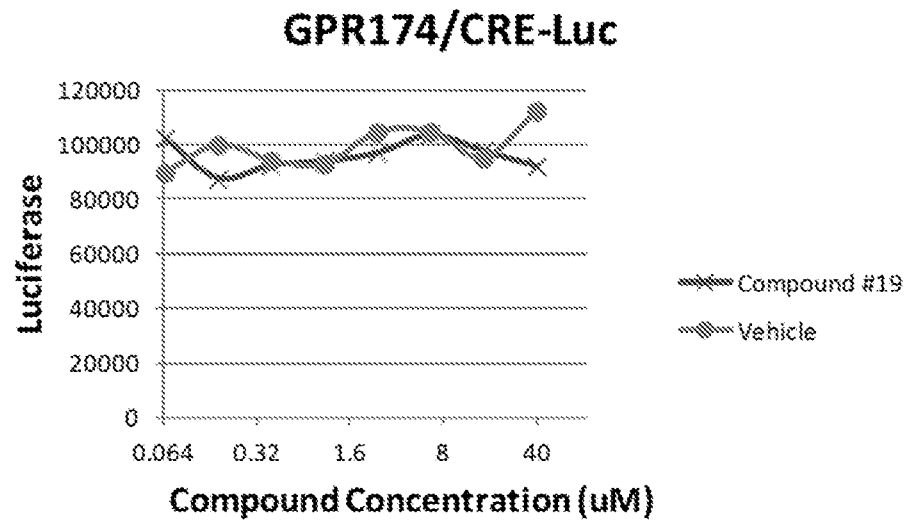


FIG. 13A

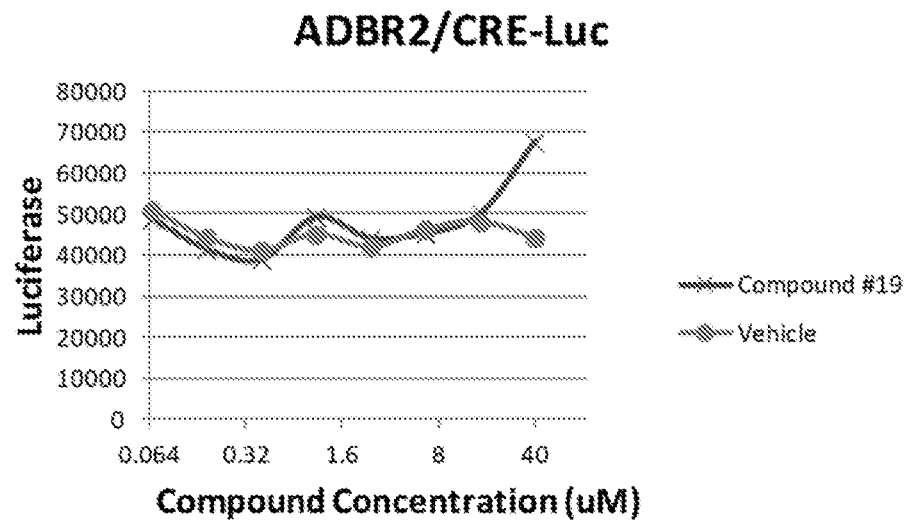


FIG. 13B

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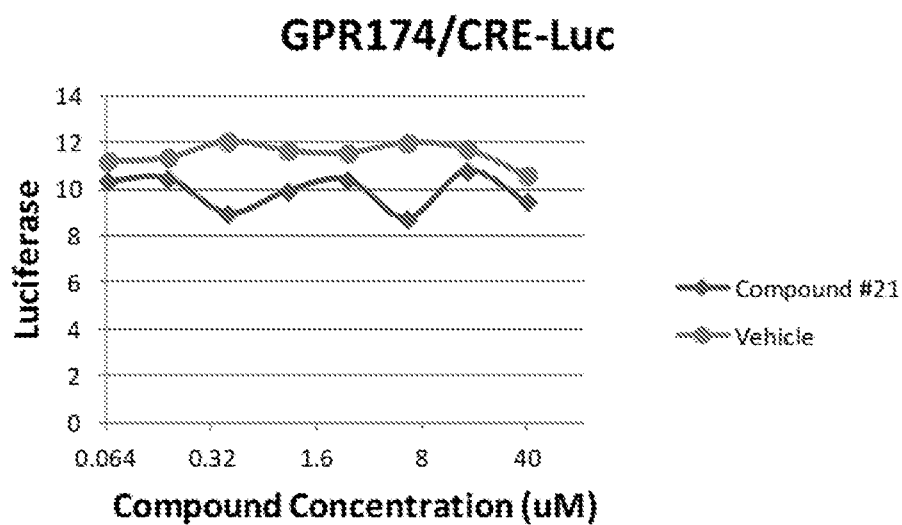


FIG. 14A

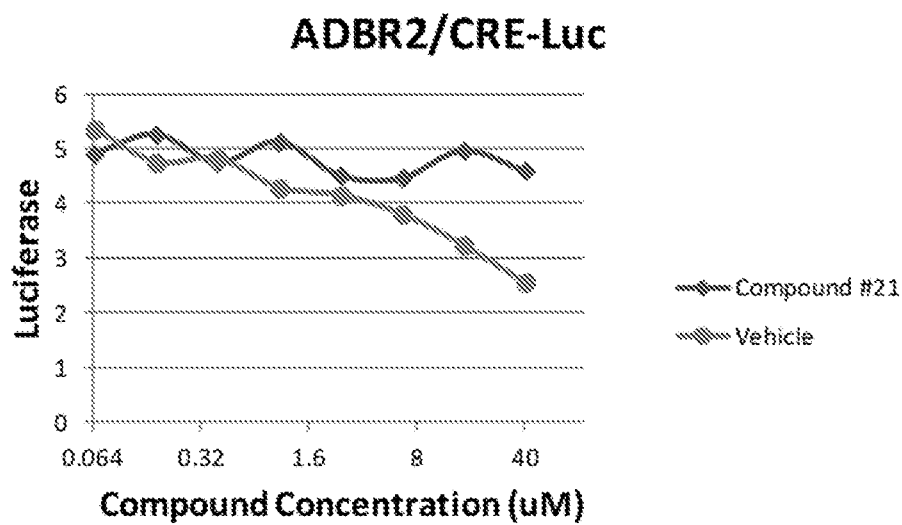


FIG. 14B

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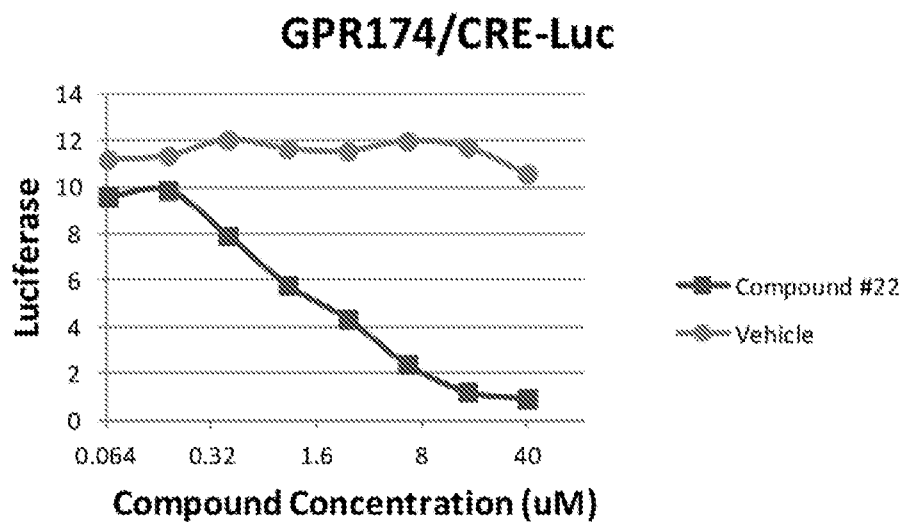


FIG. 15A

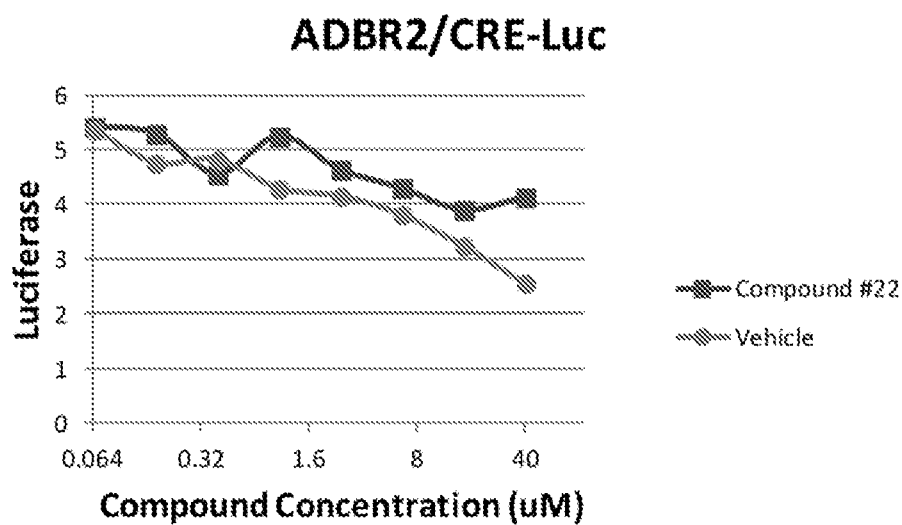


FIG. 15B

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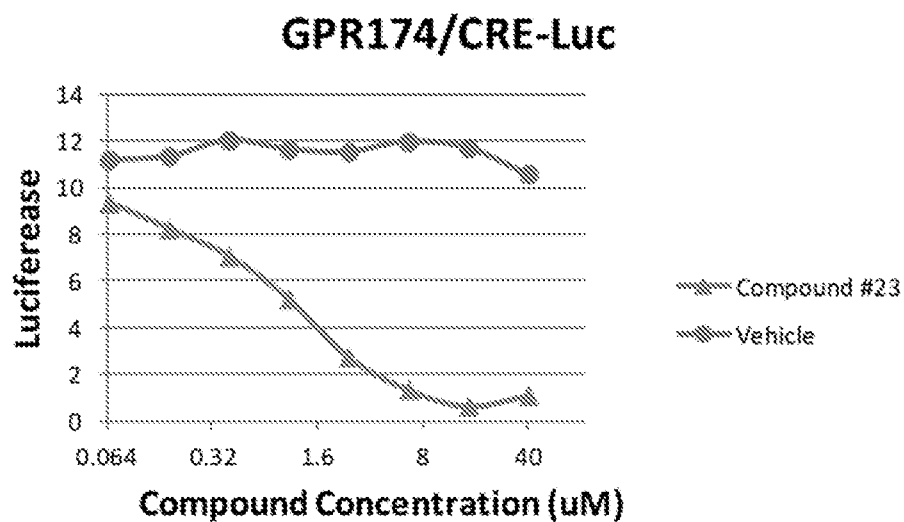


FIG. 16A

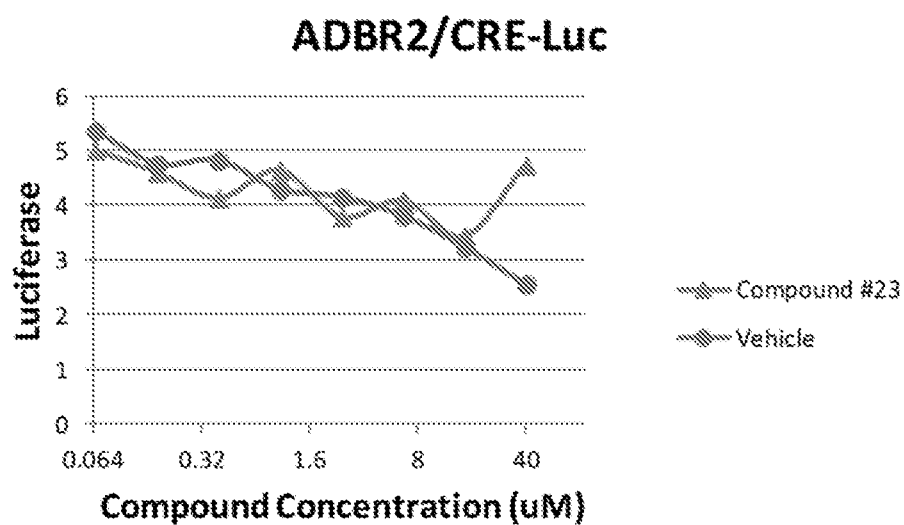


FIG. 16B

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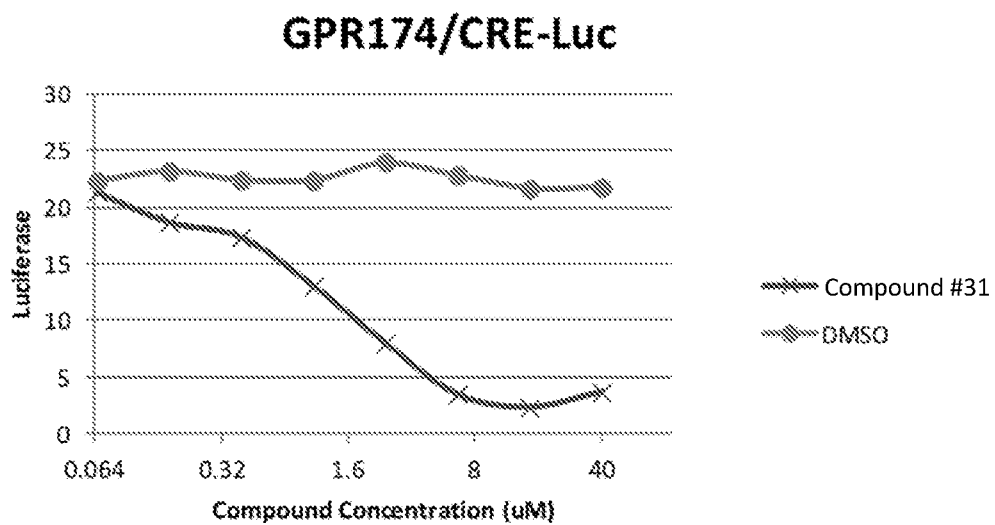


FIG. 17A

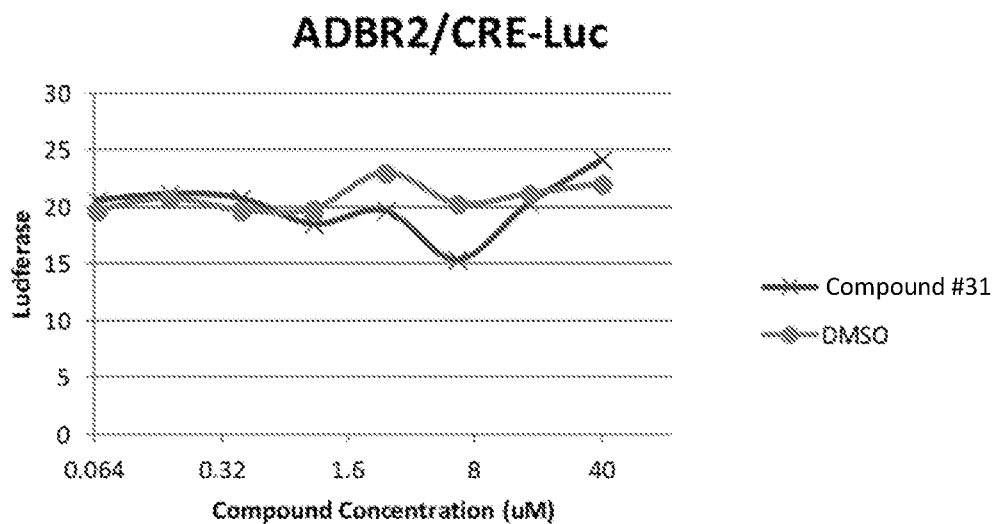


FIG. 17B

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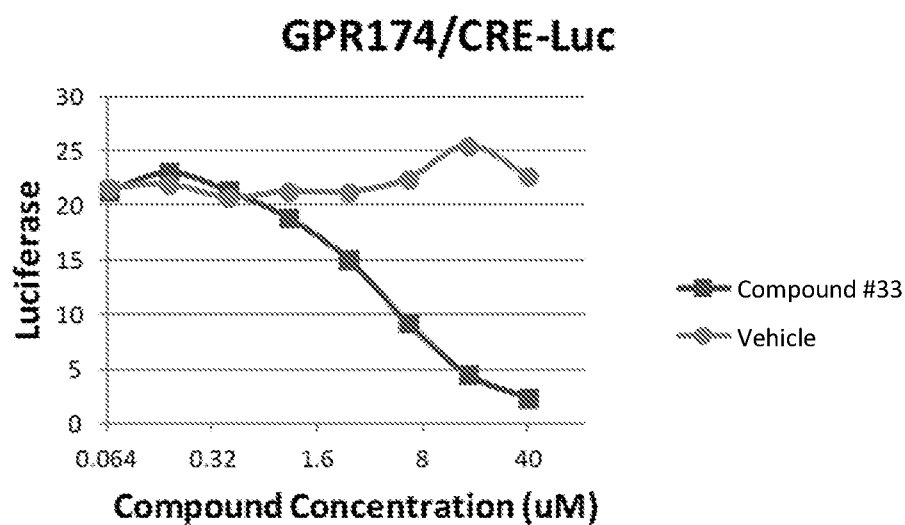


FIG. 18A

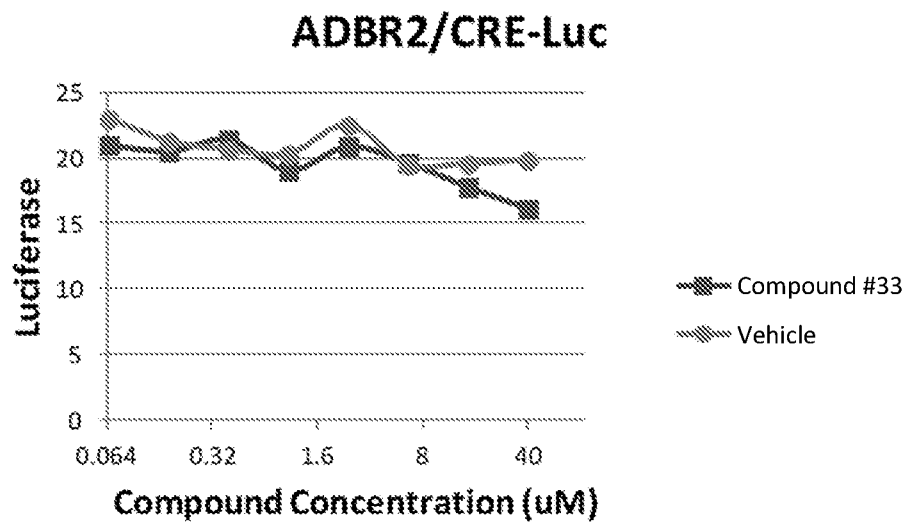


FIG. 18B

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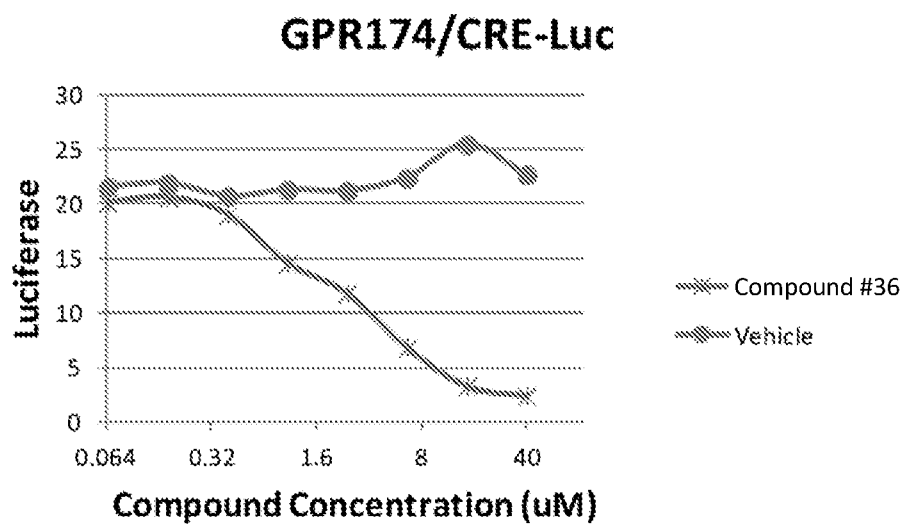


FIG. 19A

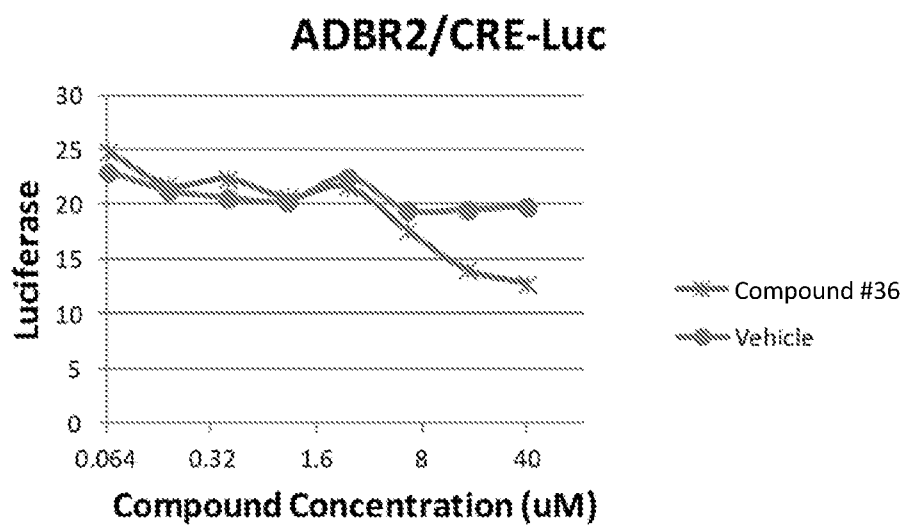


FIG. 19B

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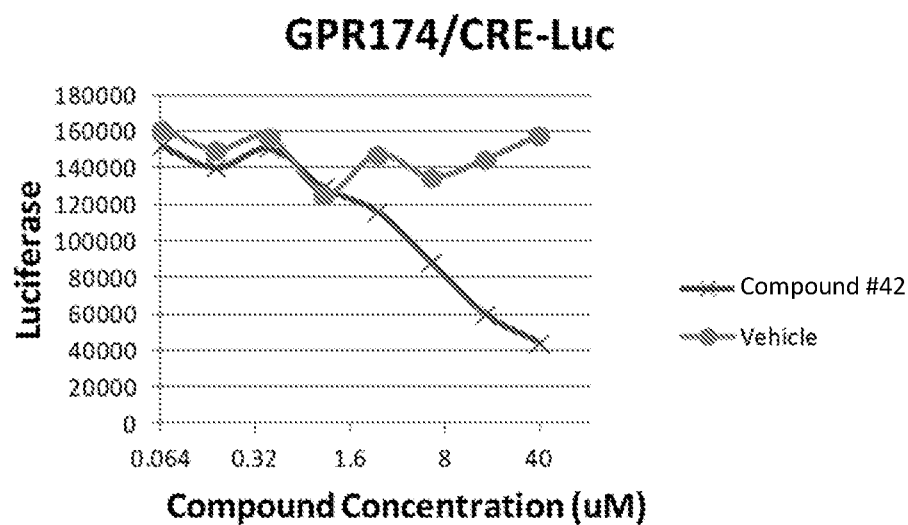


FIG. 20A

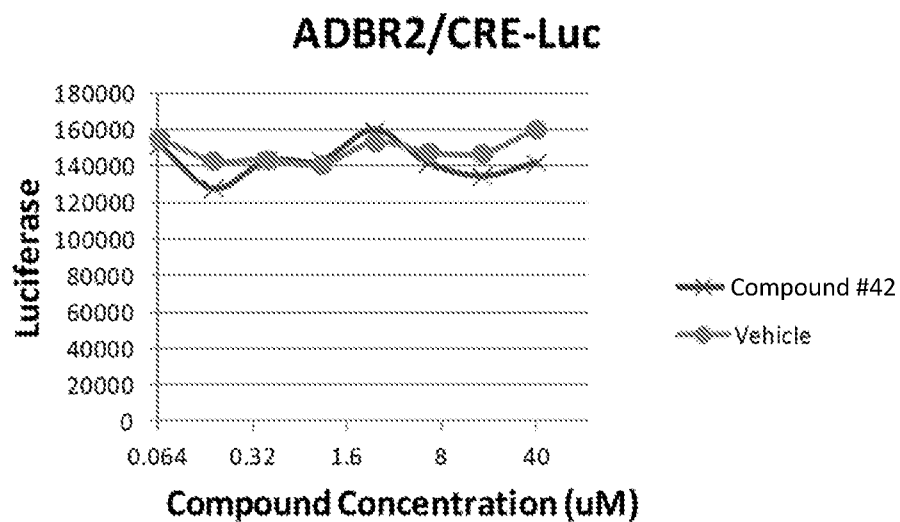


FIG. 20B

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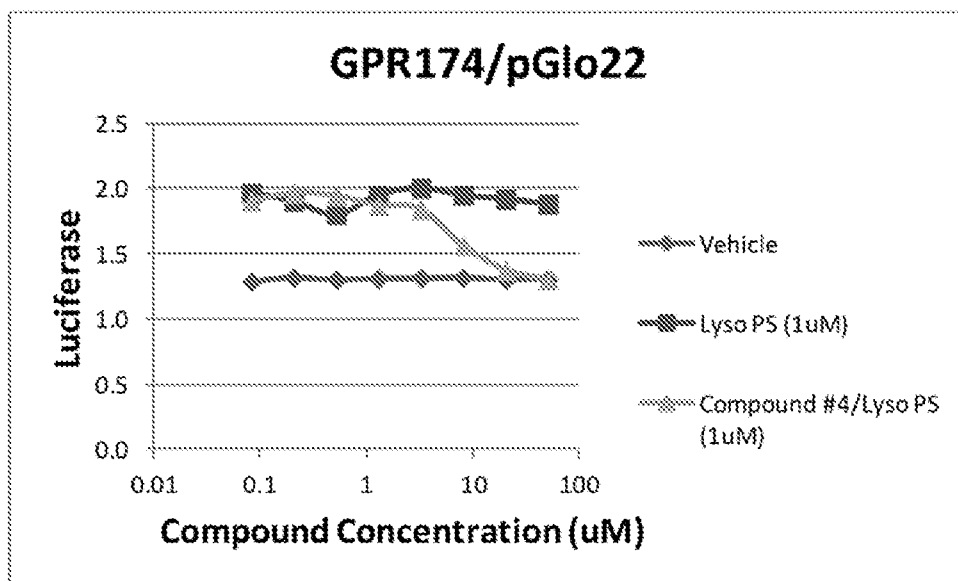


FIG. 21A

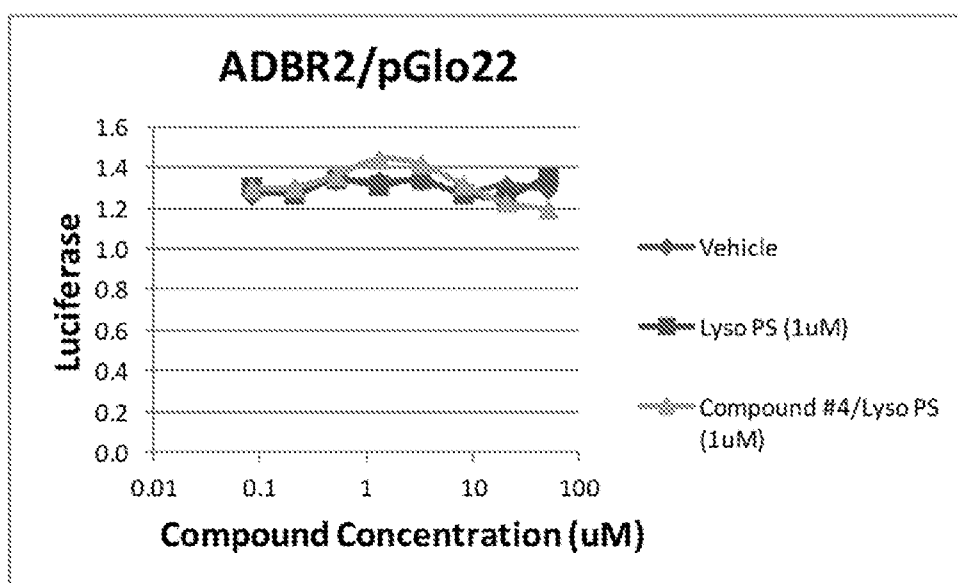


FIG. 21B

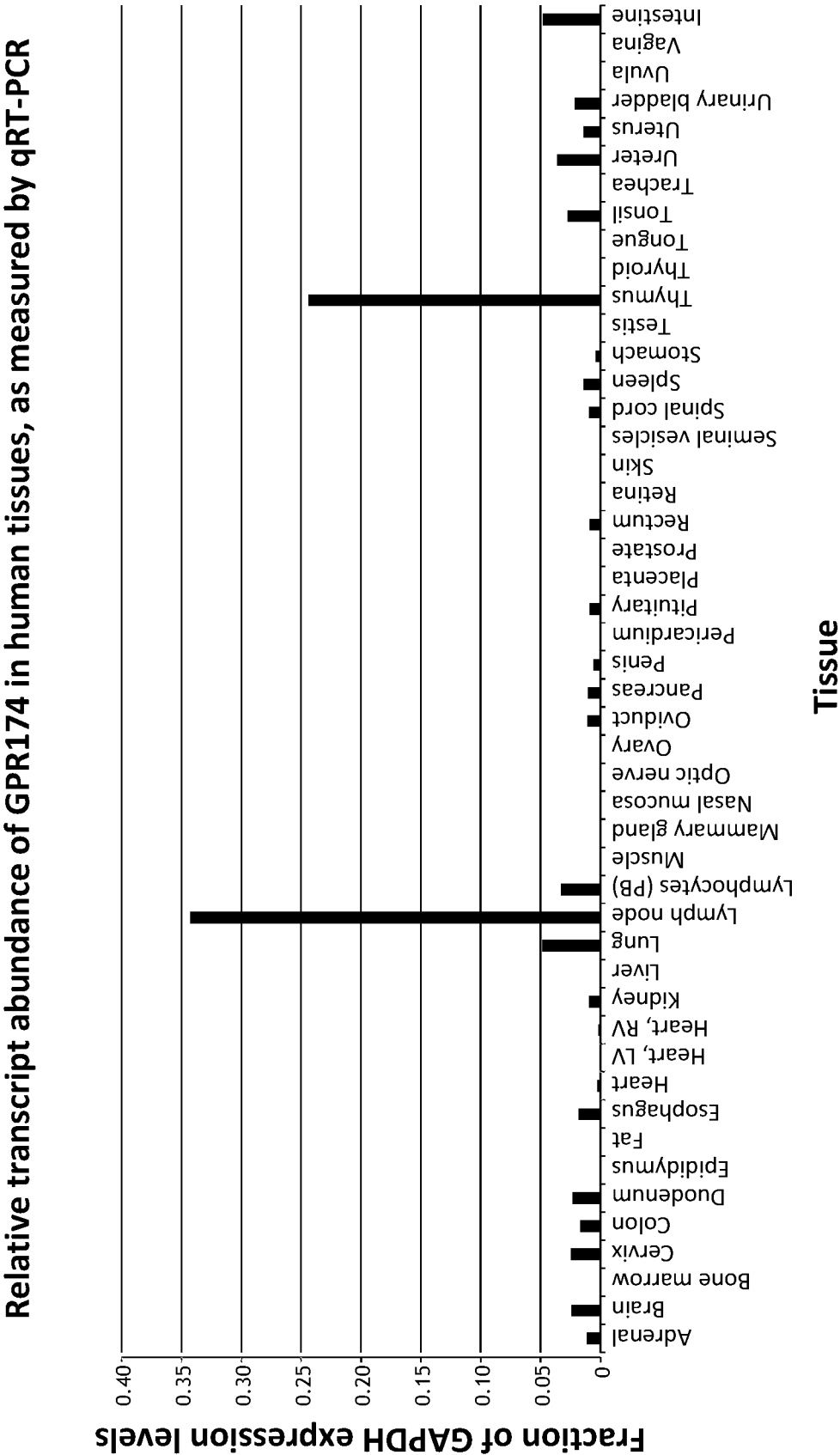


FIG. 22

Relative transcript abundance of GPR174 in human lymphoid cells, as measured by qRT-PCR

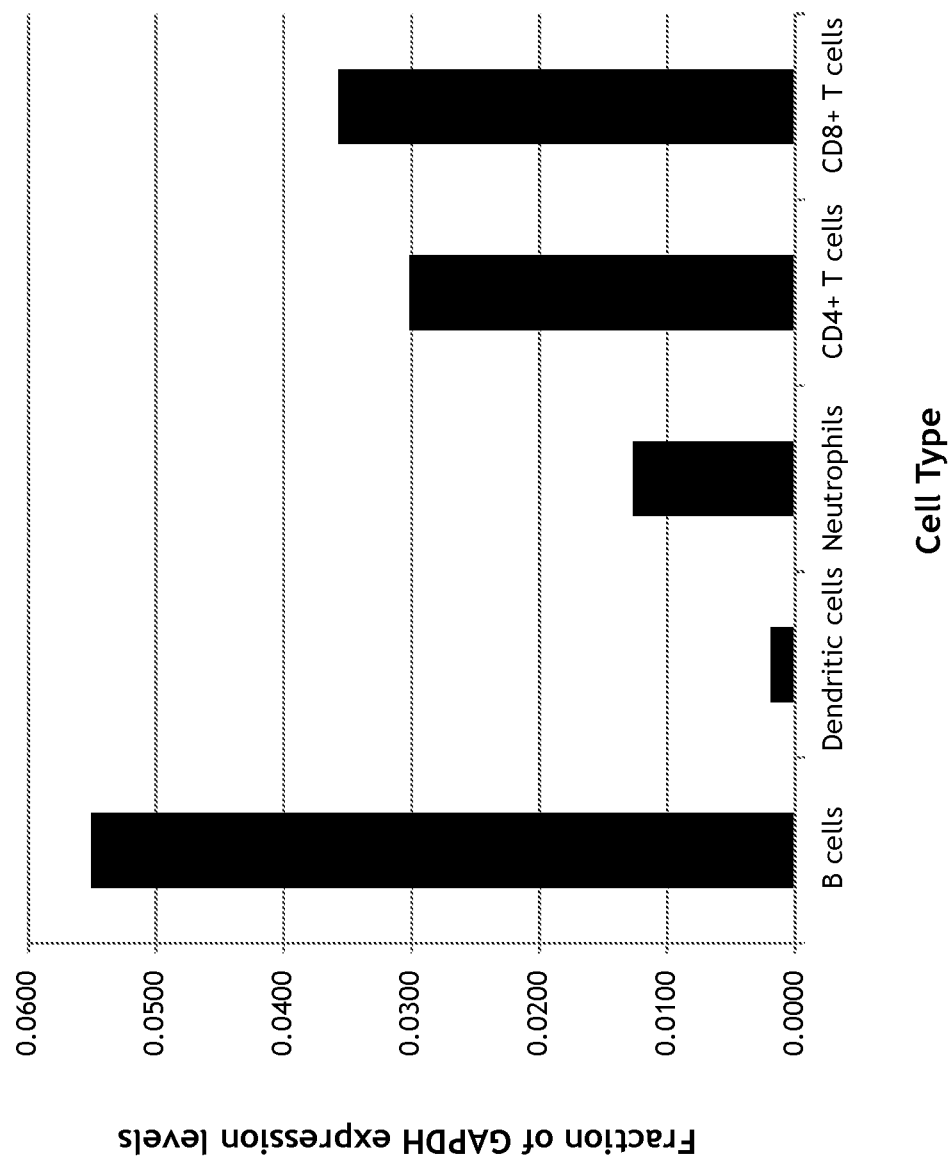


FIG. 23

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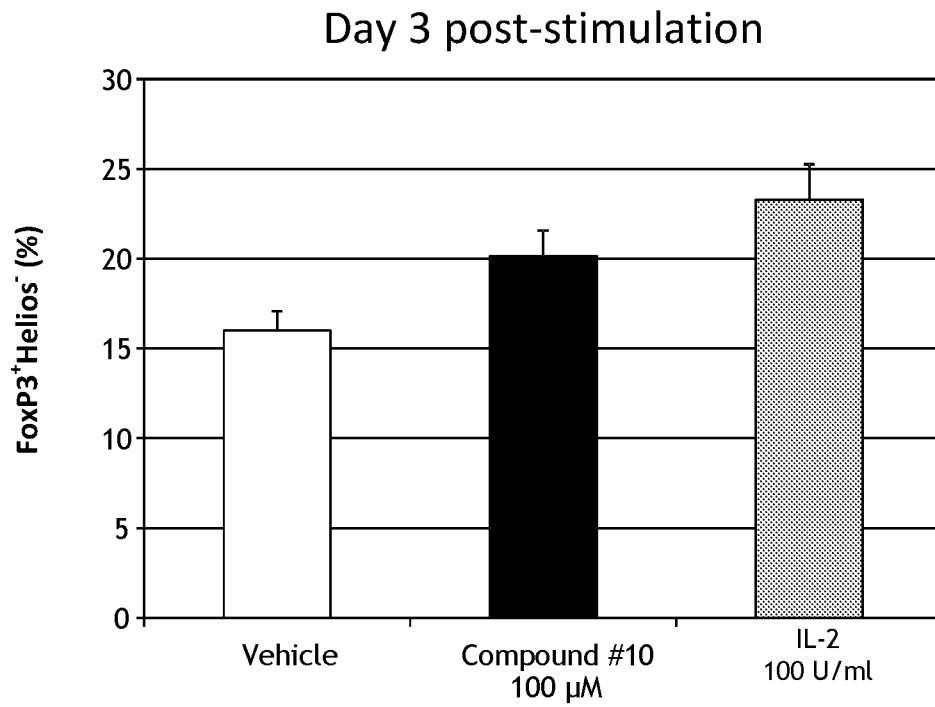


FIG. 24A

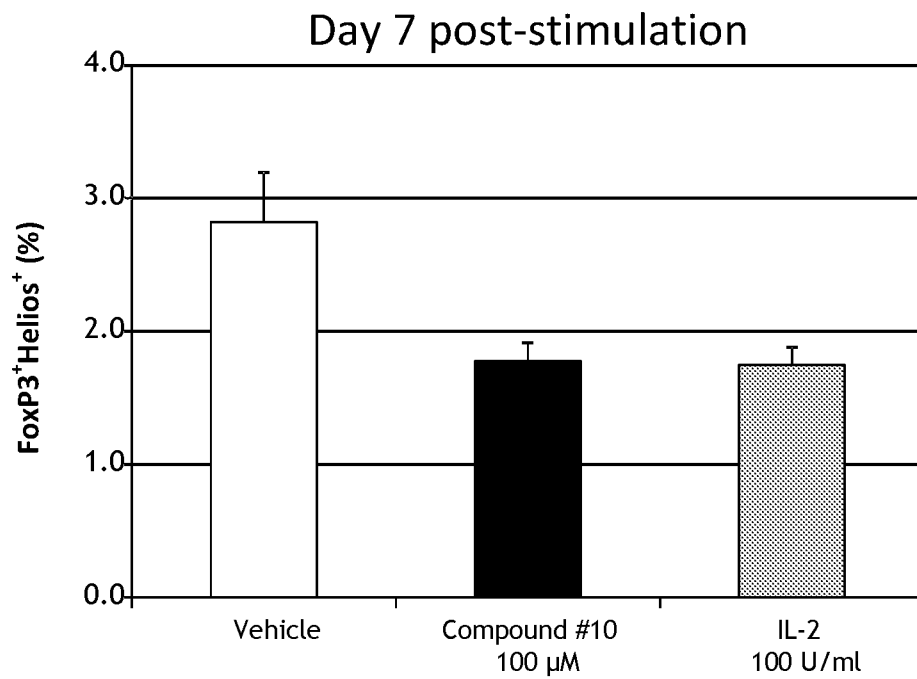


FIG. 24B

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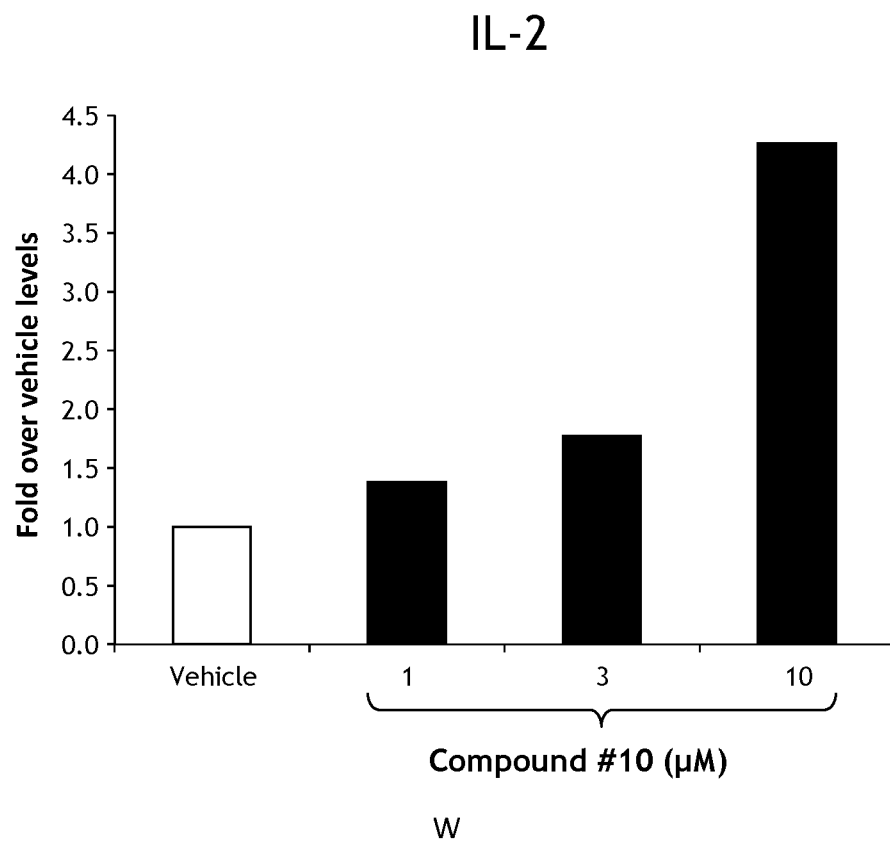


FIG. 25

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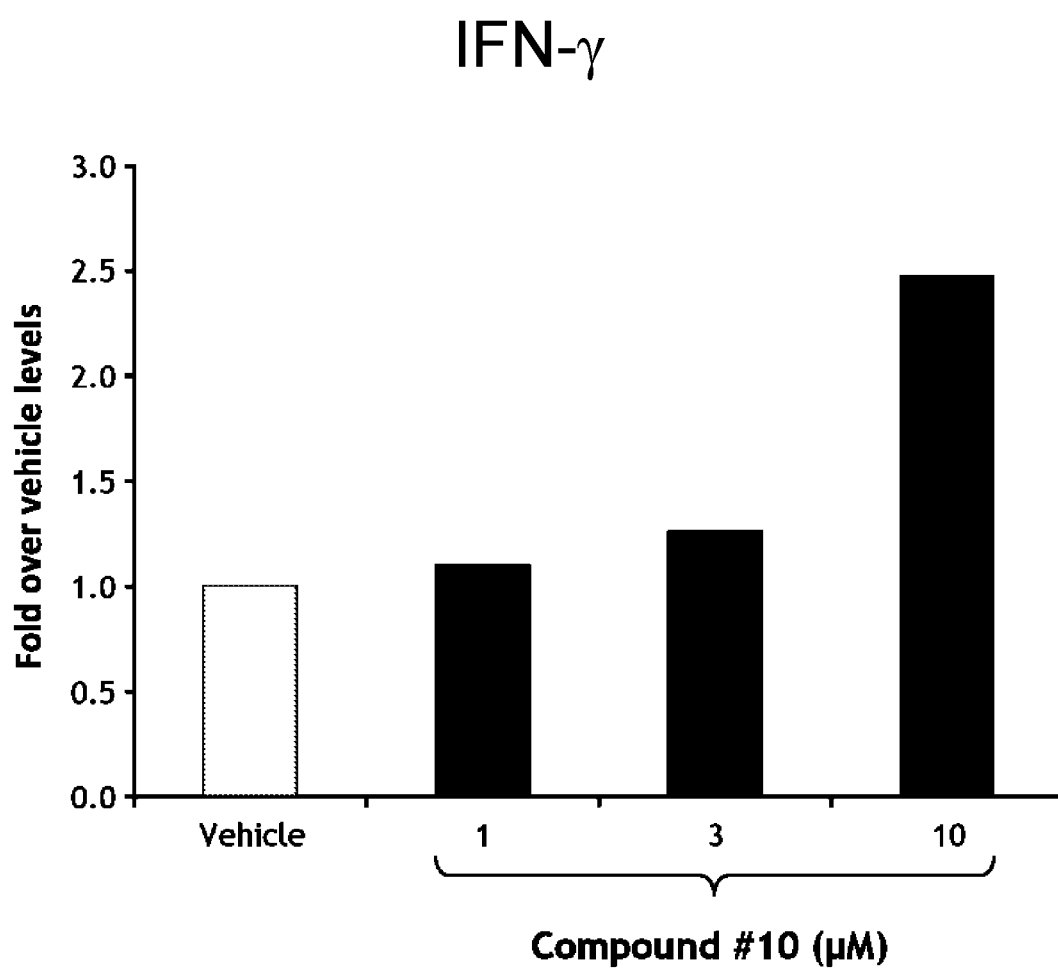


FIG. 26

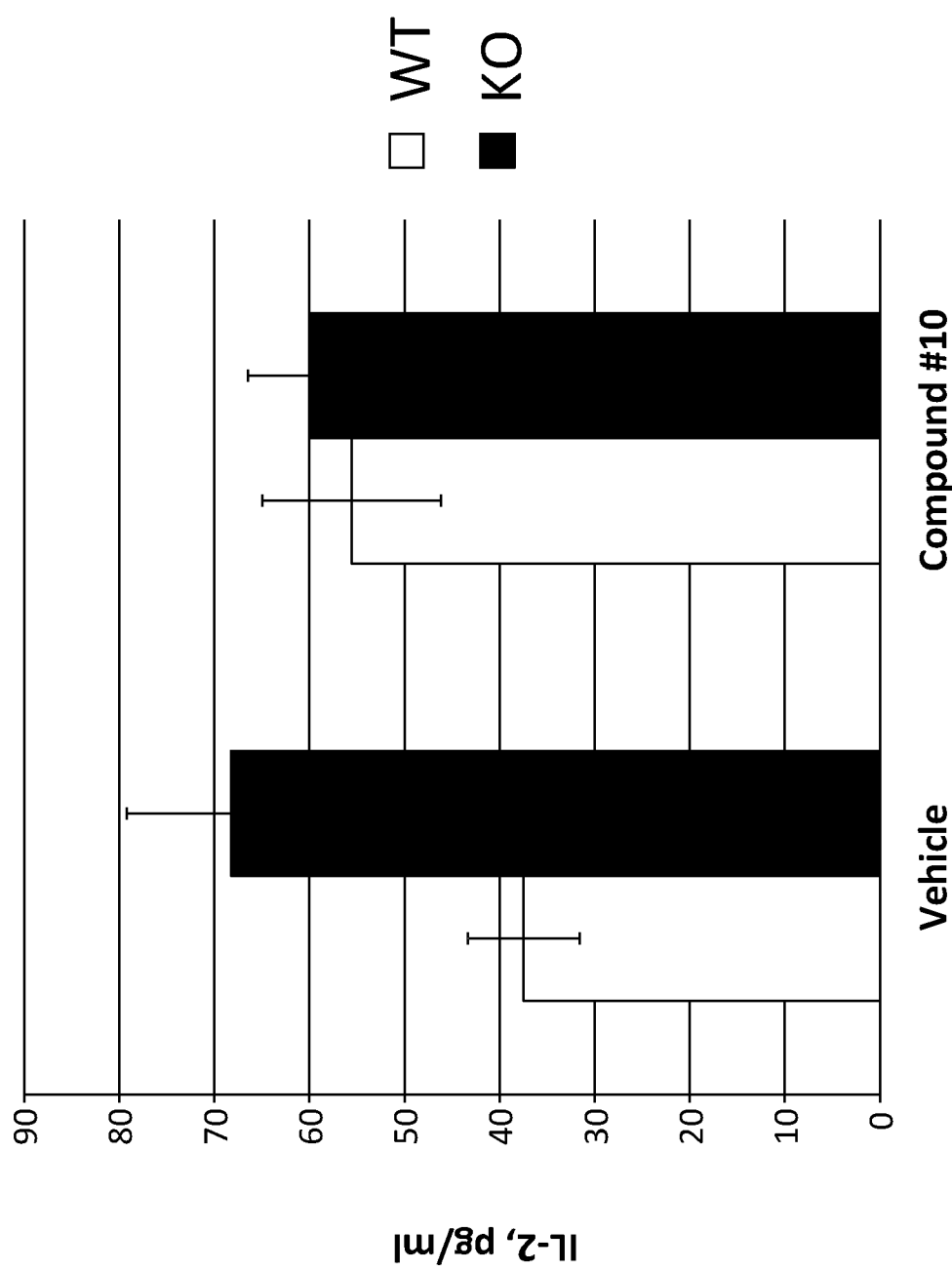


FIG. 27

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Human Treg Cells (Day 7 post-stimulation)

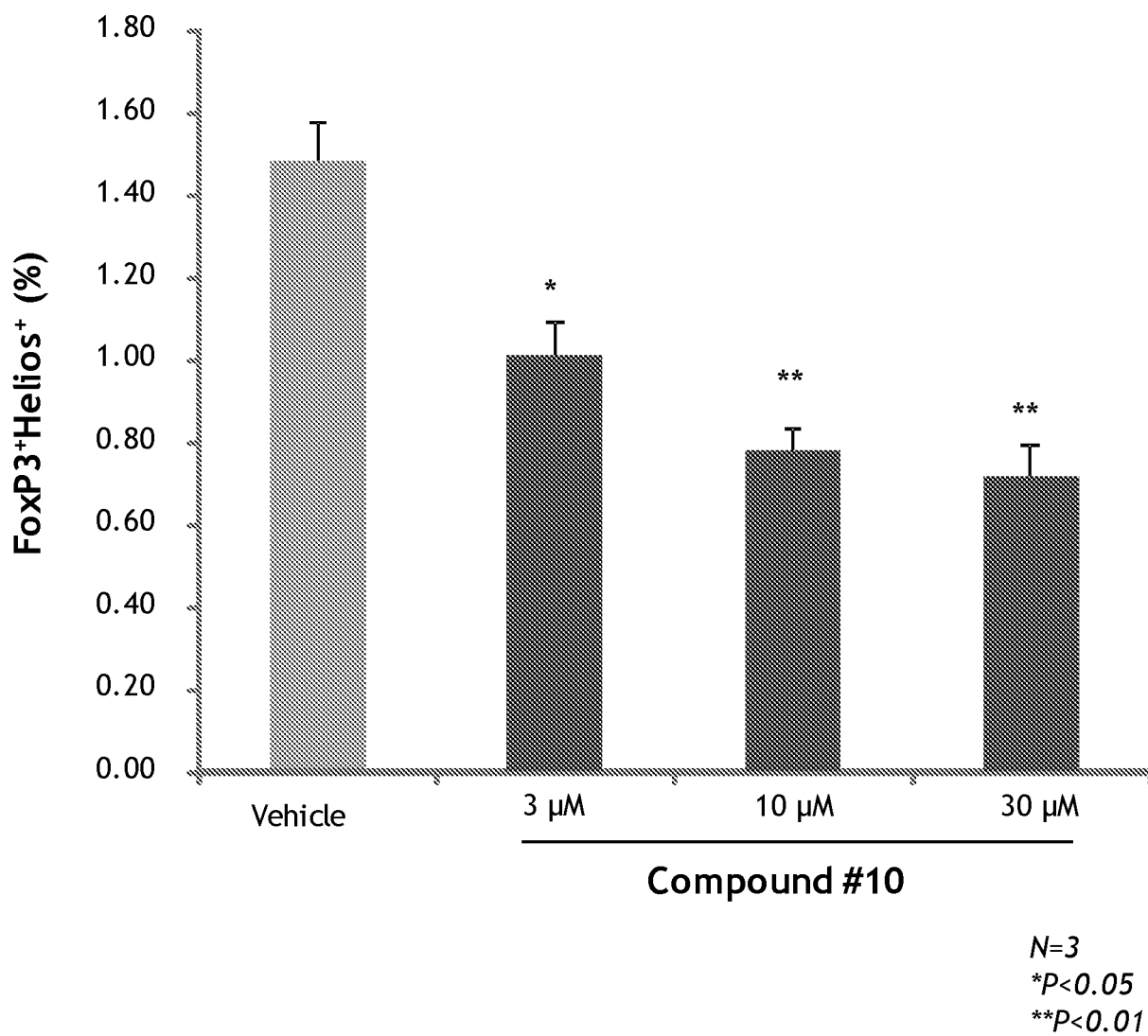


FIG. 28

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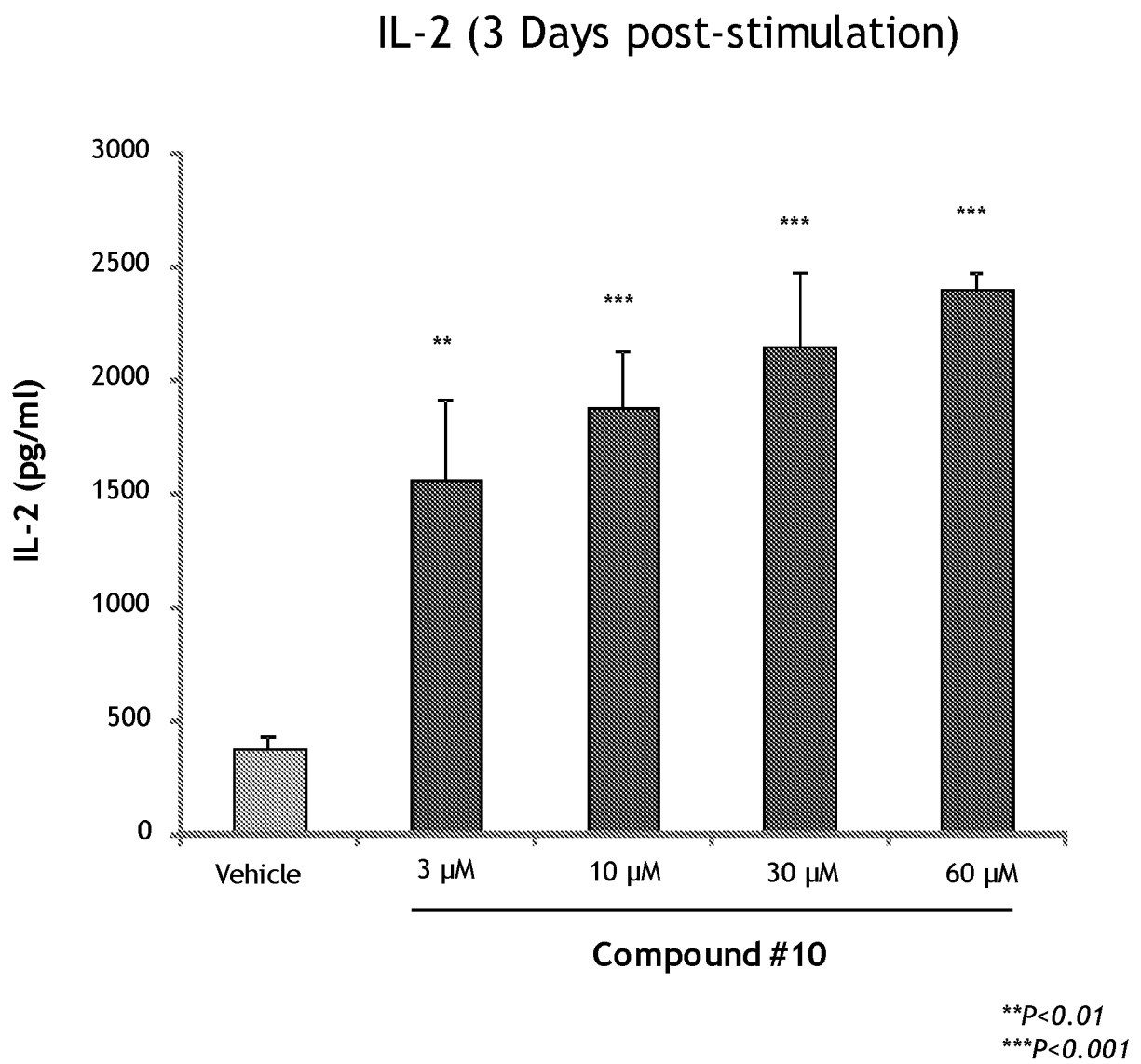


FIG. 29

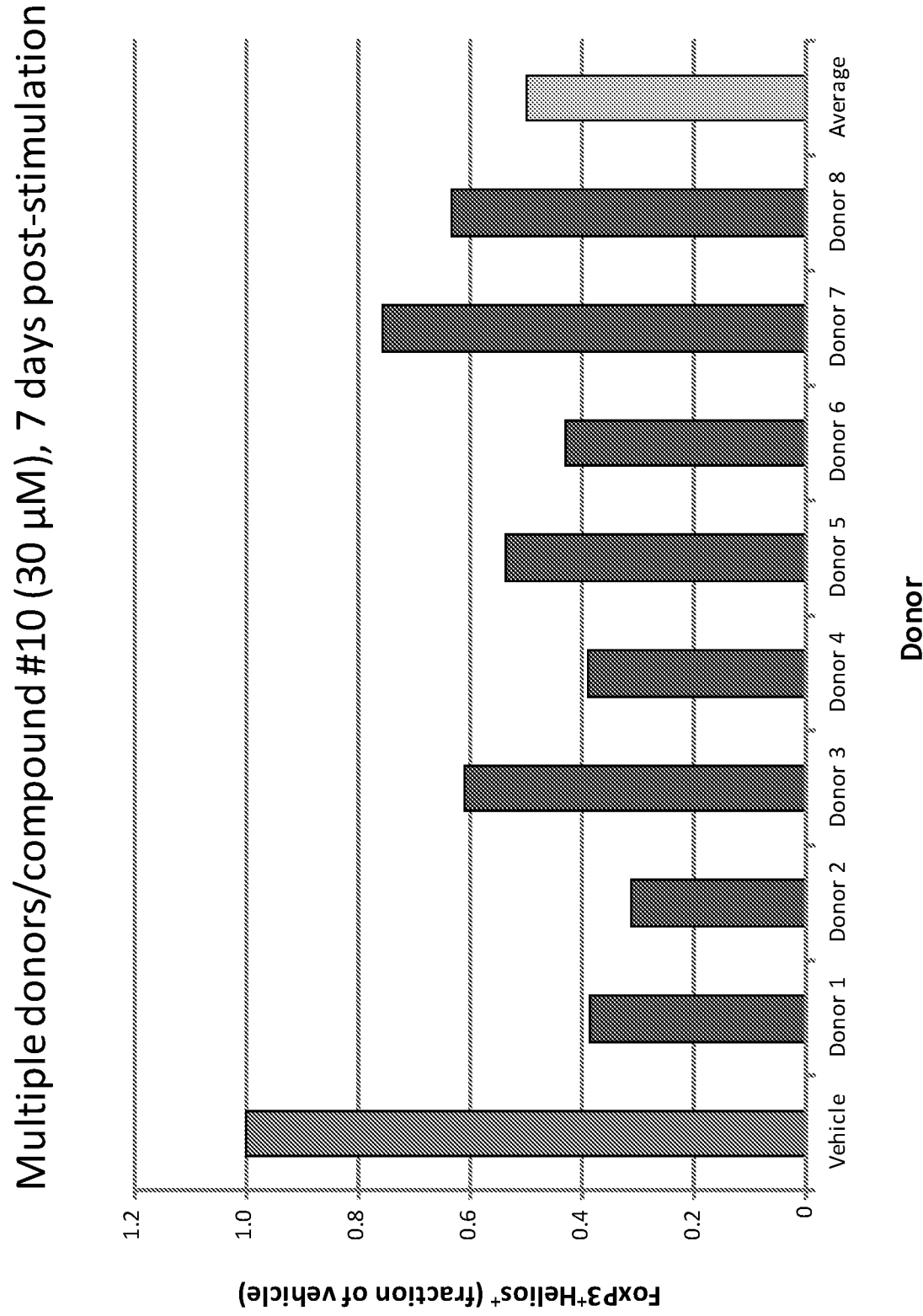


FIG. 30

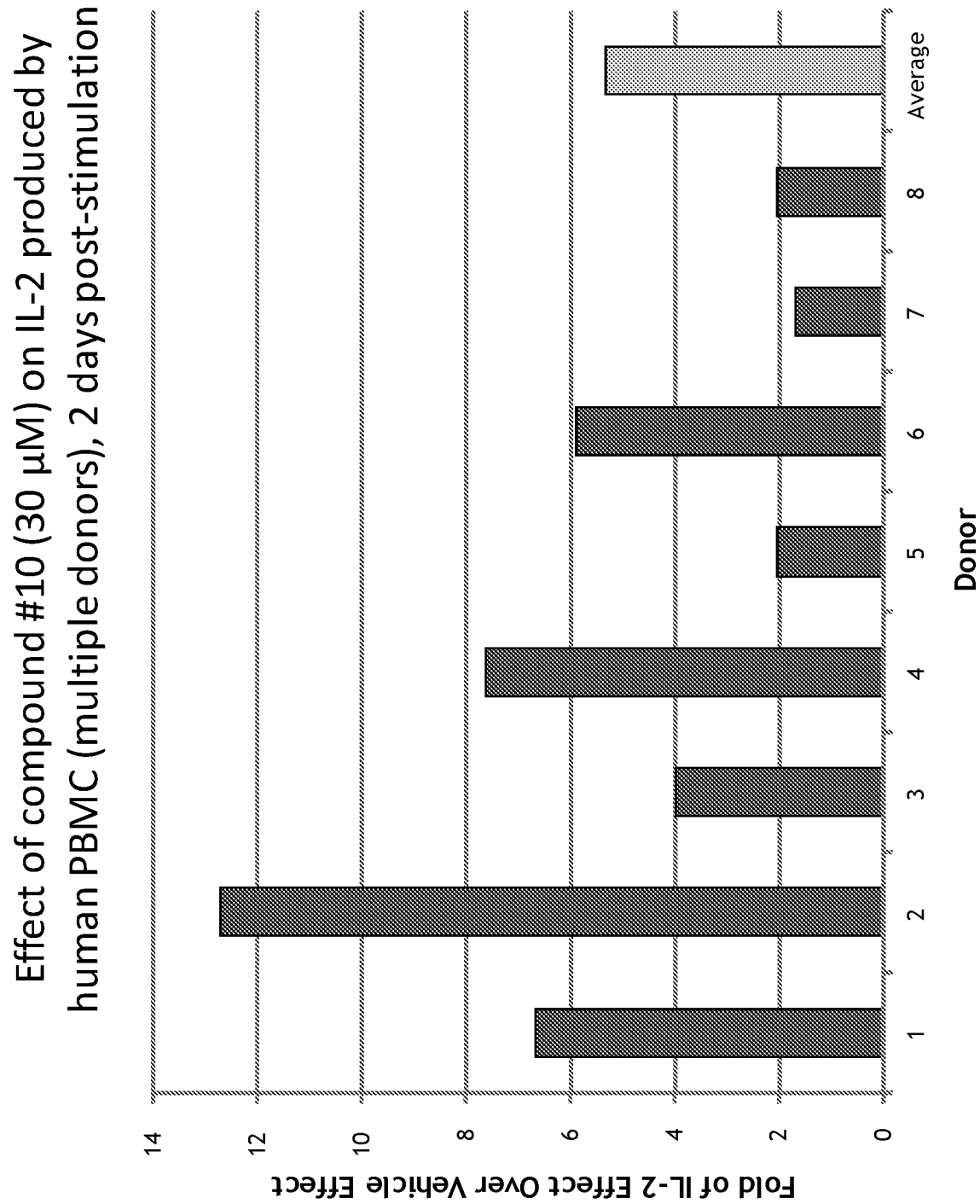


FIG. 31

Effect of compound #10 (30 μ M) on cytokines produced by pooled human PBMCs from multiple donors, 2 days post-stimulation

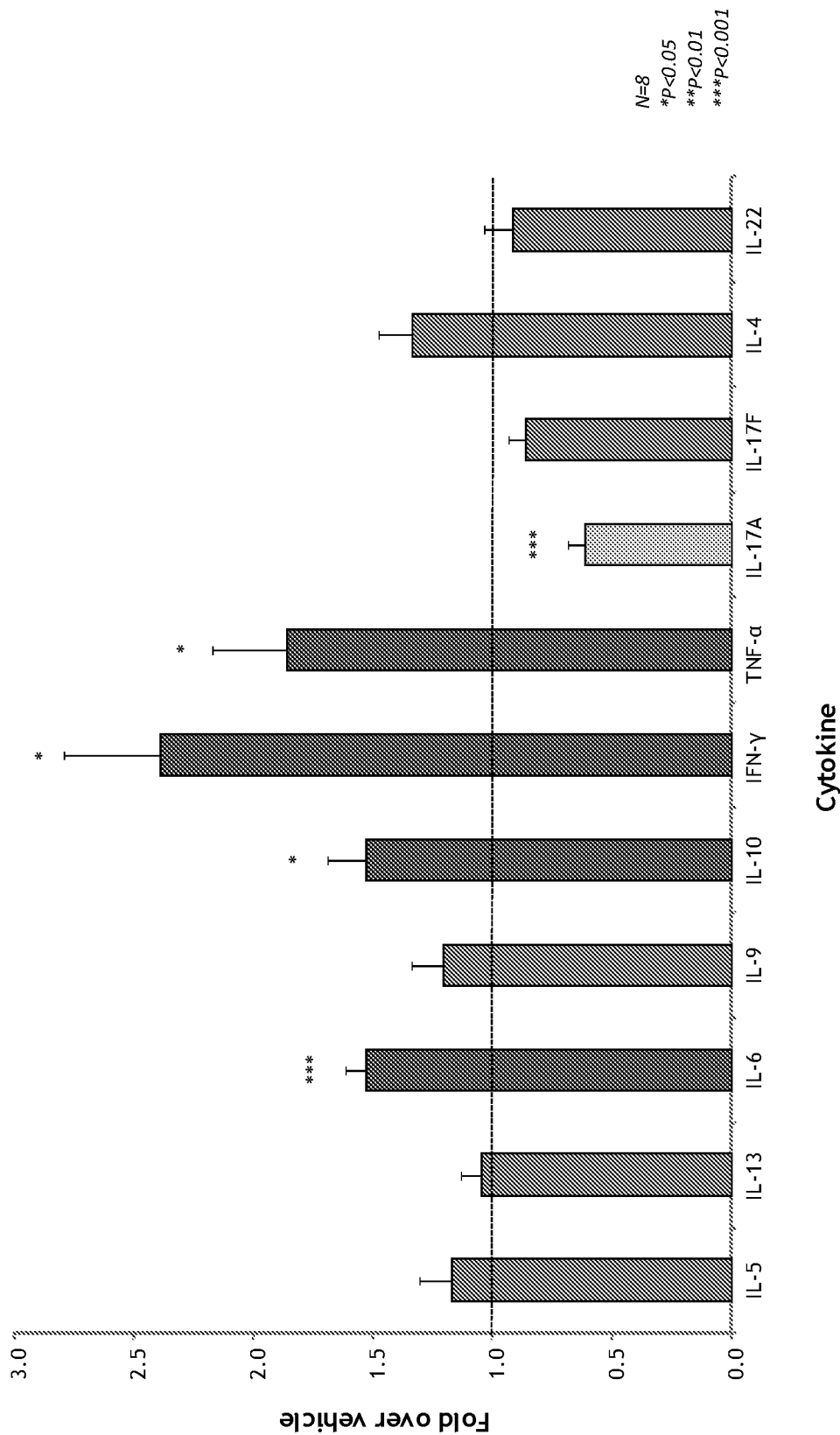


FIG. 32

Effects of compound #10 (30 μ M) on cytokine levels produced in mixed culture splenocytes from different mouse strains (co-cultured for 6 days)

C57BL/6 + DBA1

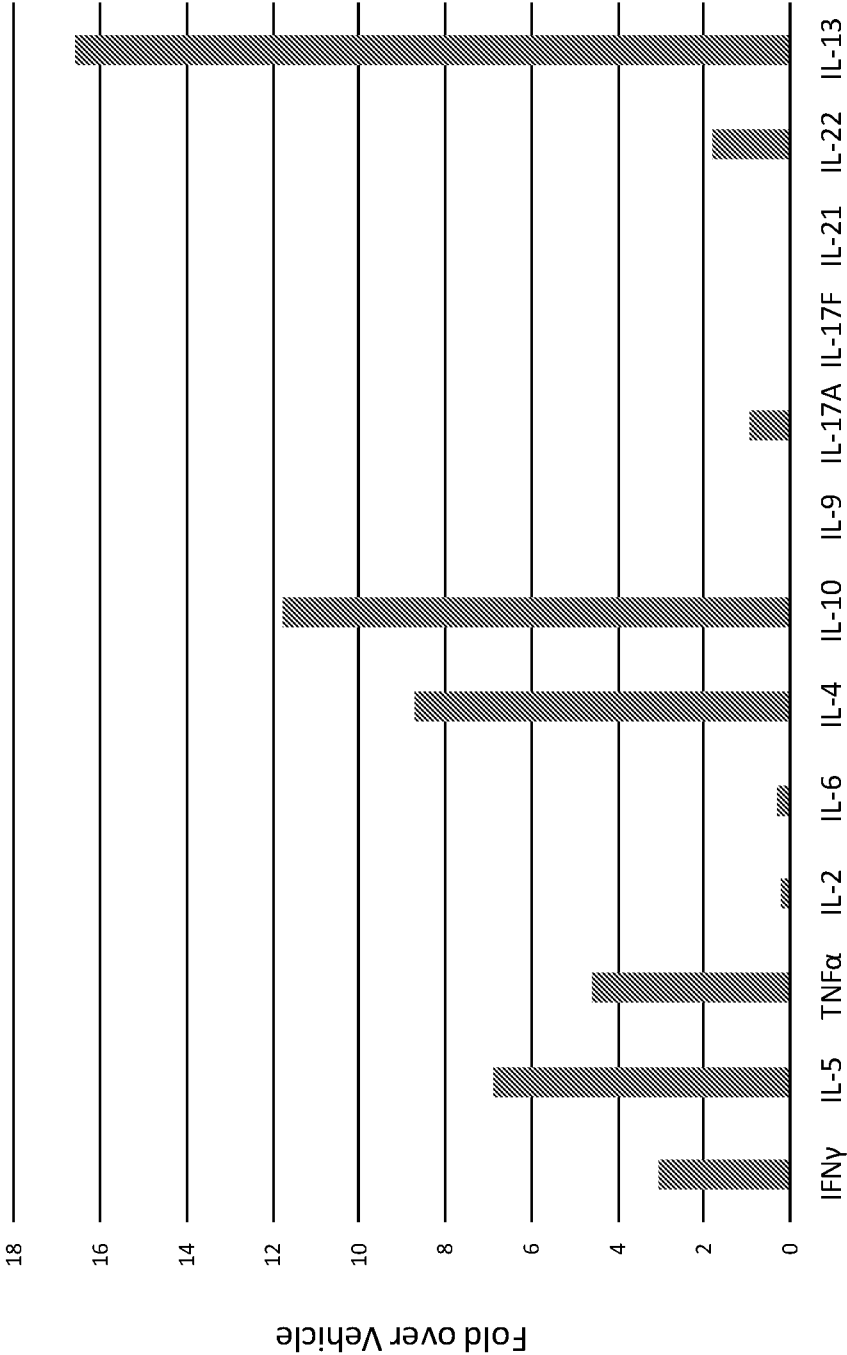


FIG. 33

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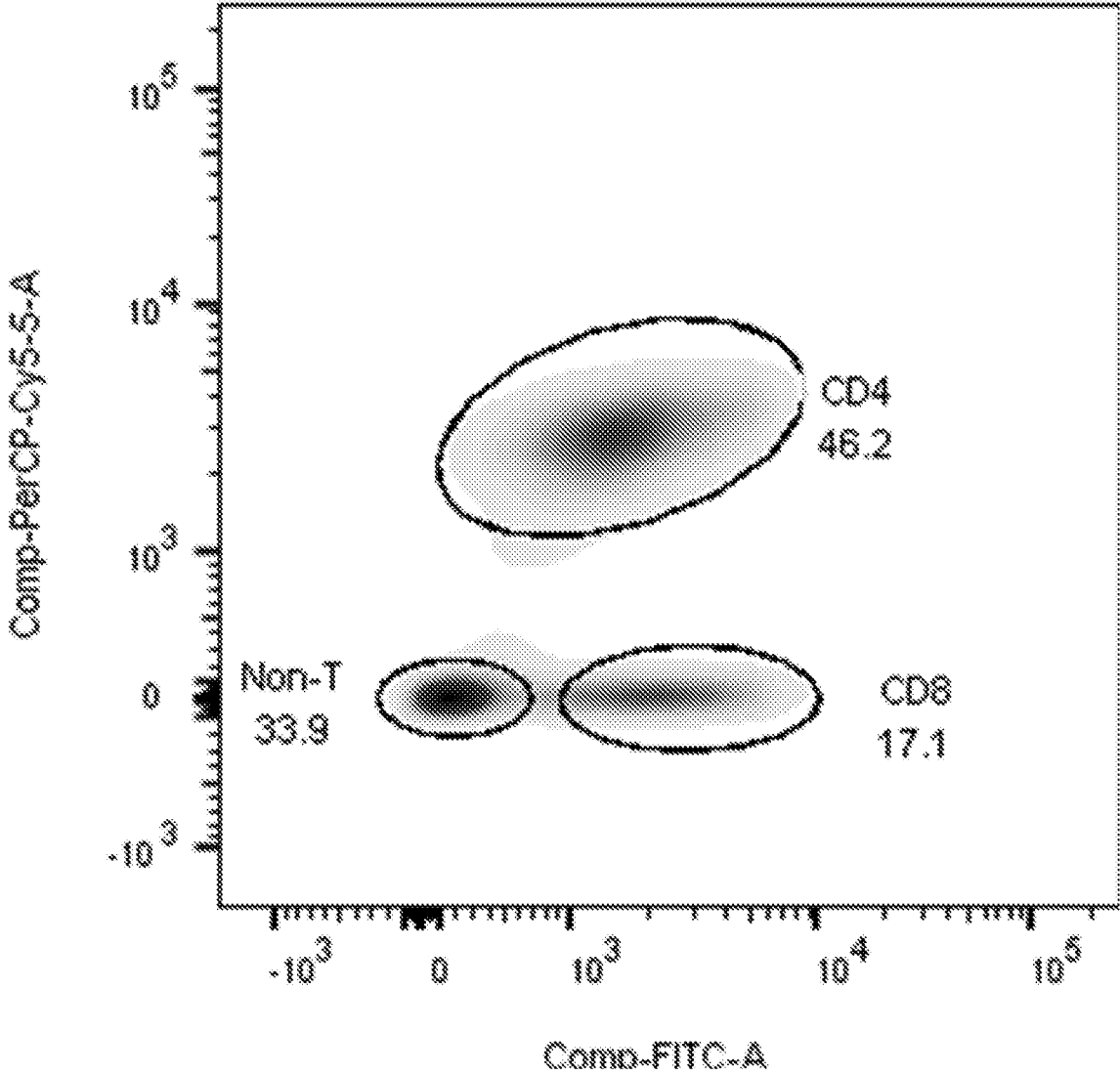


FIG. 34A

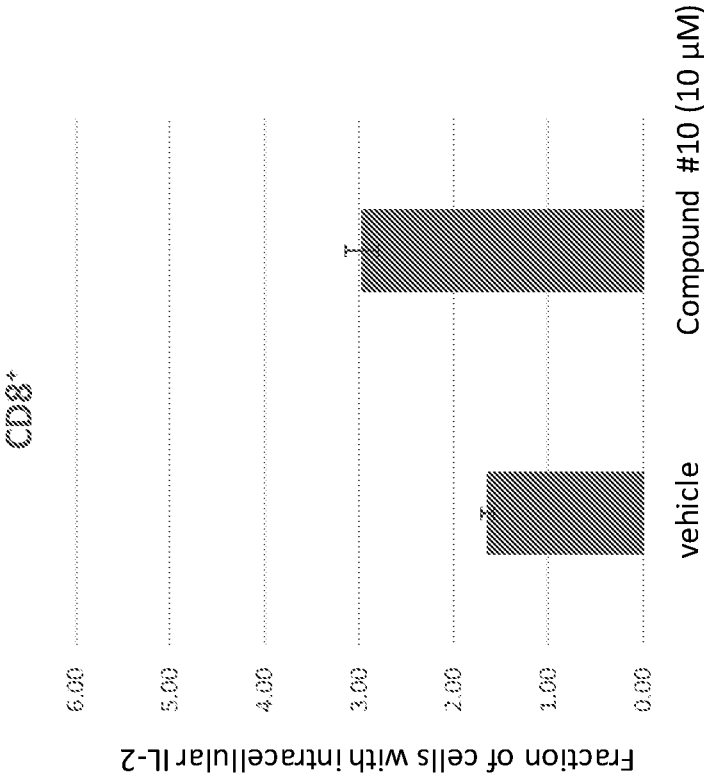


FIG. 34C

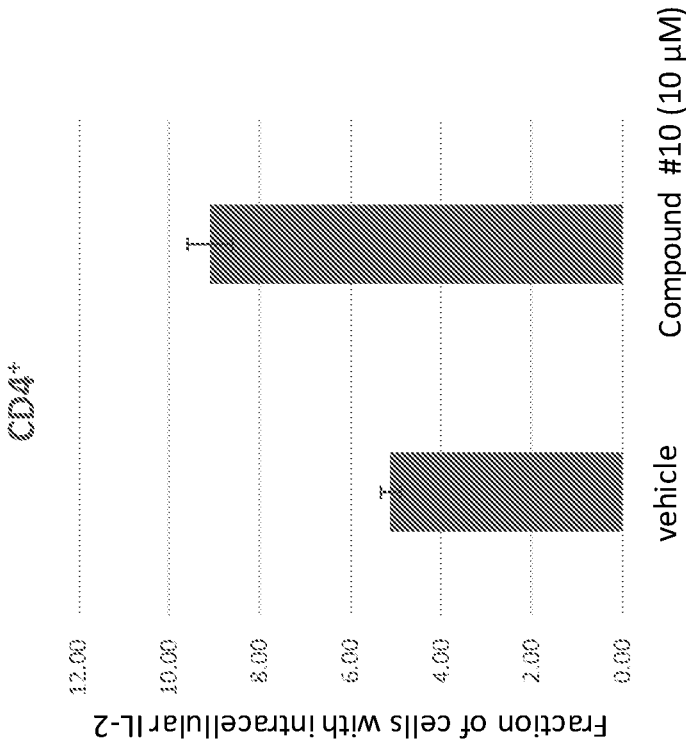


FIG. 34B

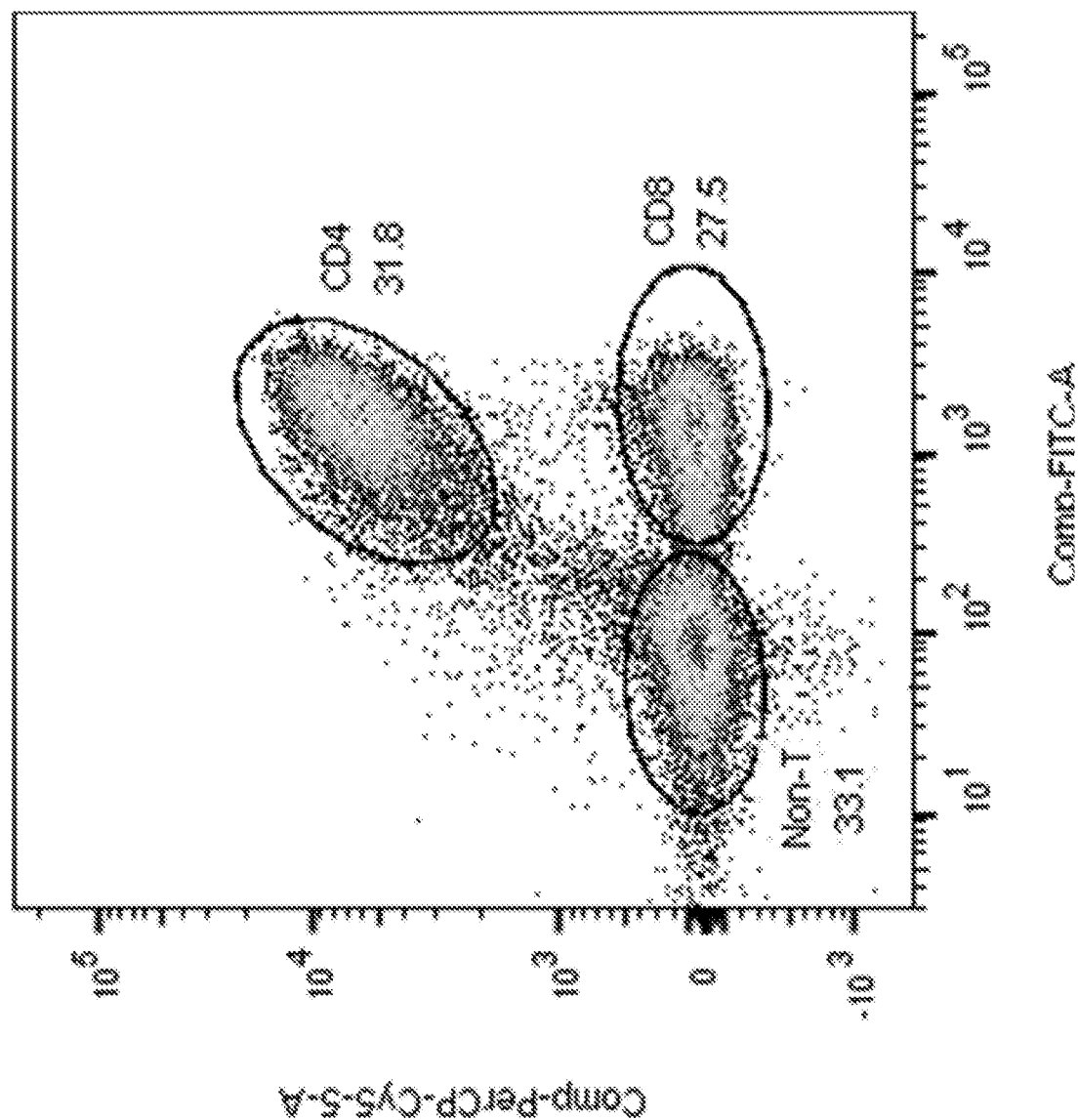


FIG. 35A

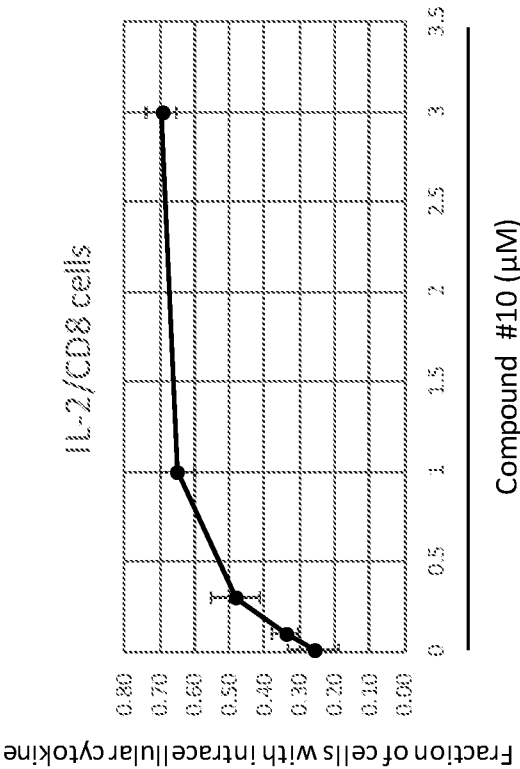


FIG. 35C

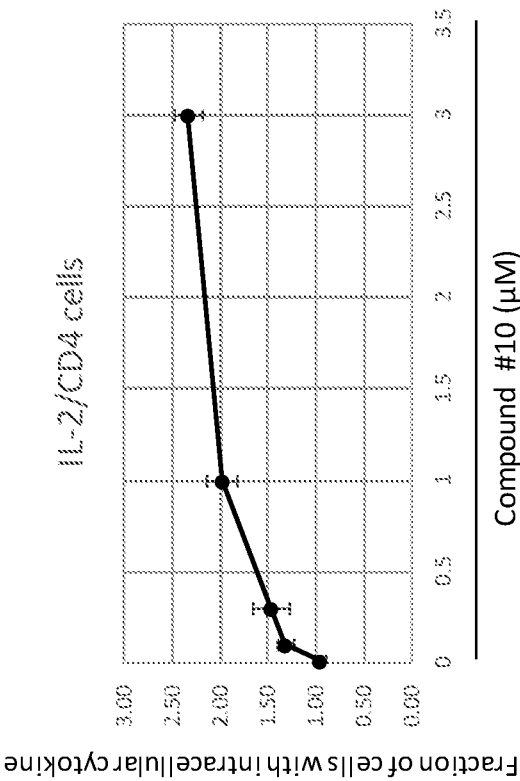


FIG. 35B

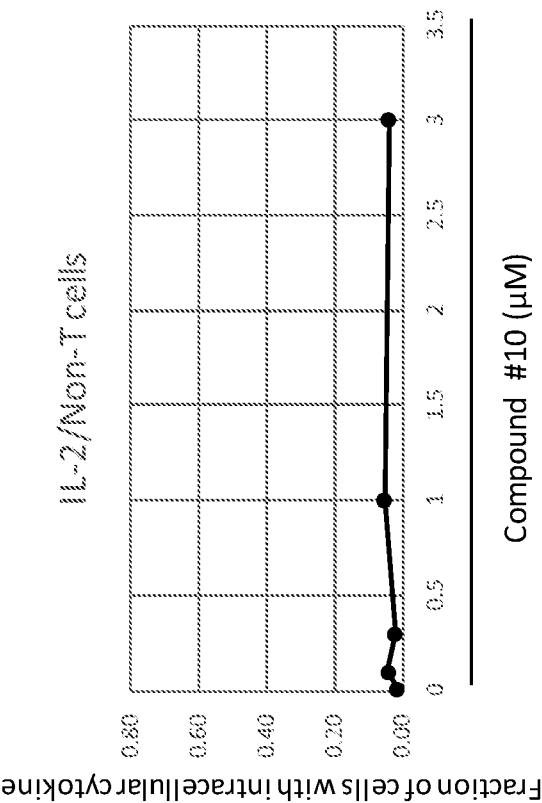


FIG. 35D

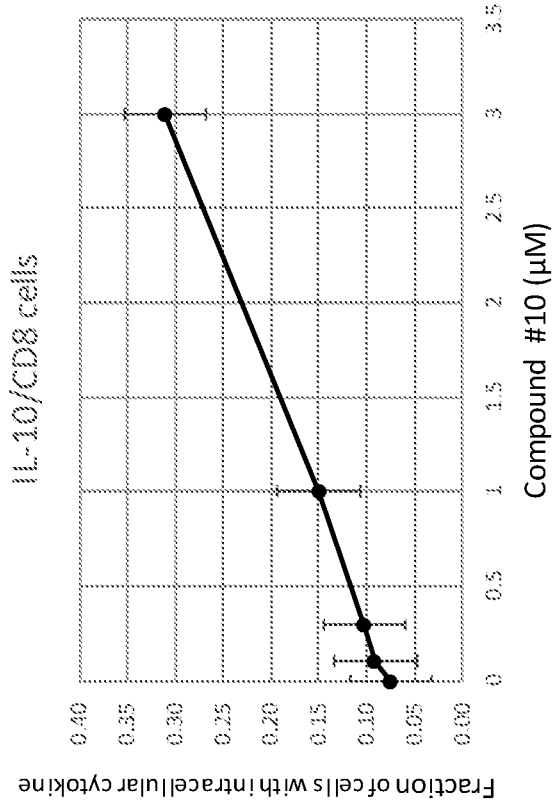


FIG. 35F

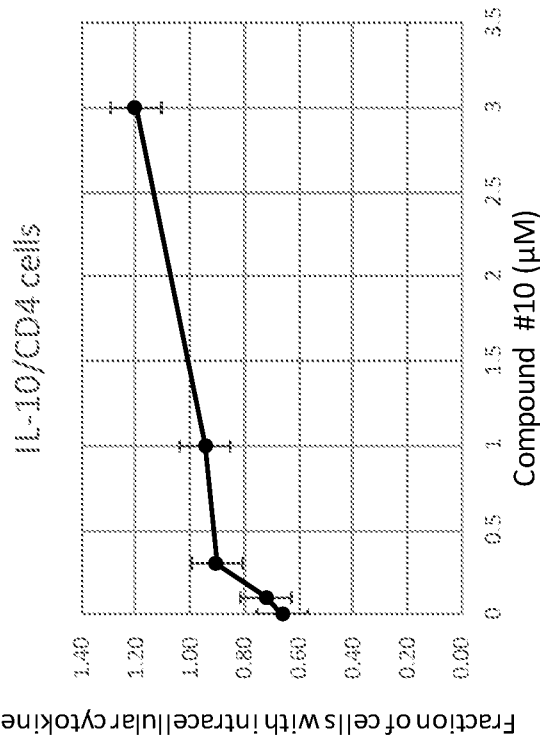


FIG. 35E

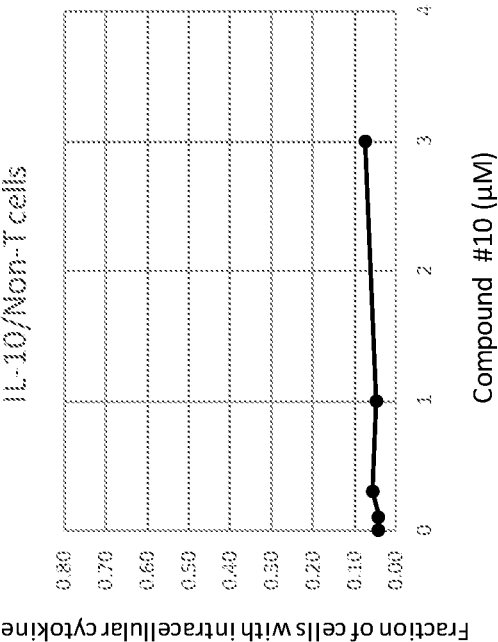


FIG. 35G

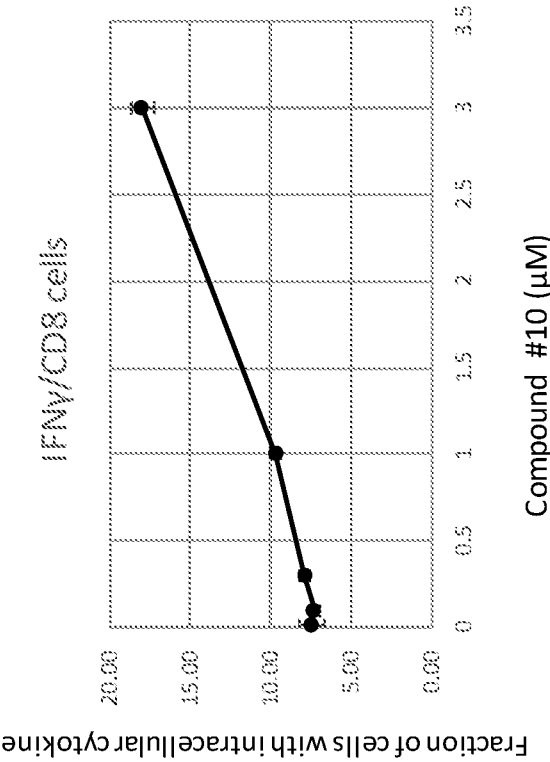


FIG. 35I

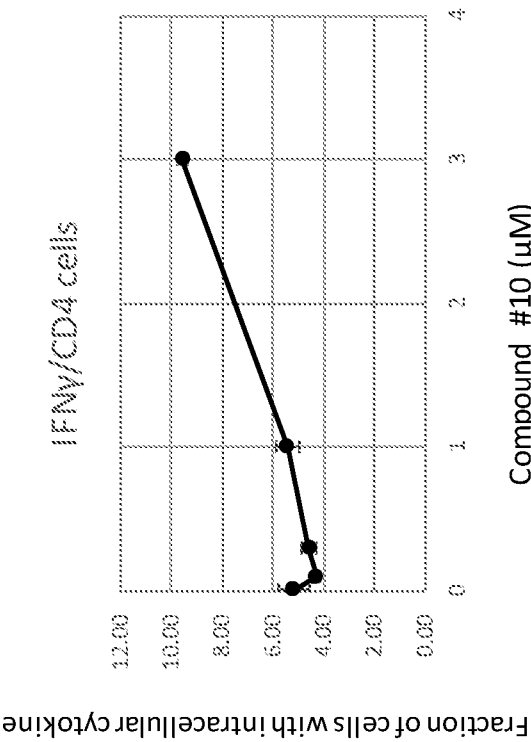


FIG. 35H

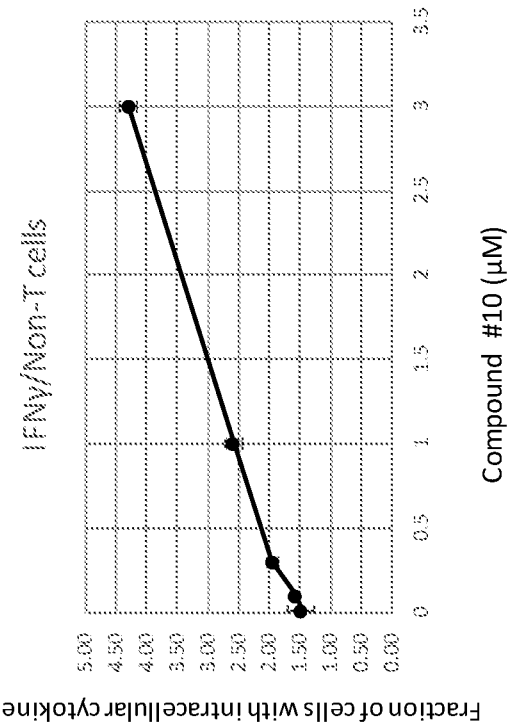


FIG. 35J

Induction of TNF- α by compound #10

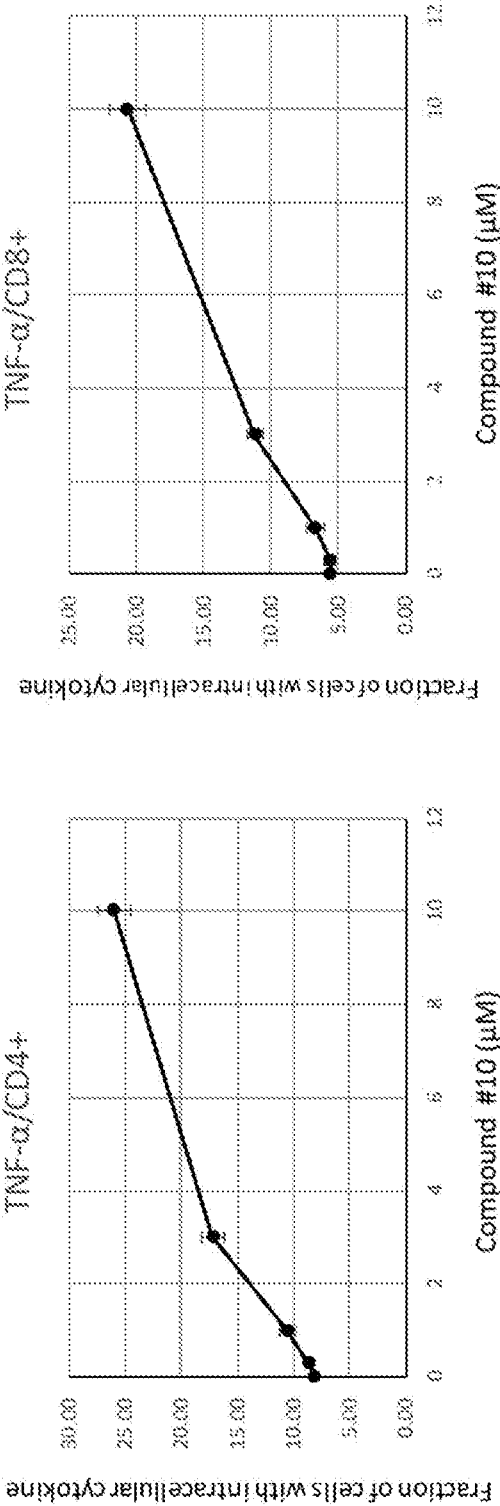


FIG. 35K

FIG. 35L

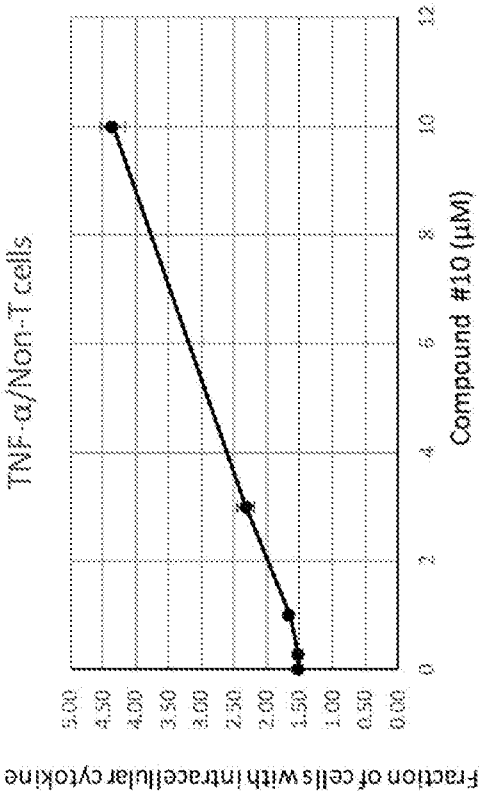


FIG. 35M

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Additional analysis of non-T cell population from FIG. 35A

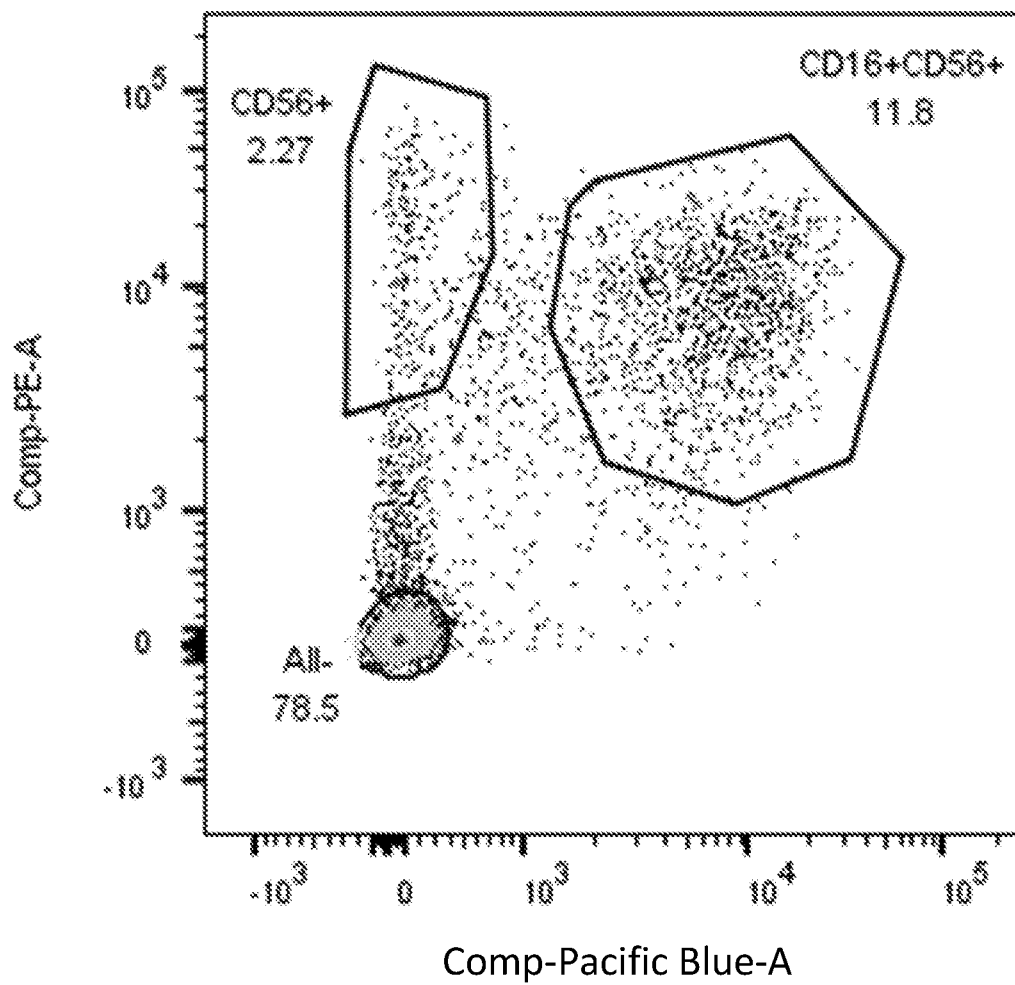


FIG. 36A

Induction of IFN γ by compound #10 in NK cells

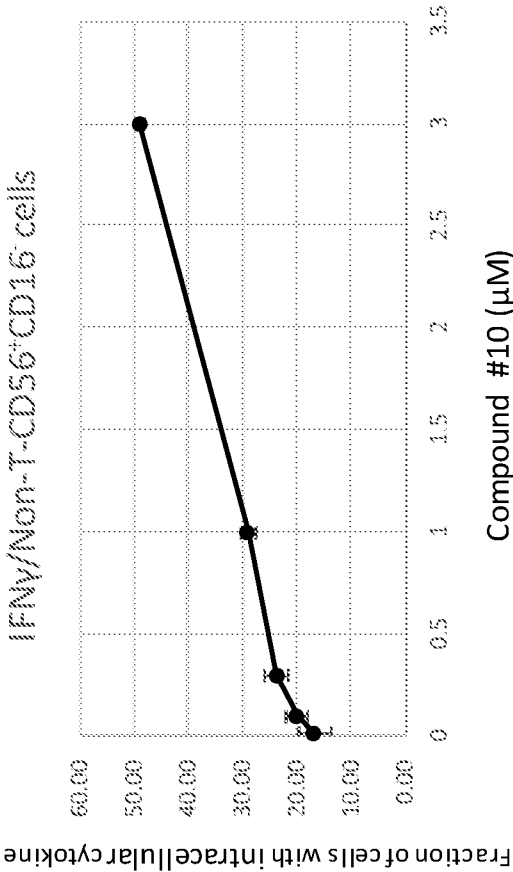


FIG. 36C

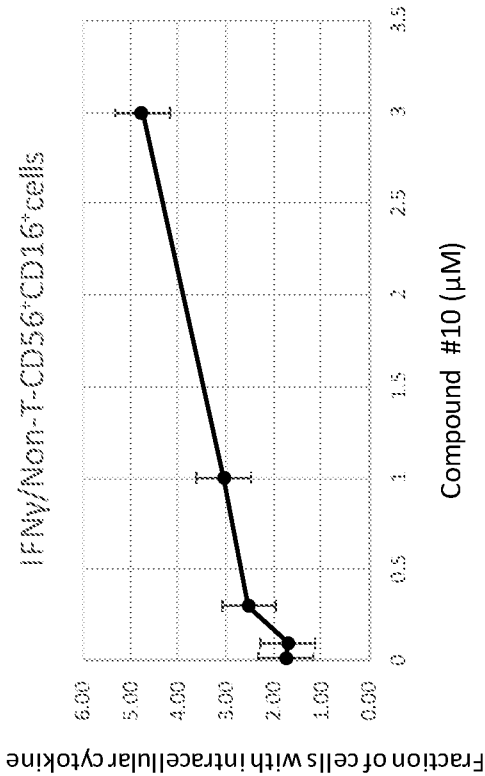


FIG. 36B

Induction of TNF- α by compound #10 in NK cells

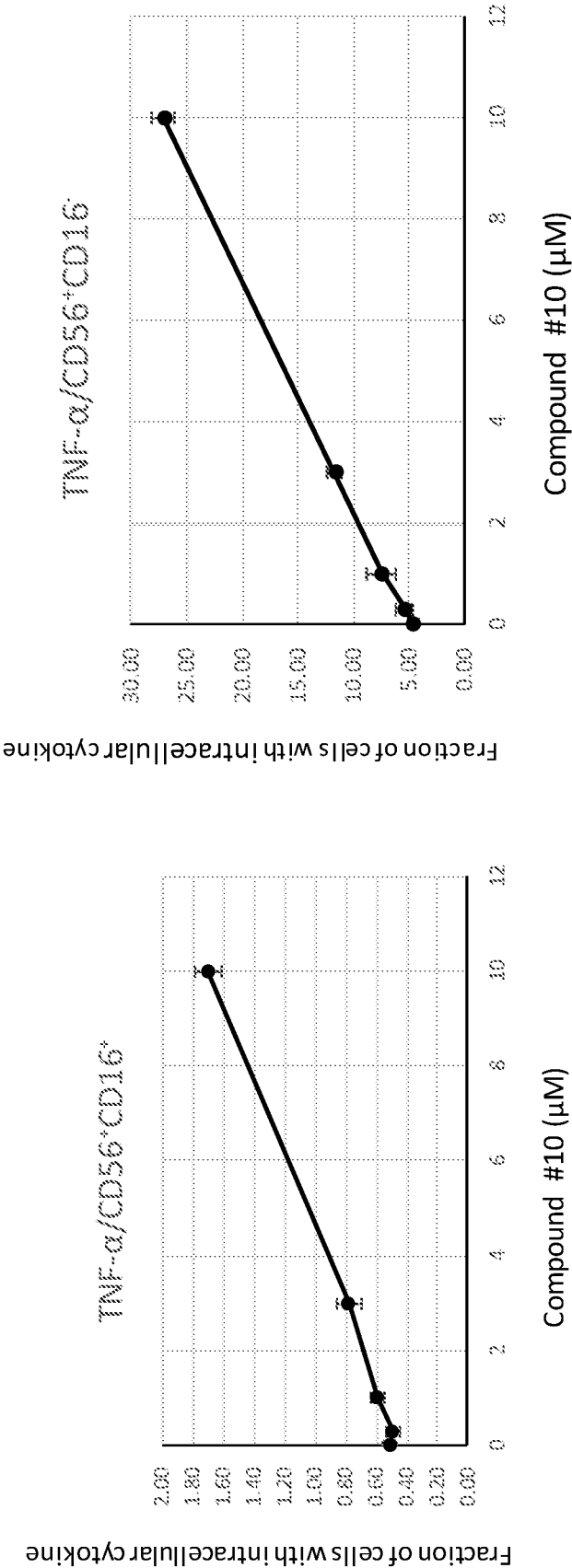


FIG. 36D

FIG. 36E

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Effect of GPR174 on in Vivo-Expanded Flu-Specific CD8⁺ Cells
Upon Flu PR8 Infection of Mice

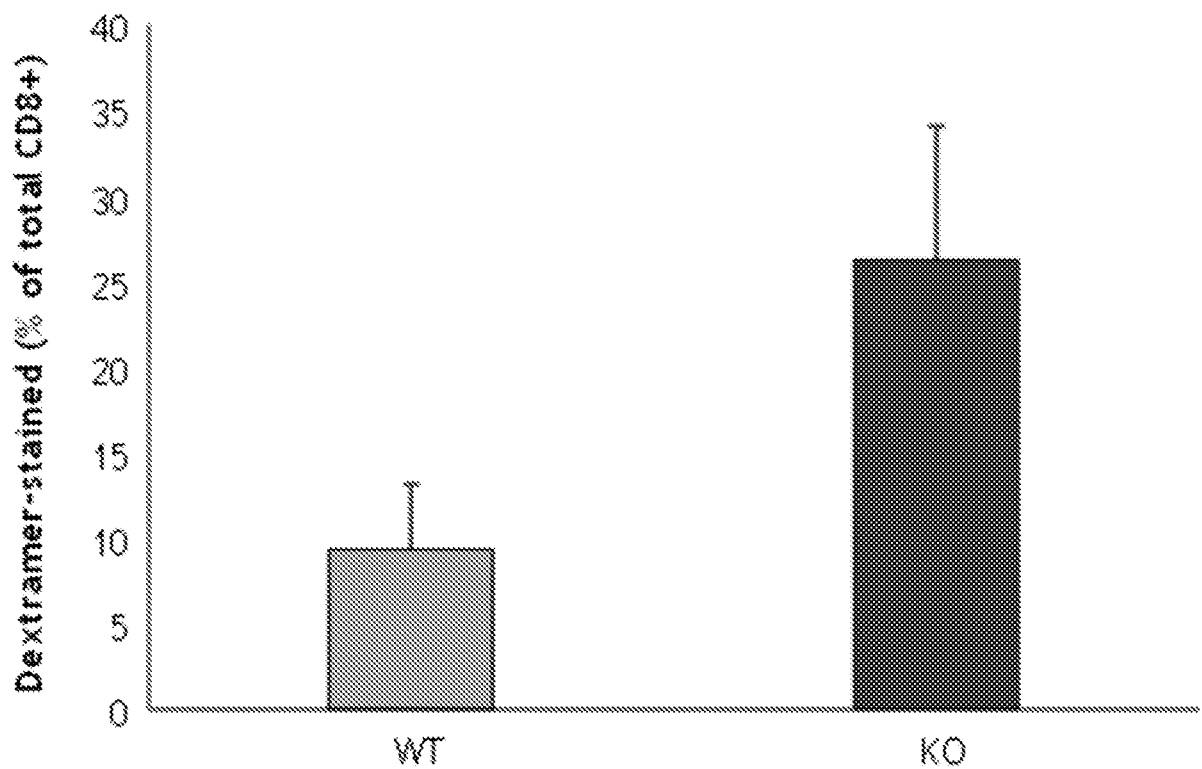


FIG. 37

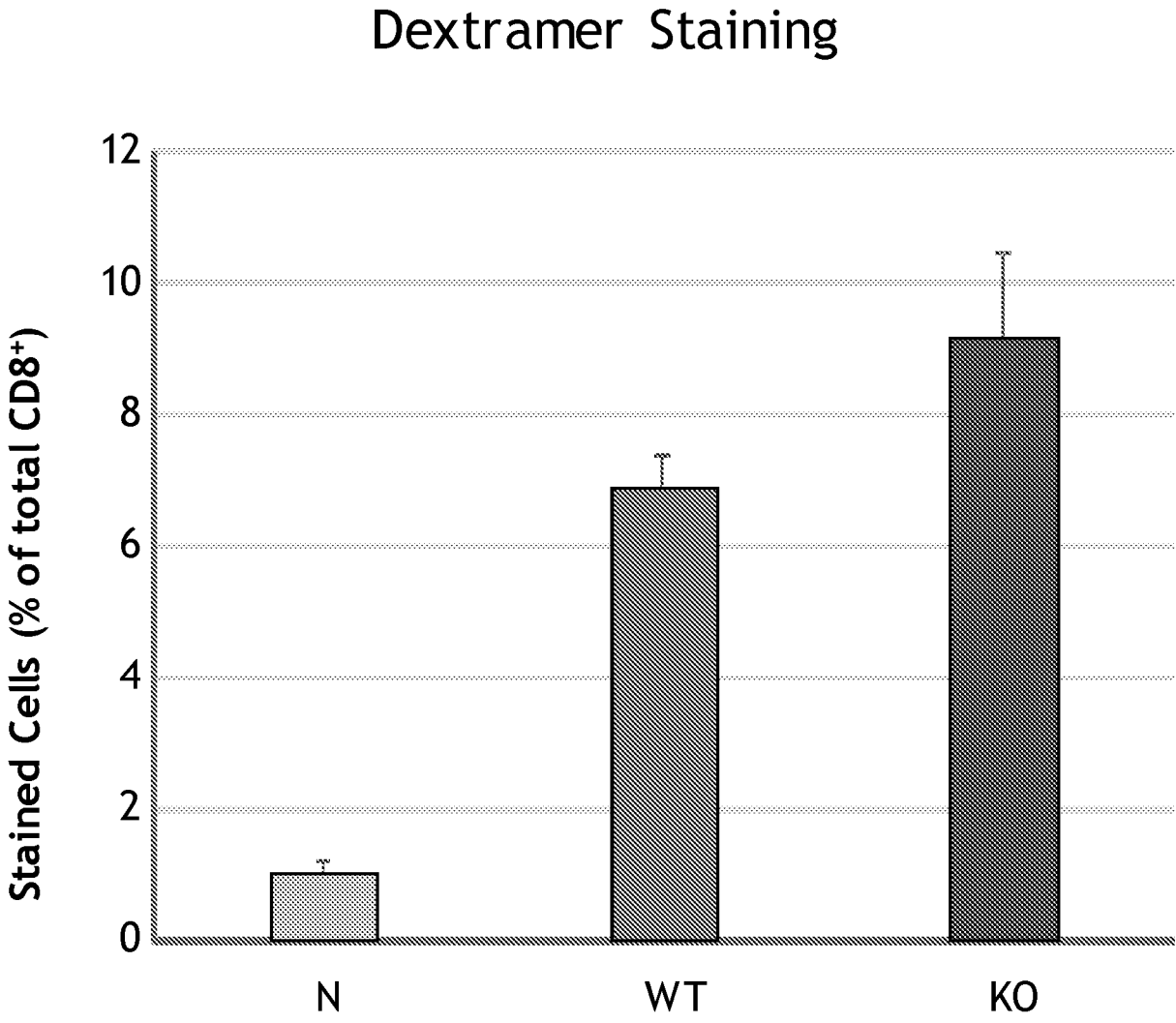


FIG. 38

Effect of GPR174i on CTLA4 Expression on Human Naïve T Cells
(one day post-stimulation)

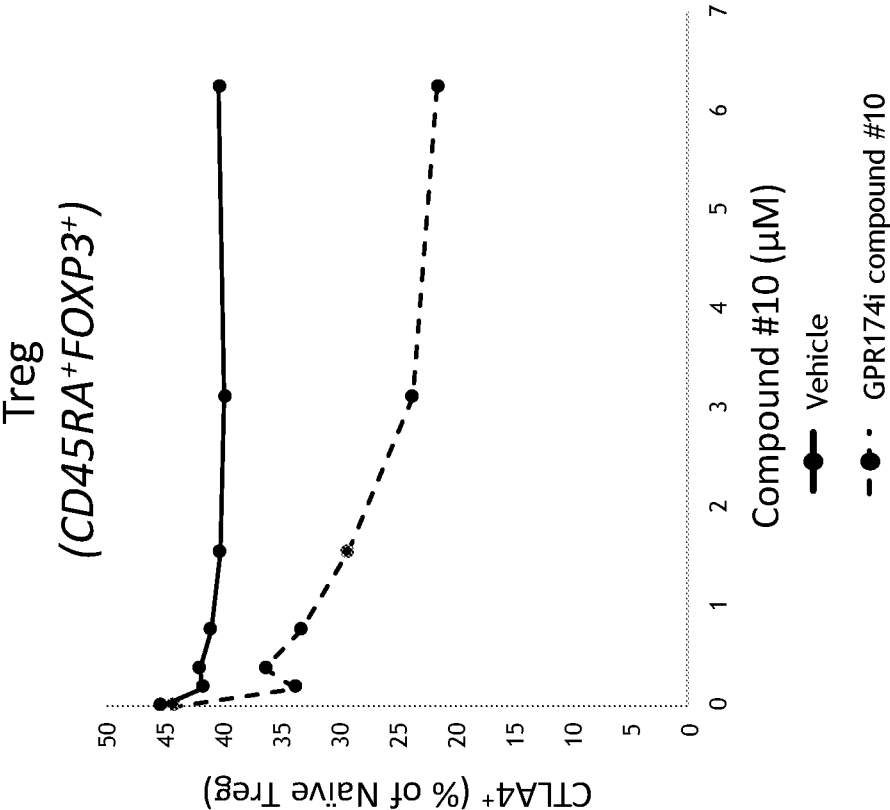


FIG. 39A

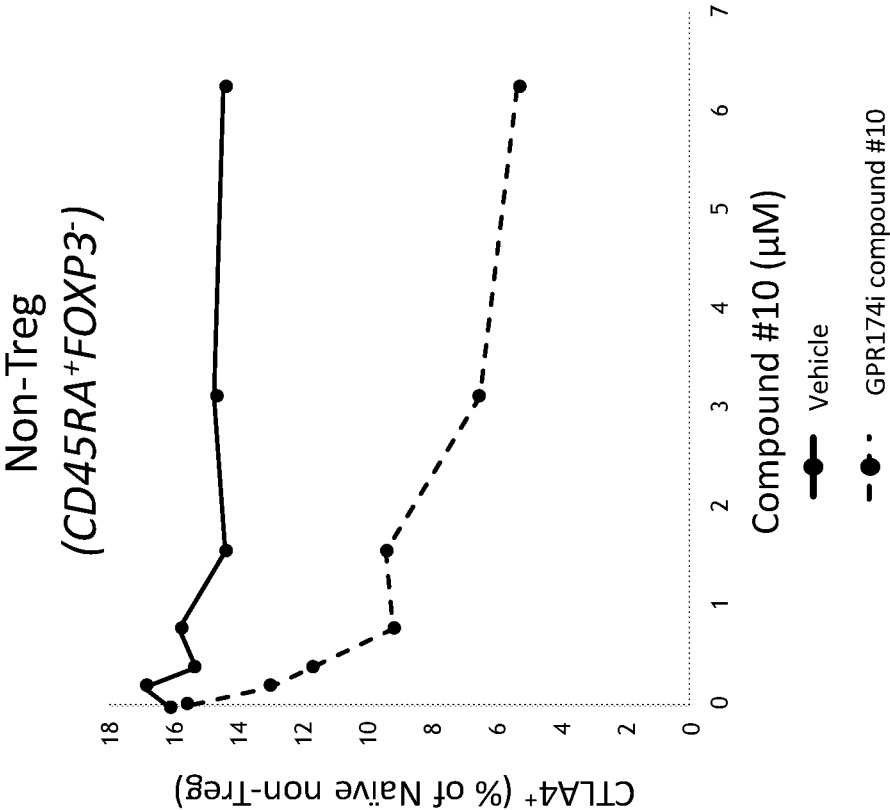


FIG. 39B

Effect of GPR174i on CTLA4 Expression on Human Memory T Cells
(one day post-stimulation)

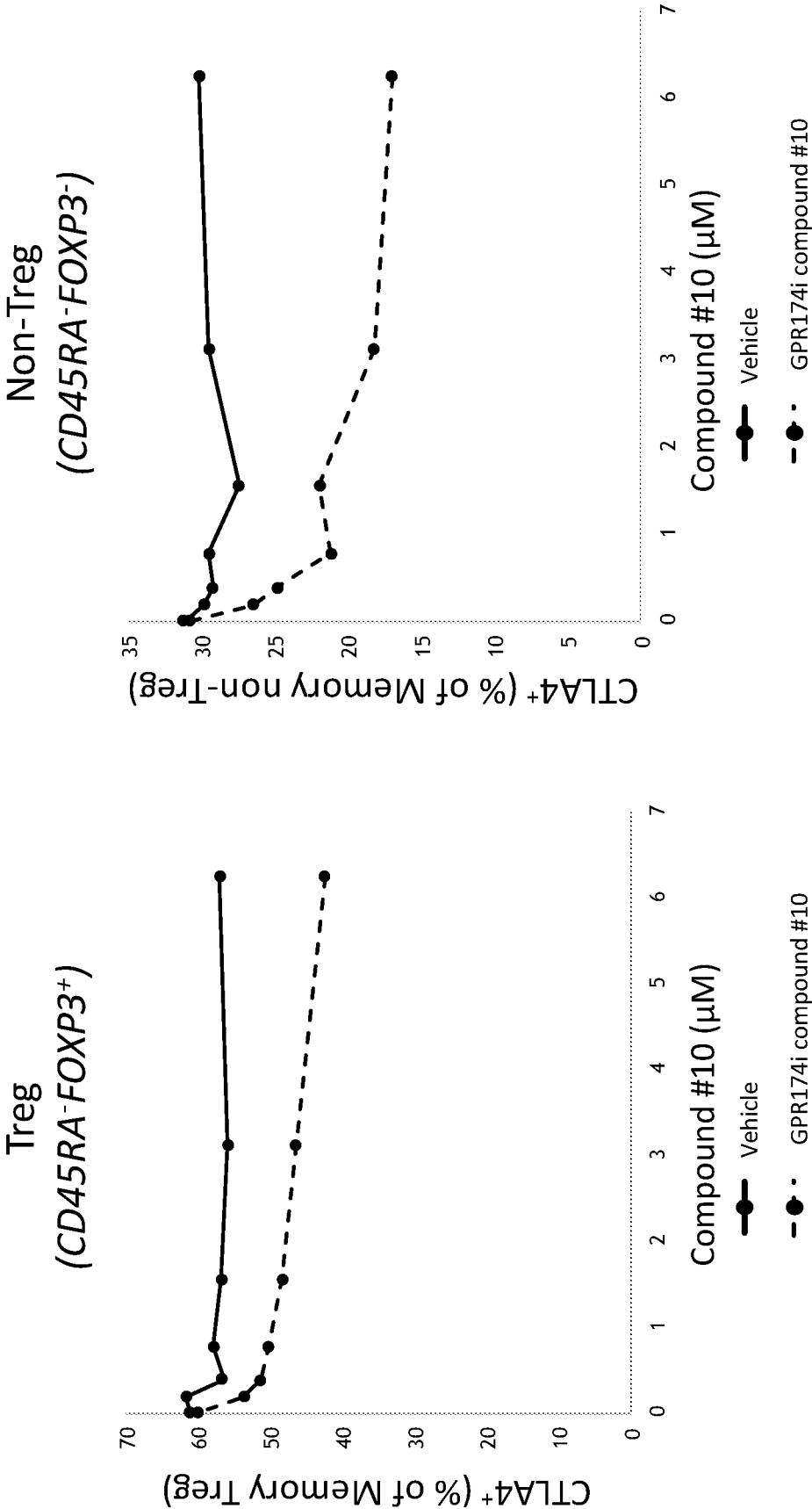


FIG. 40A

FIG. 40B

Effect of GPR174i on PD-L1 Expression on Human CD4 T Cells
(one day post-stimulation)

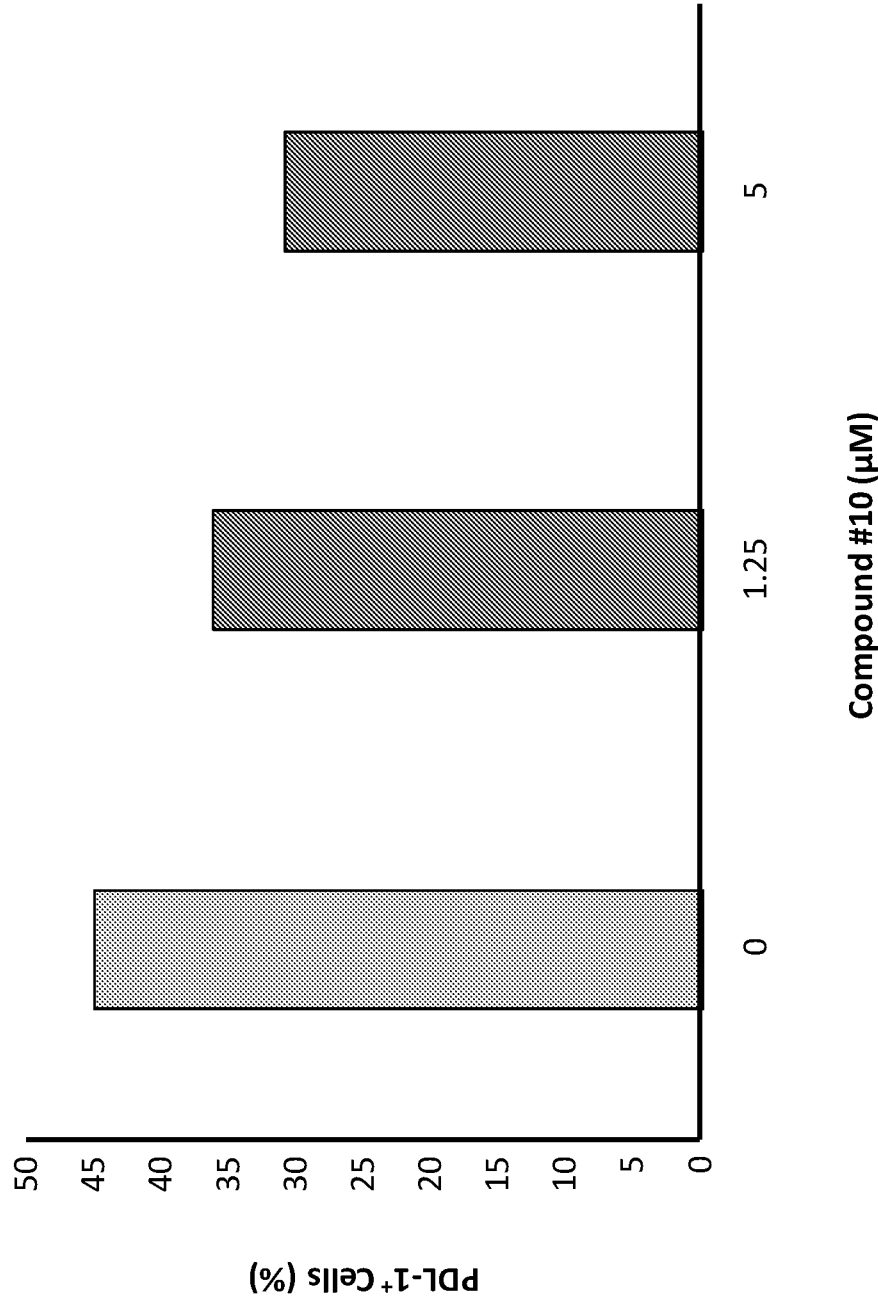


FIG. 41

**Effect of GPR174i on TIGIT Expression on Human CD8 T Cells
(one day post-stimulation)**

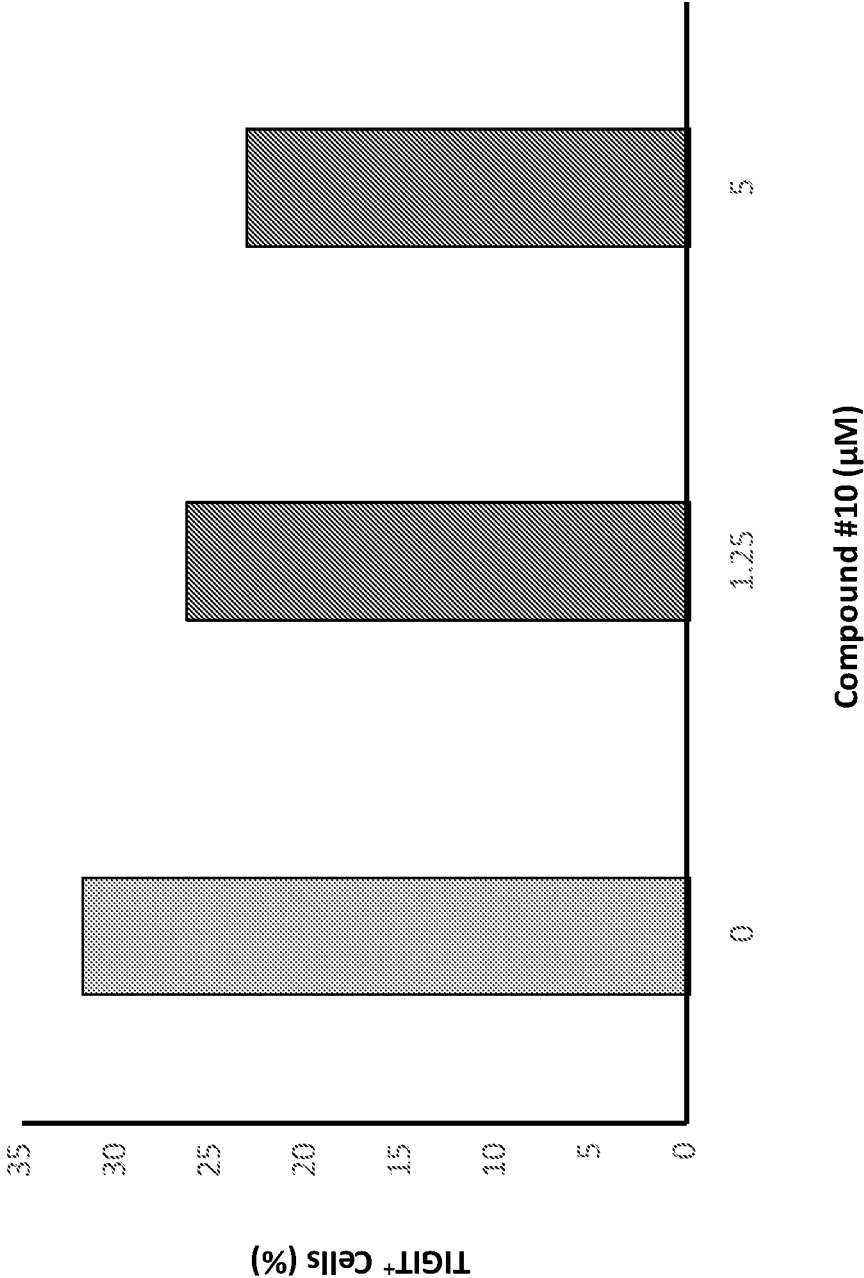


FIG. 42

Effect of GPR174i on AREG Expression on Human CD4 T Cells
(one day post-stimulation)

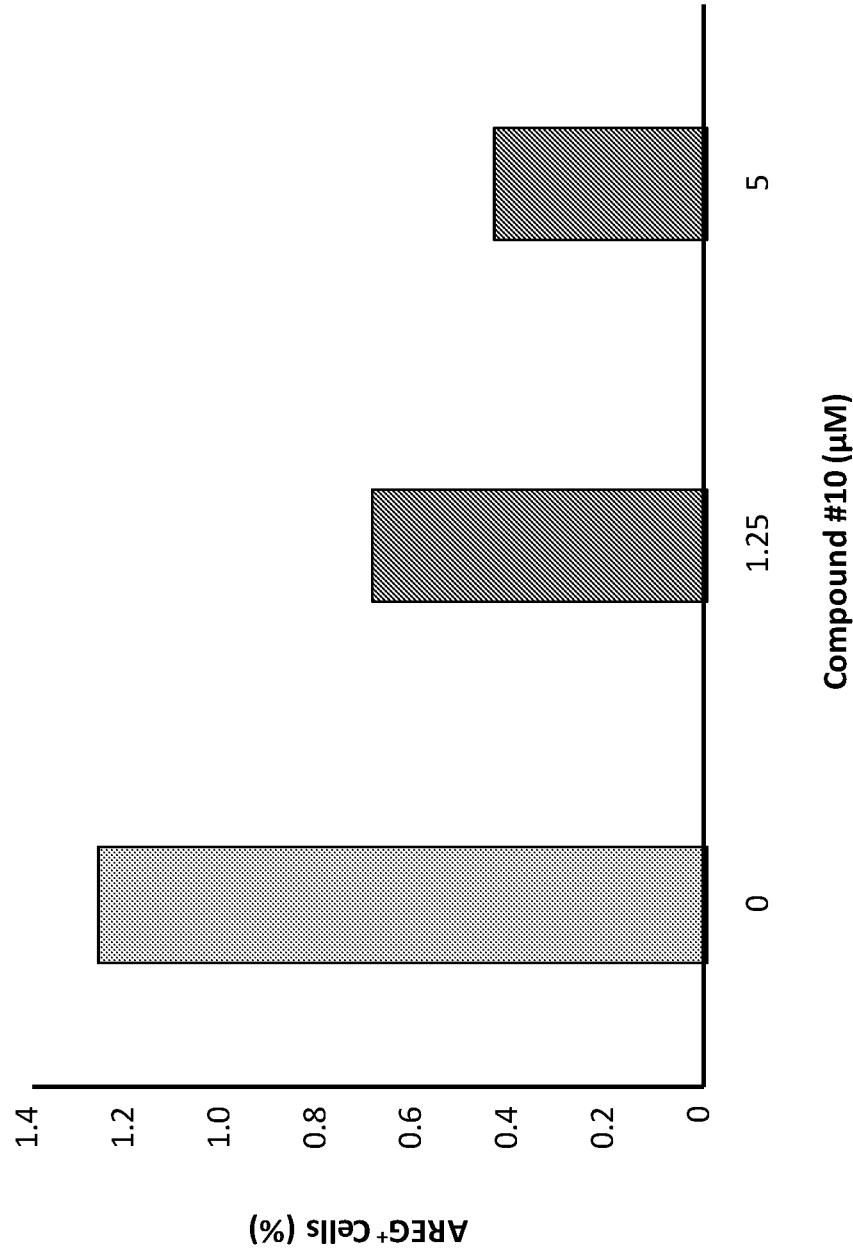


FIG. 43

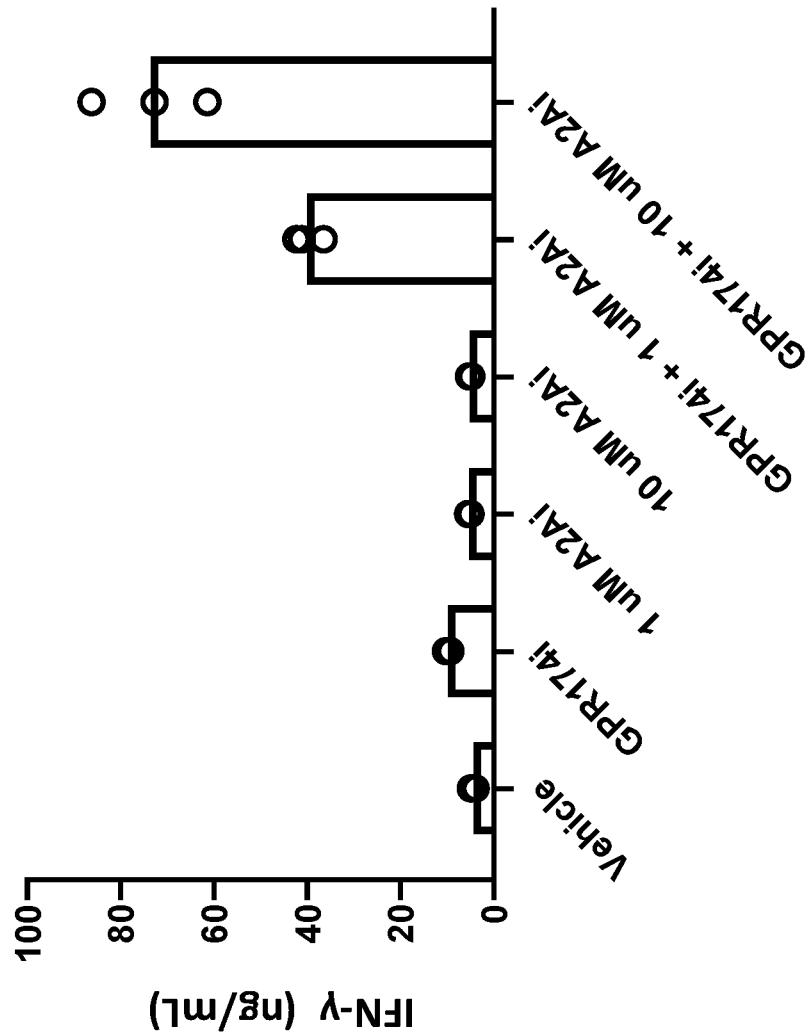


FIG. 44

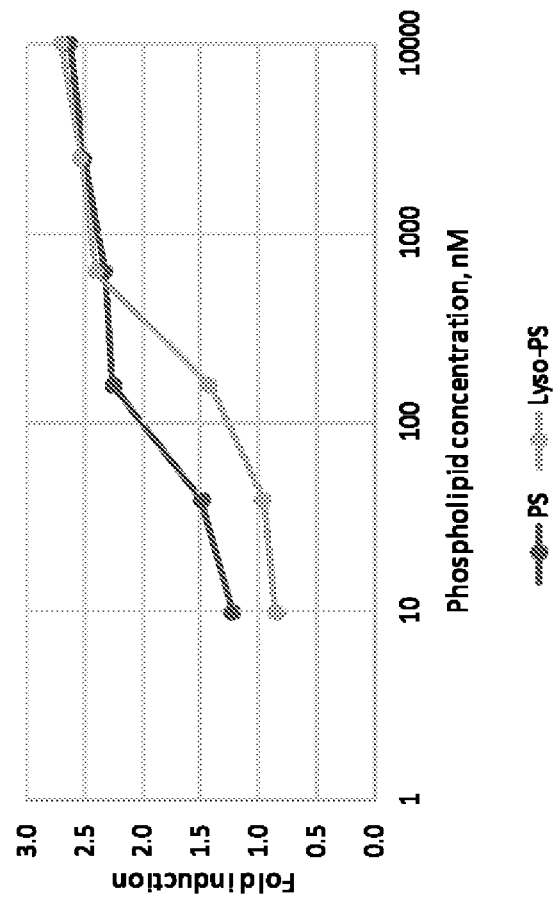


FIG. 45A

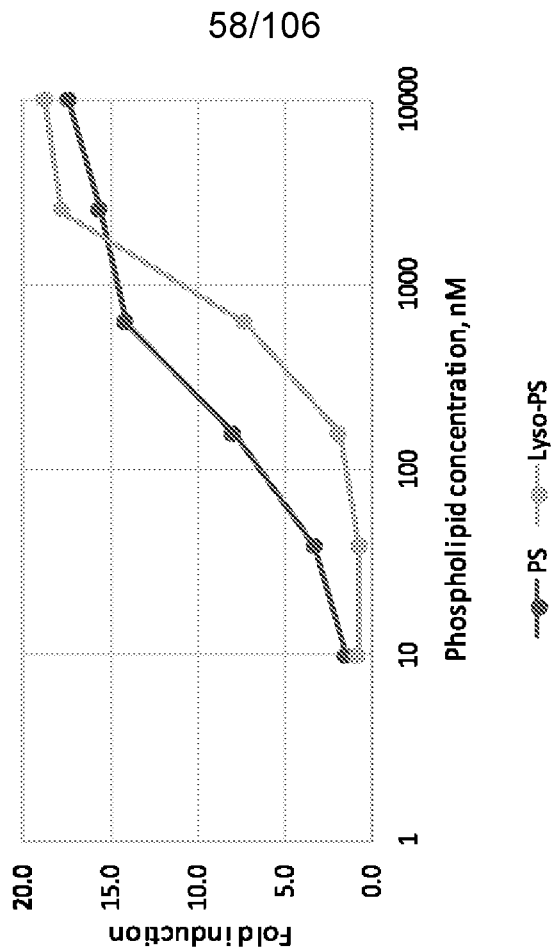


FIG. 45B

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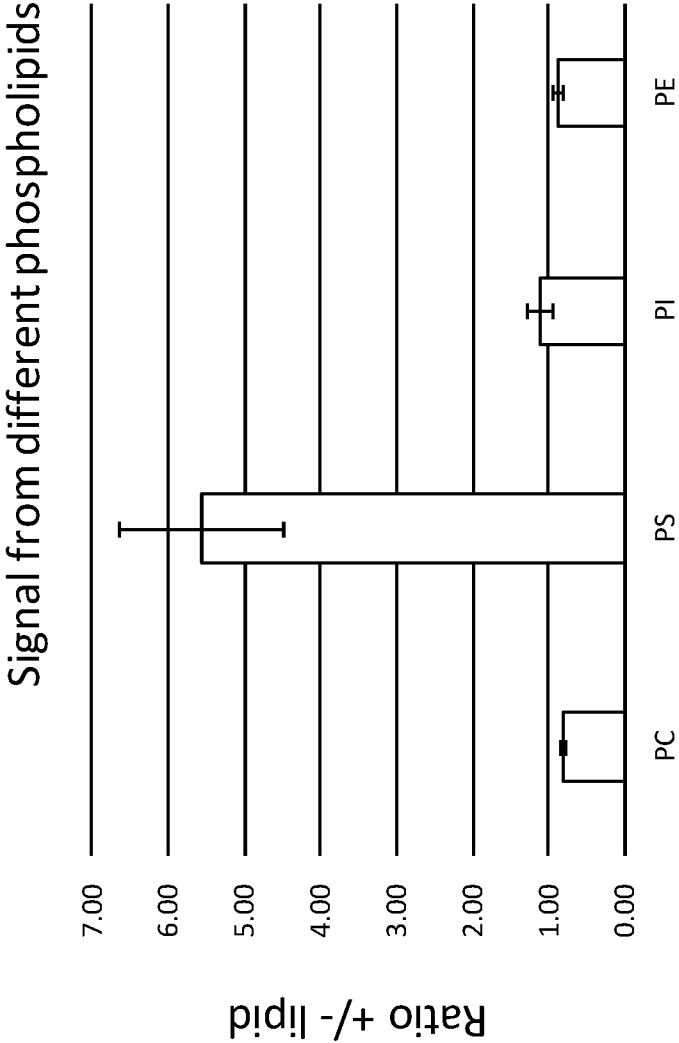


FIG. 46

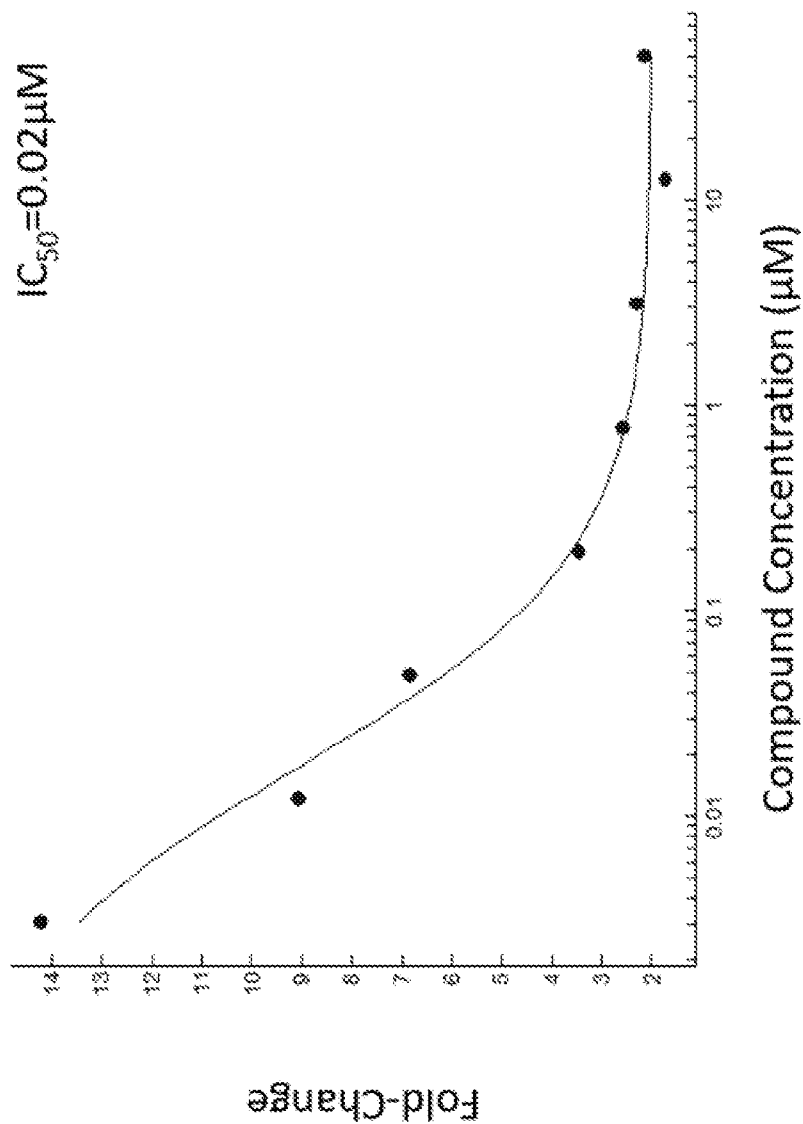


FIG. 47A

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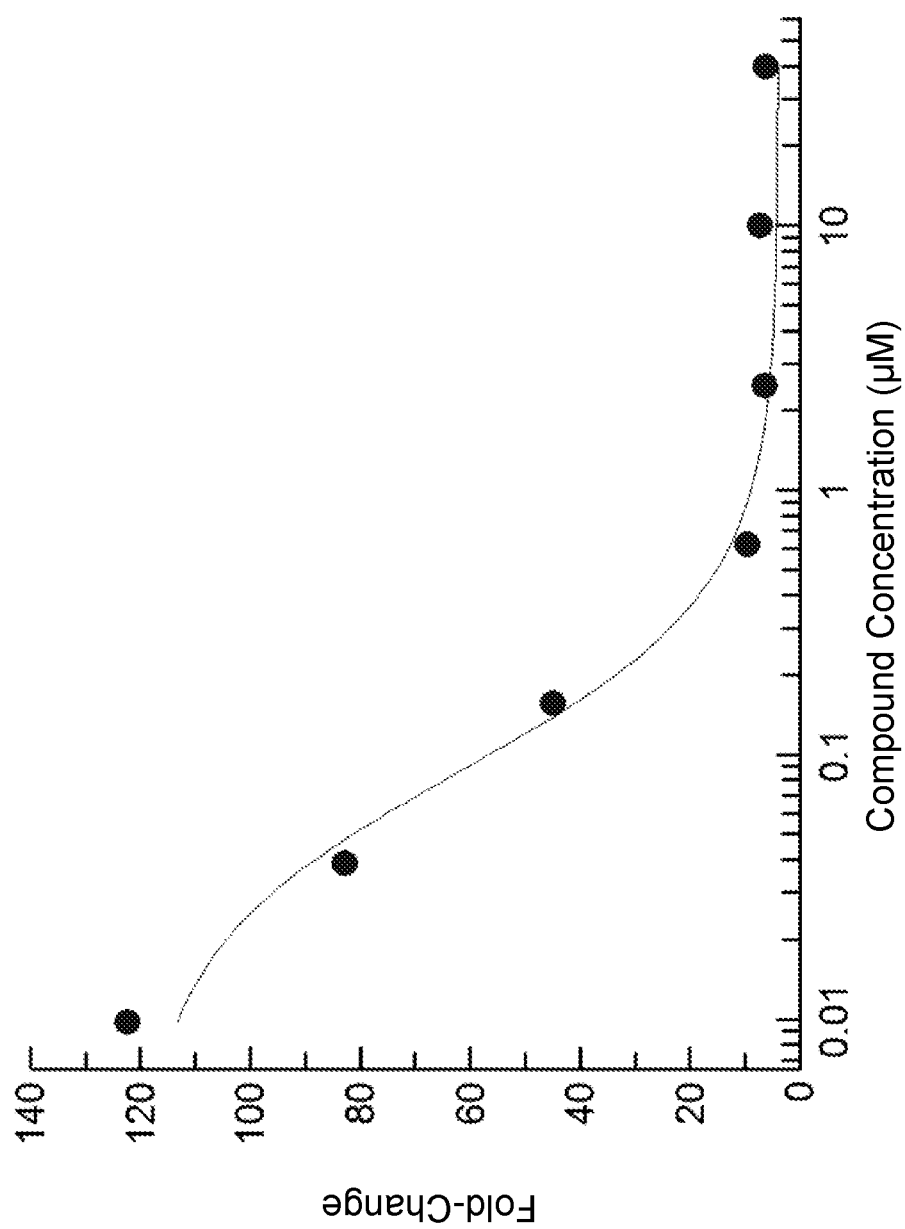


FIG. 47B

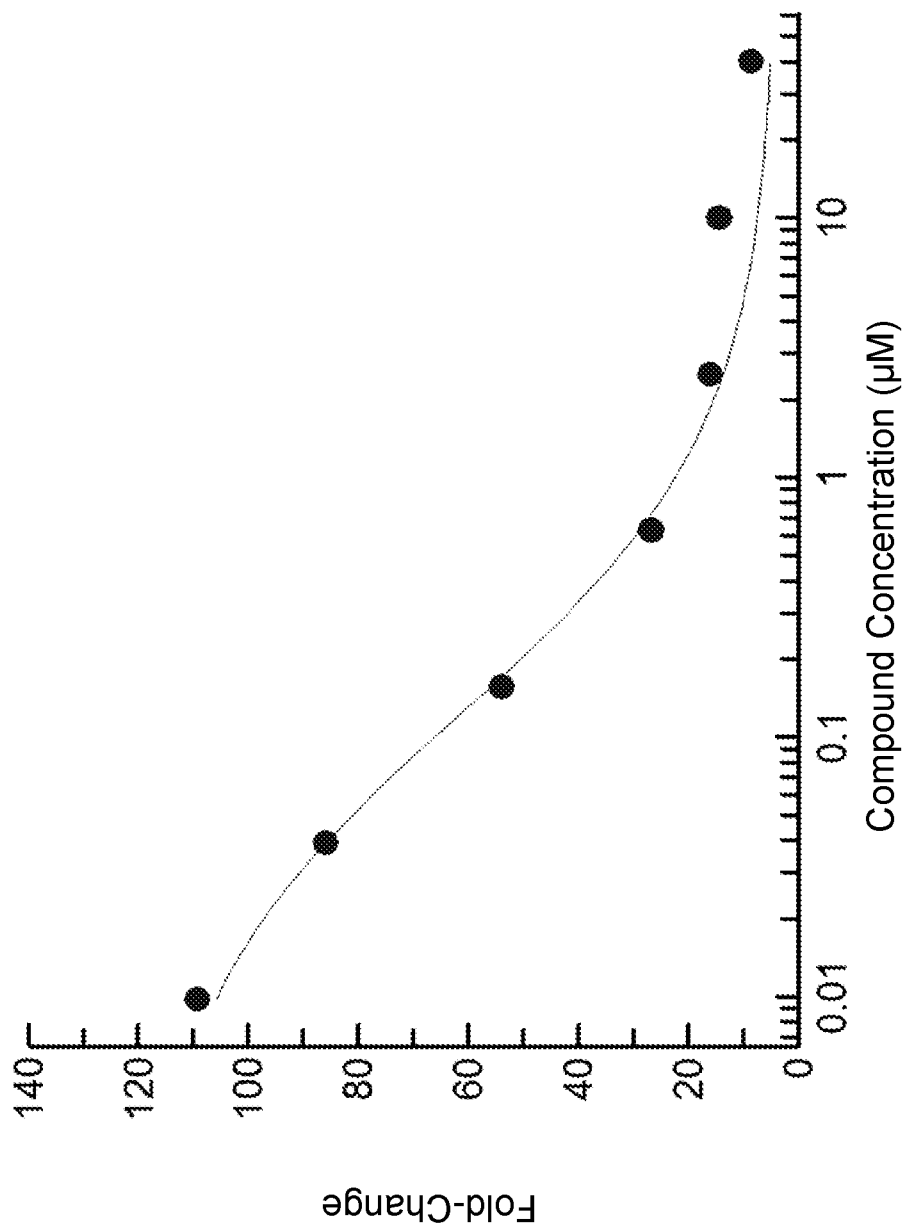


FIG. 47C

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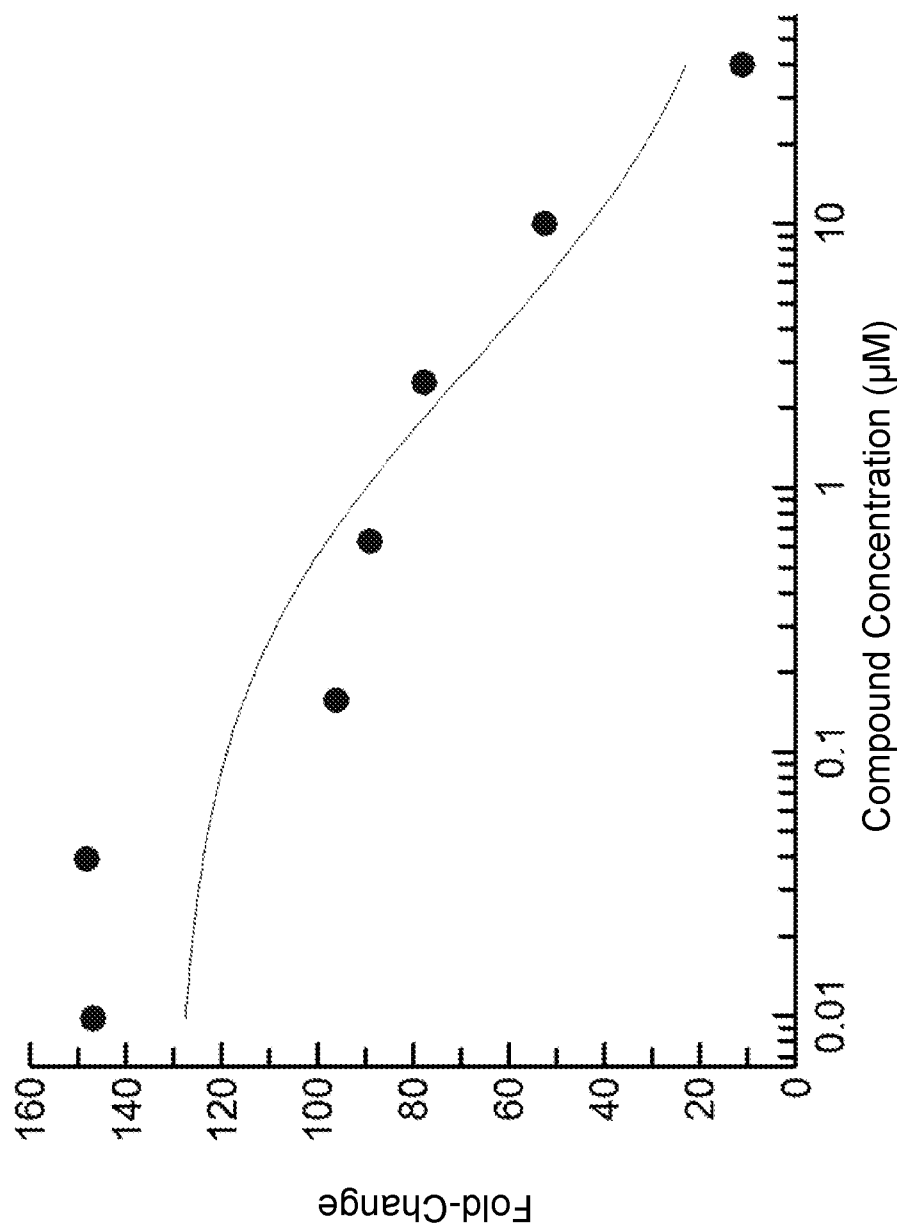


FIG. 47D

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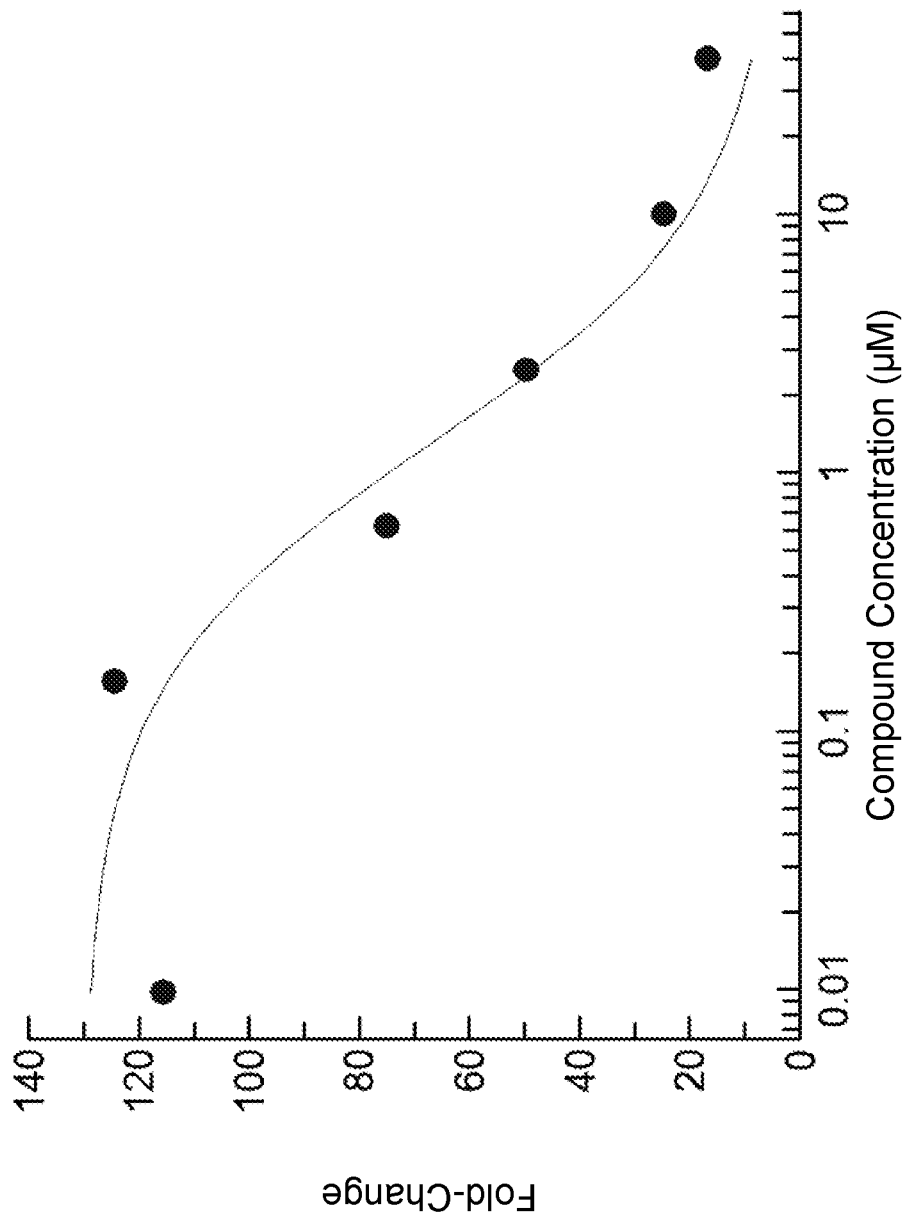


FIG. 47E

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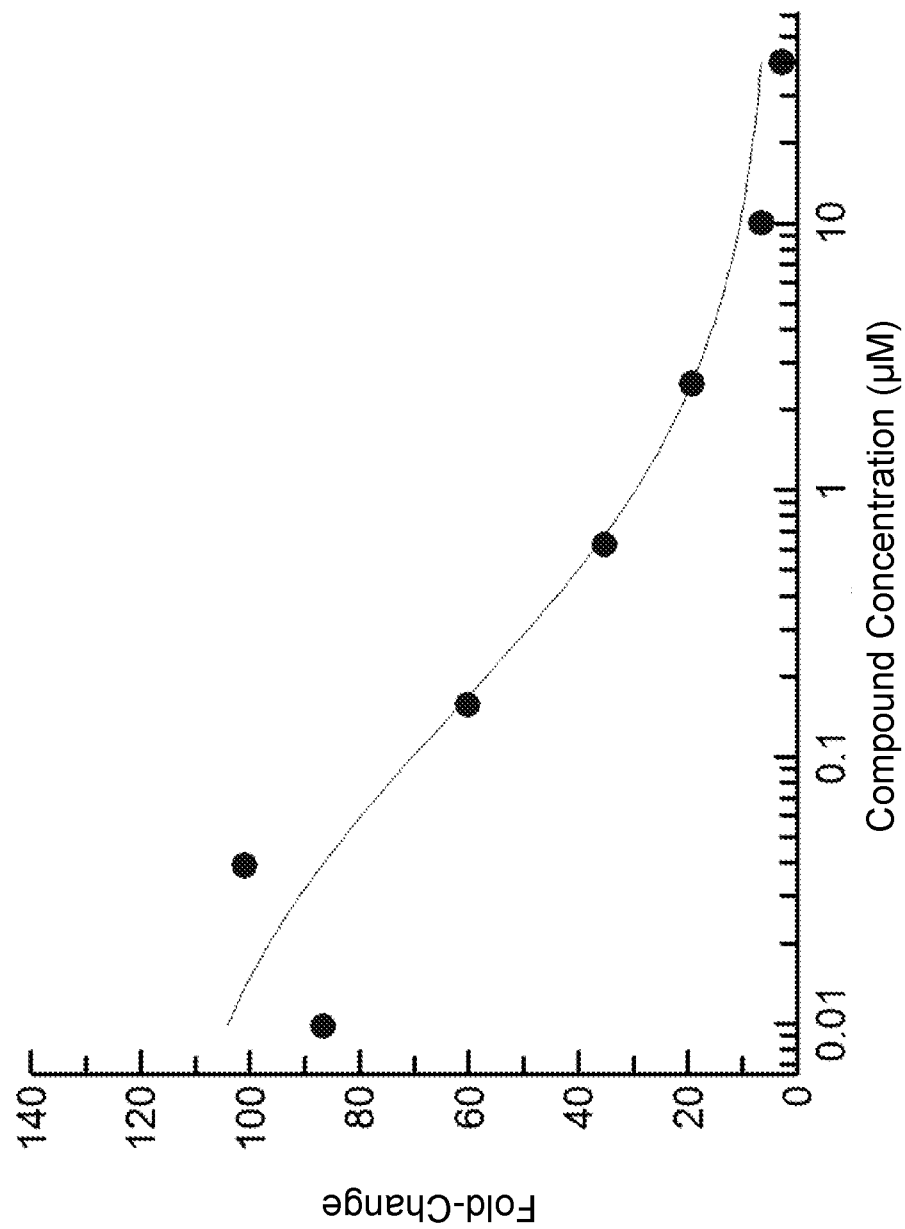


FIG. 47F

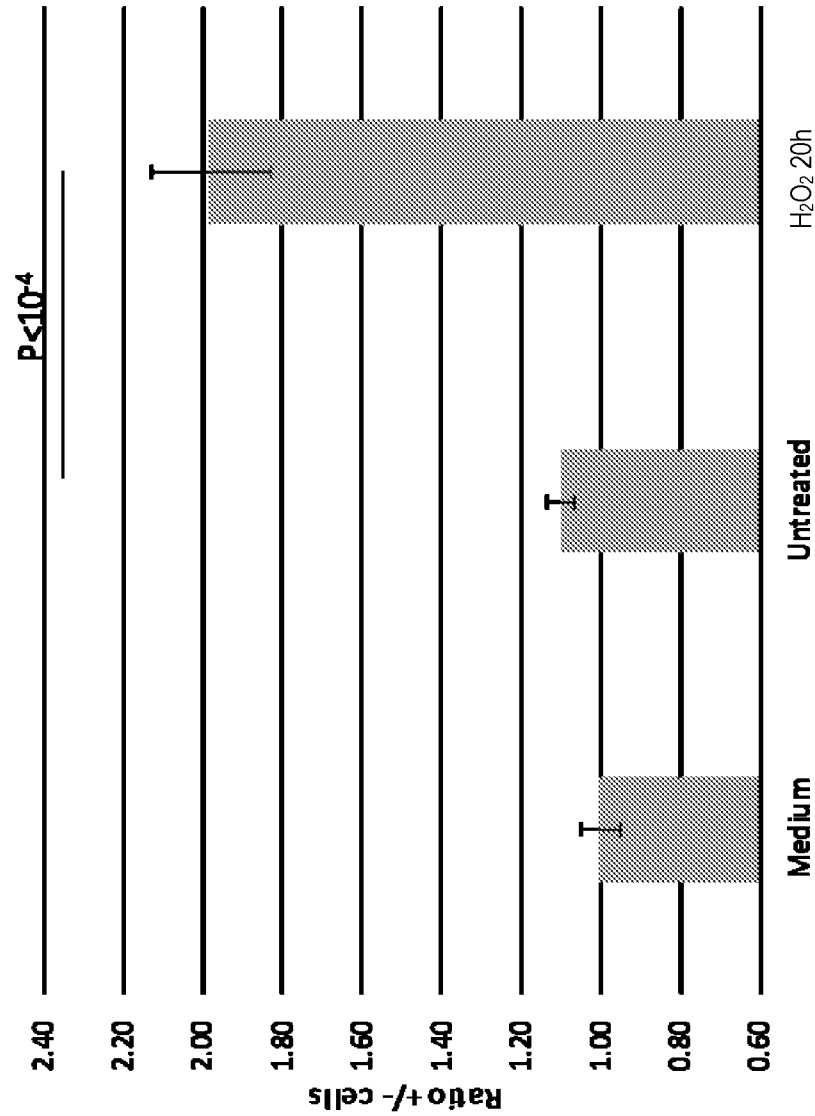


FIG. 48A

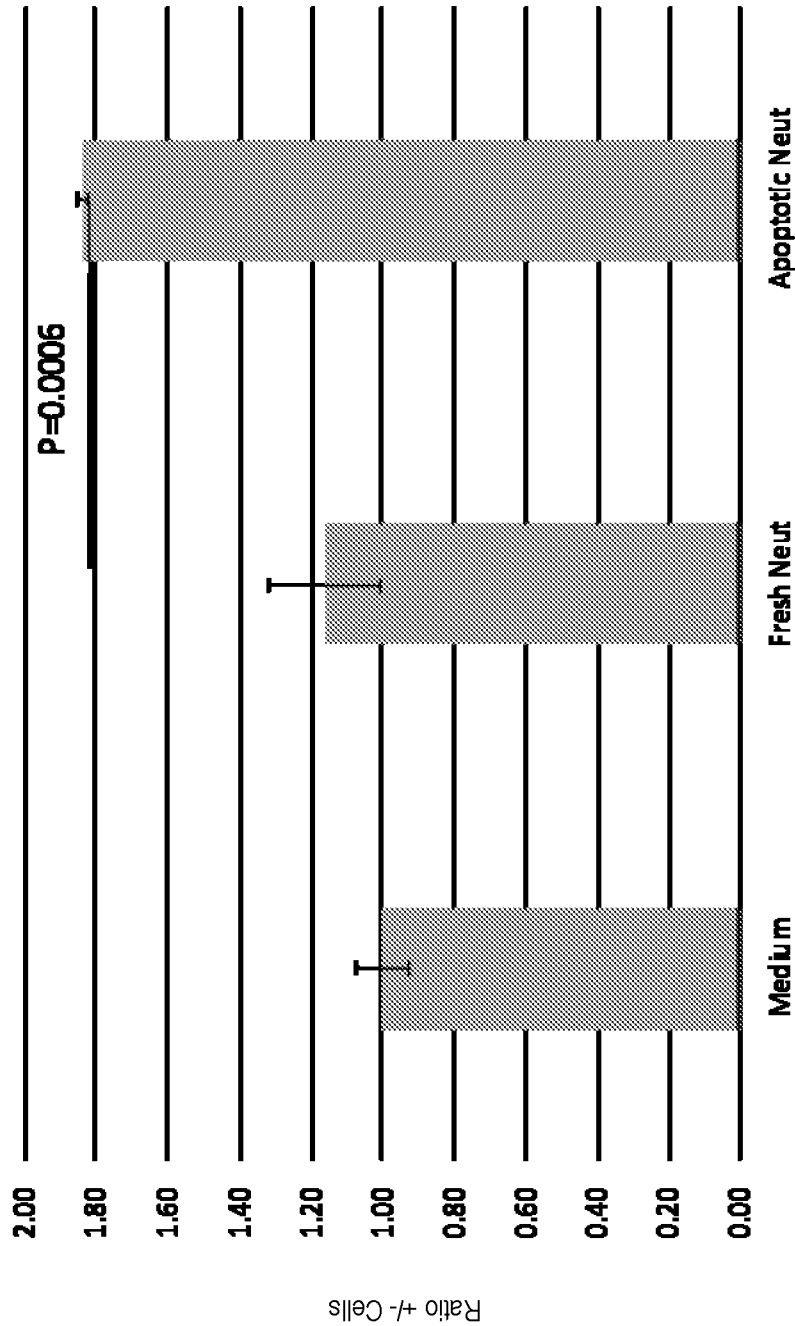


FIG. 48B

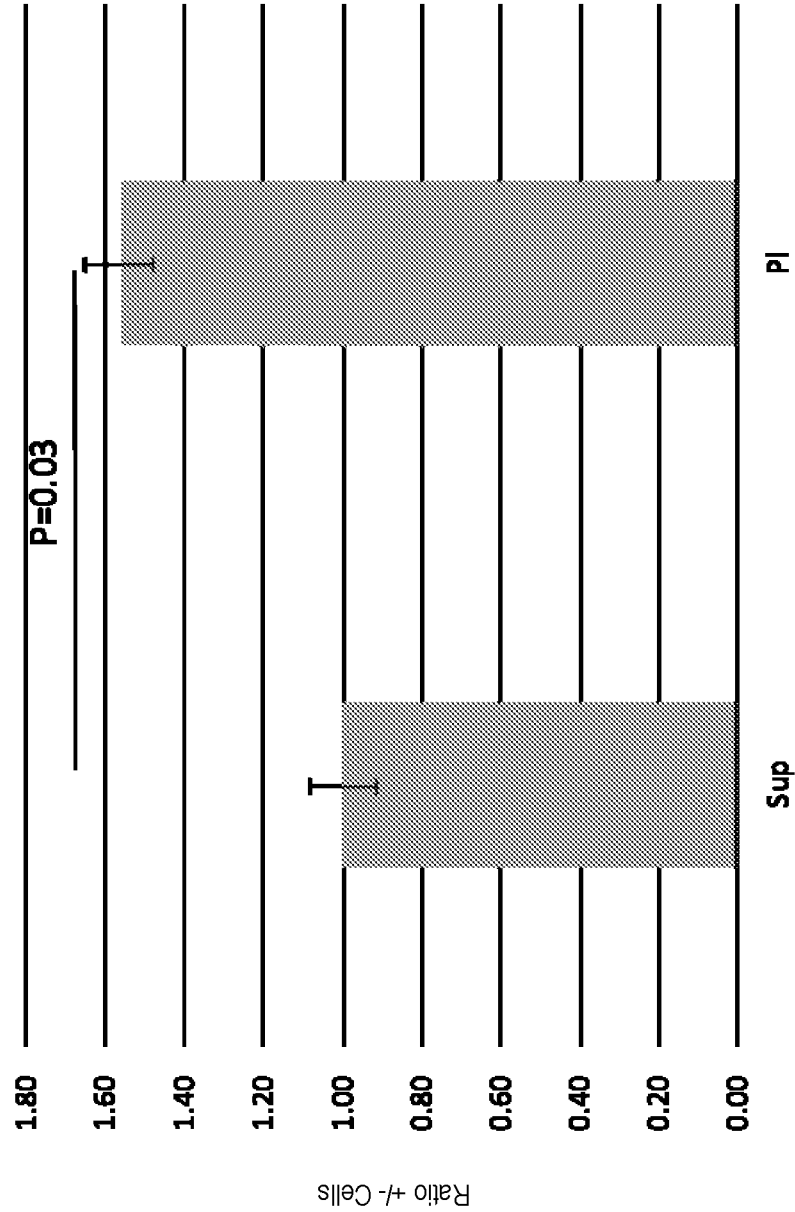


FIG. 48C

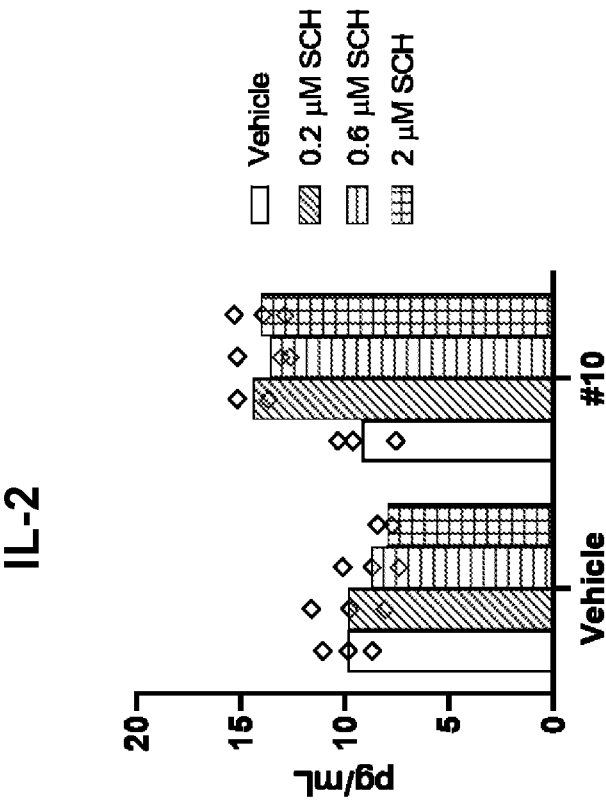


FIG. 49B

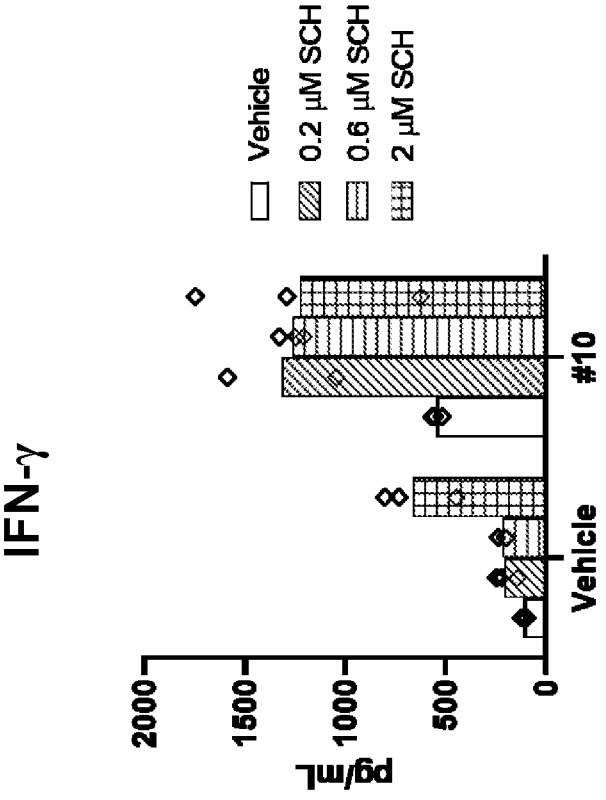


FIG. 49A

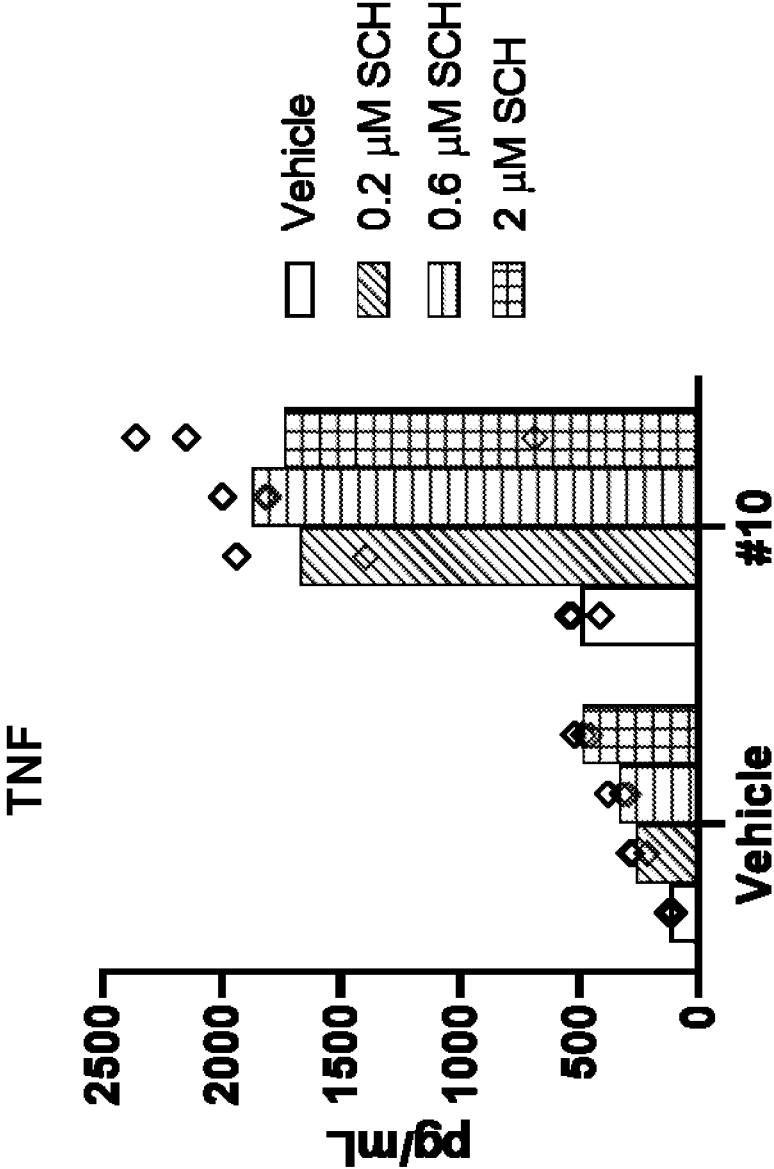


FIG. 49C

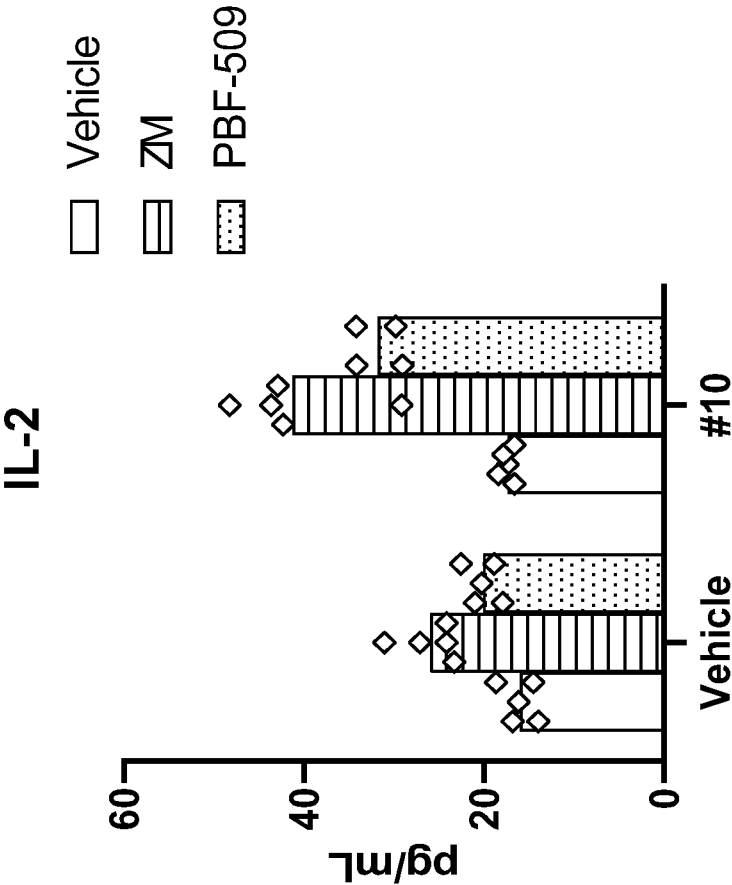


FIG. 50B

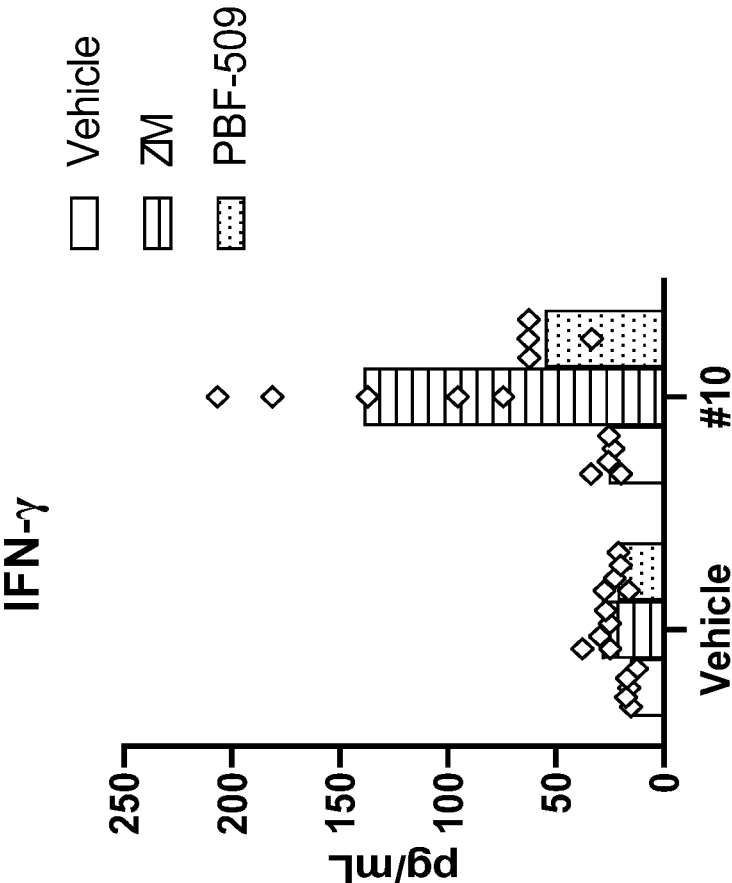


FIG. 50A

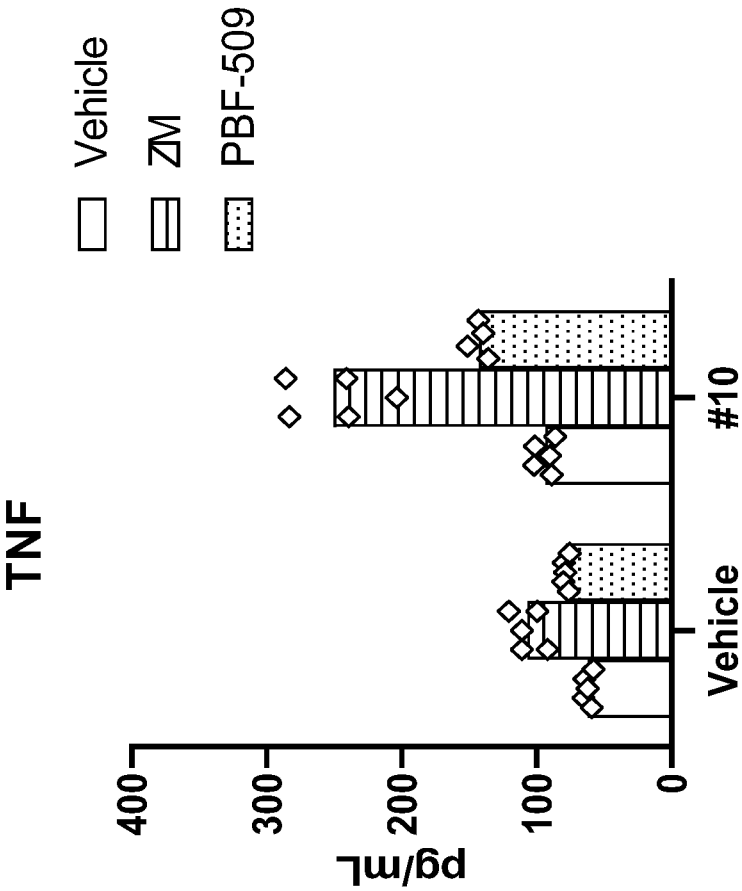


FIG. 50C

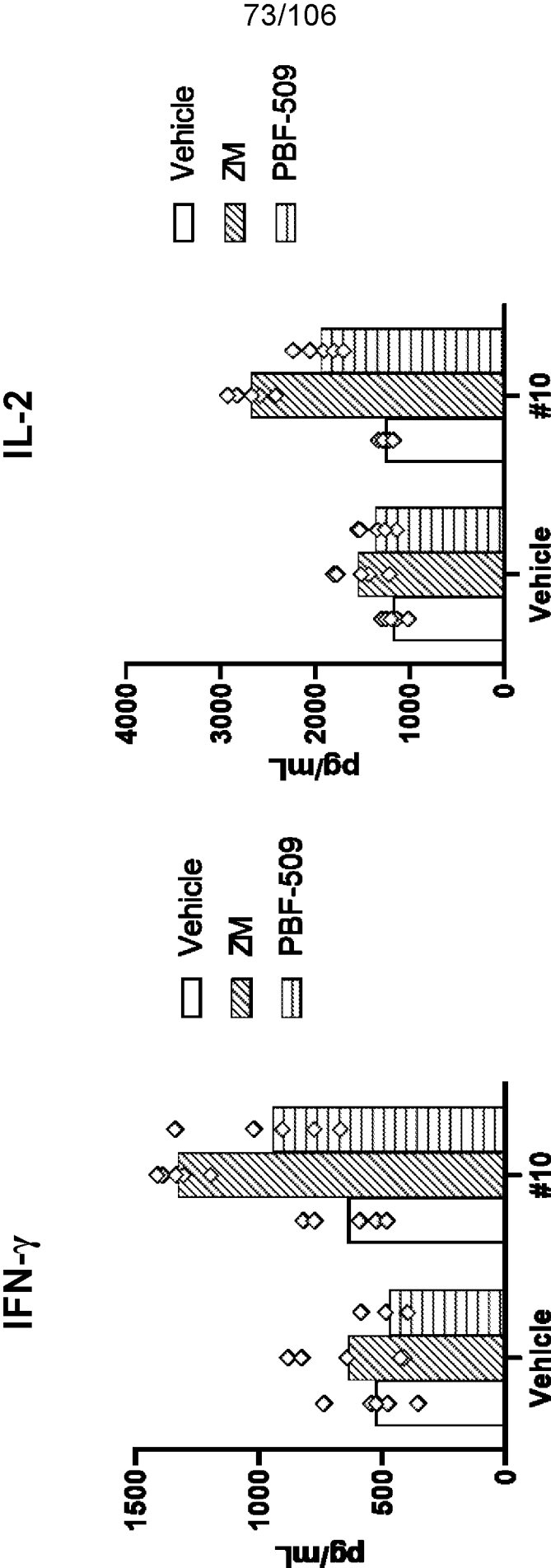


FIG. 51B

FIG. 51A

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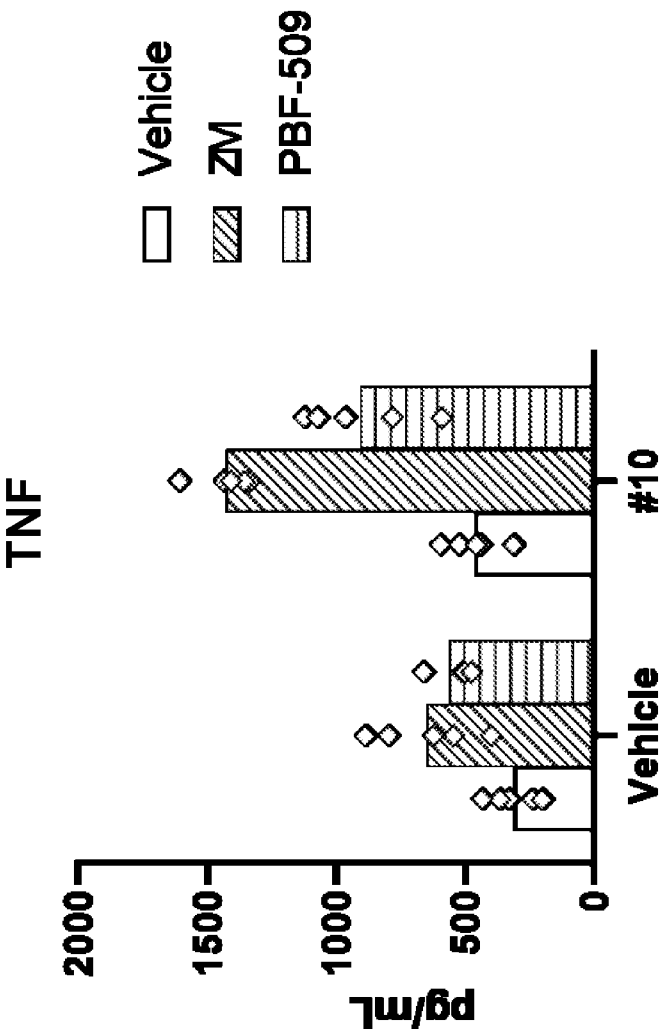


FIG. 51C

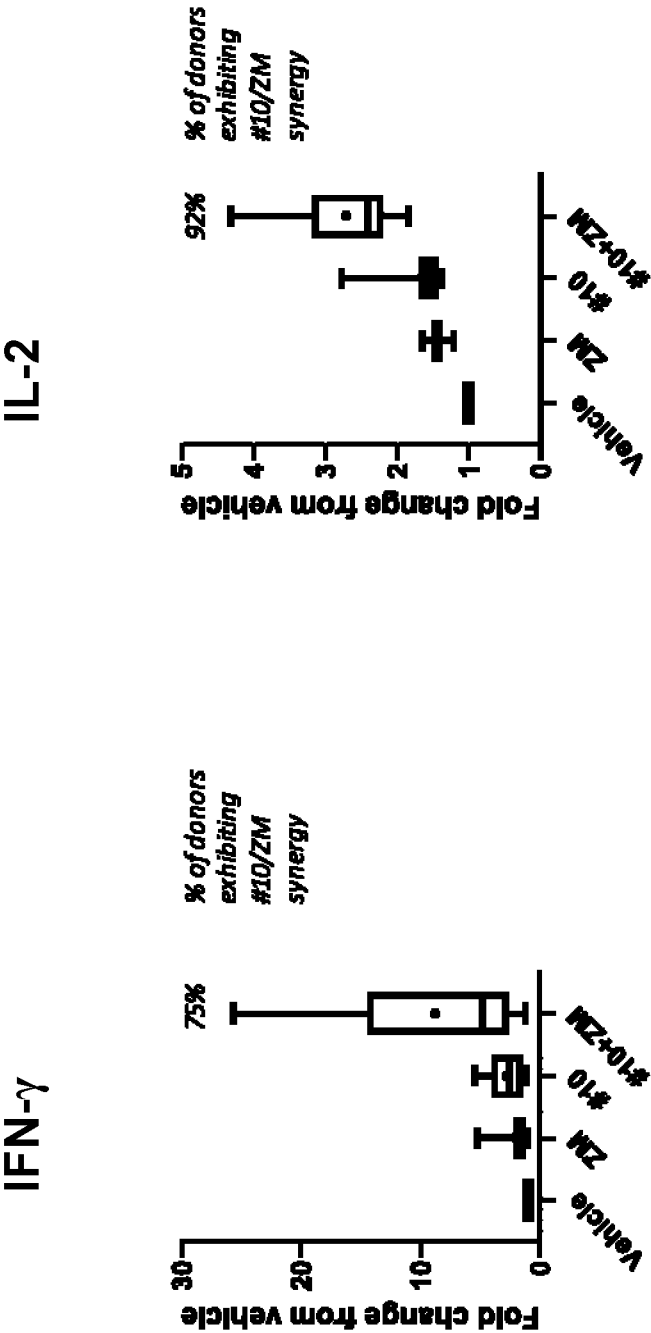


FIG. 52A

FIG. 52B

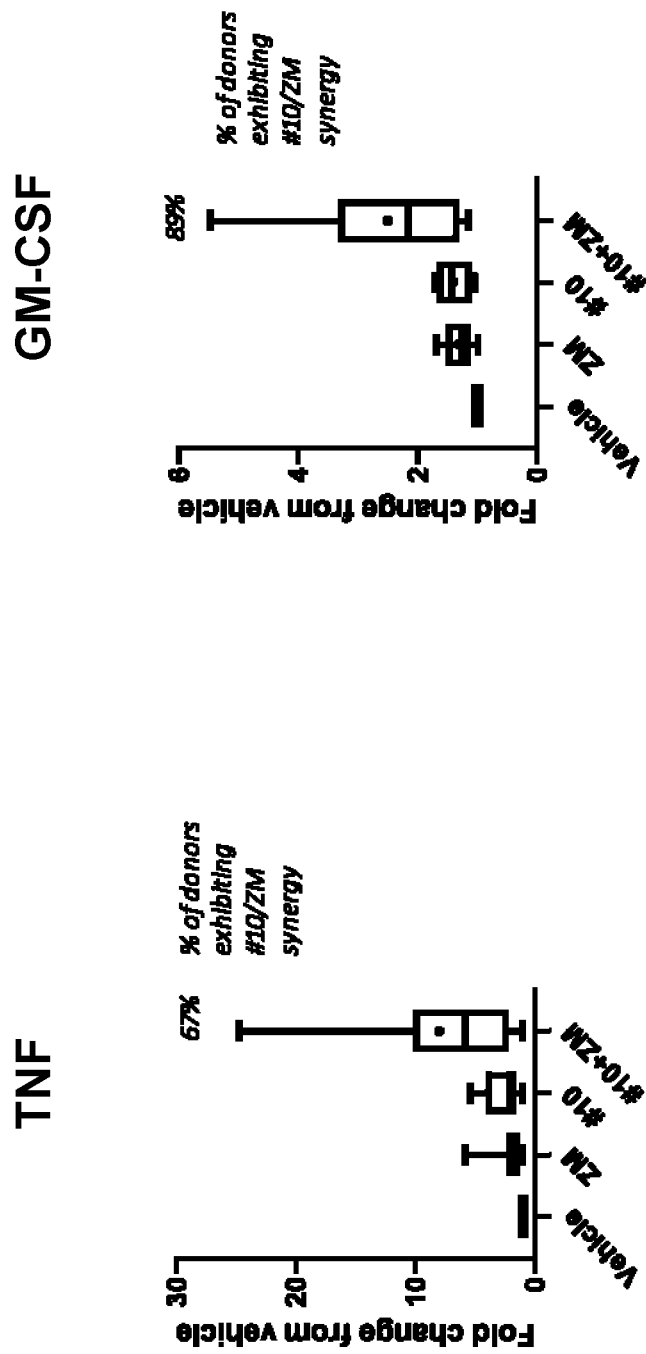


FIG. 52C

FIG. 52D

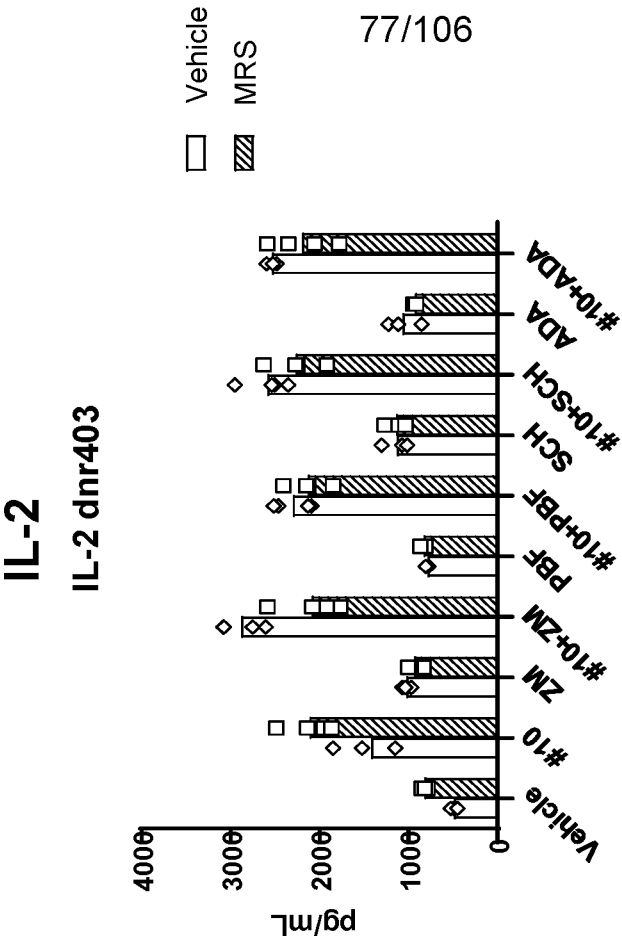


FIG. 53B

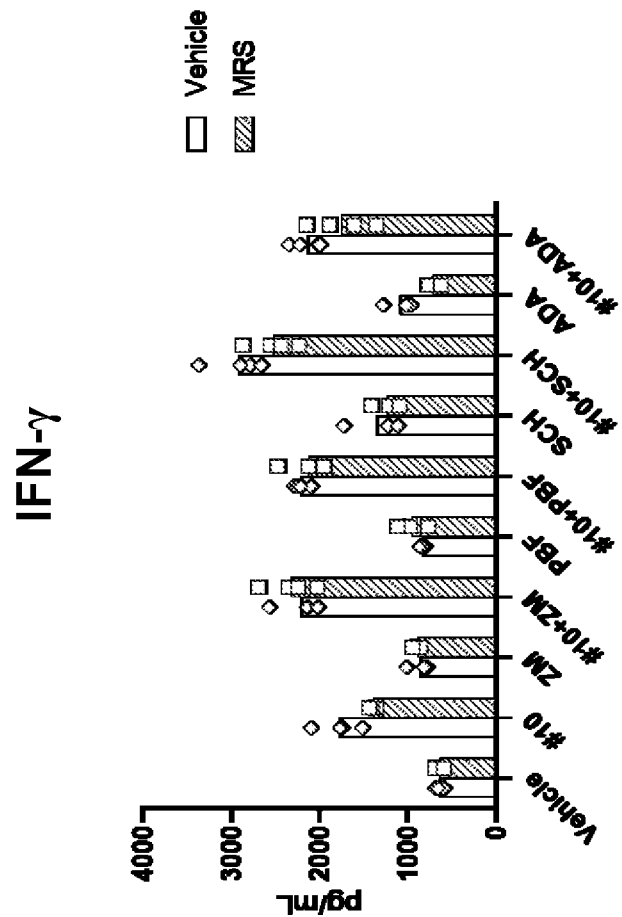


FIG. 53A

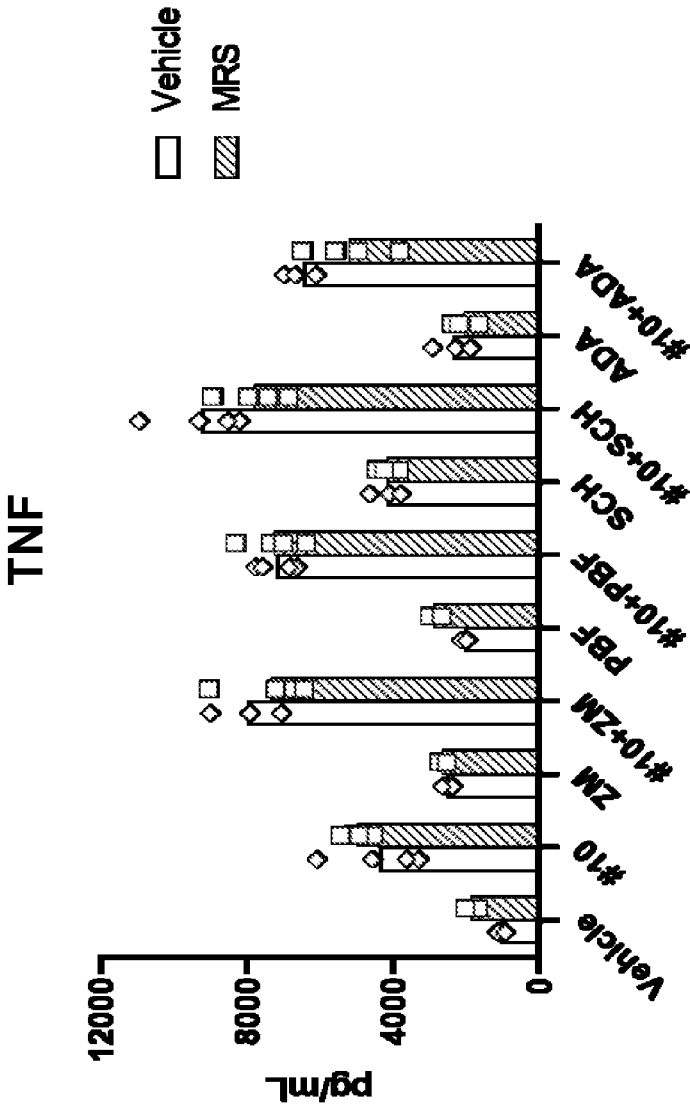


FIG. 53C

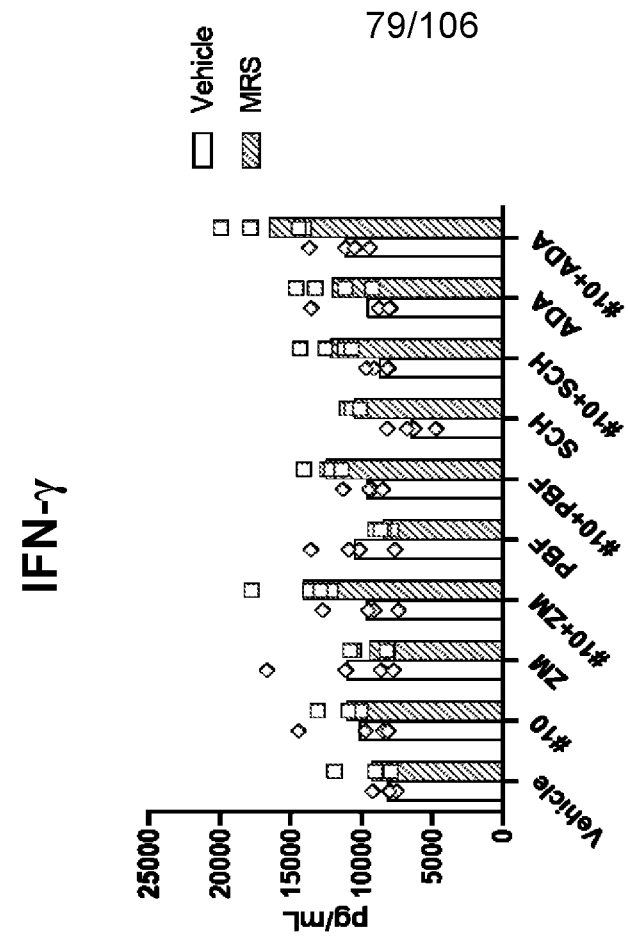


FIG. 54A

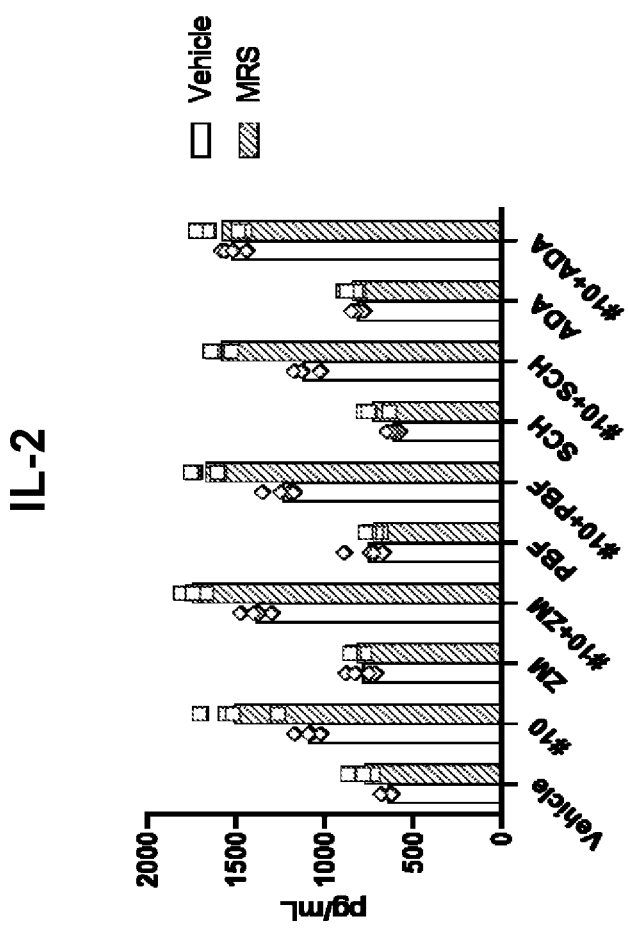


FIG. 54B

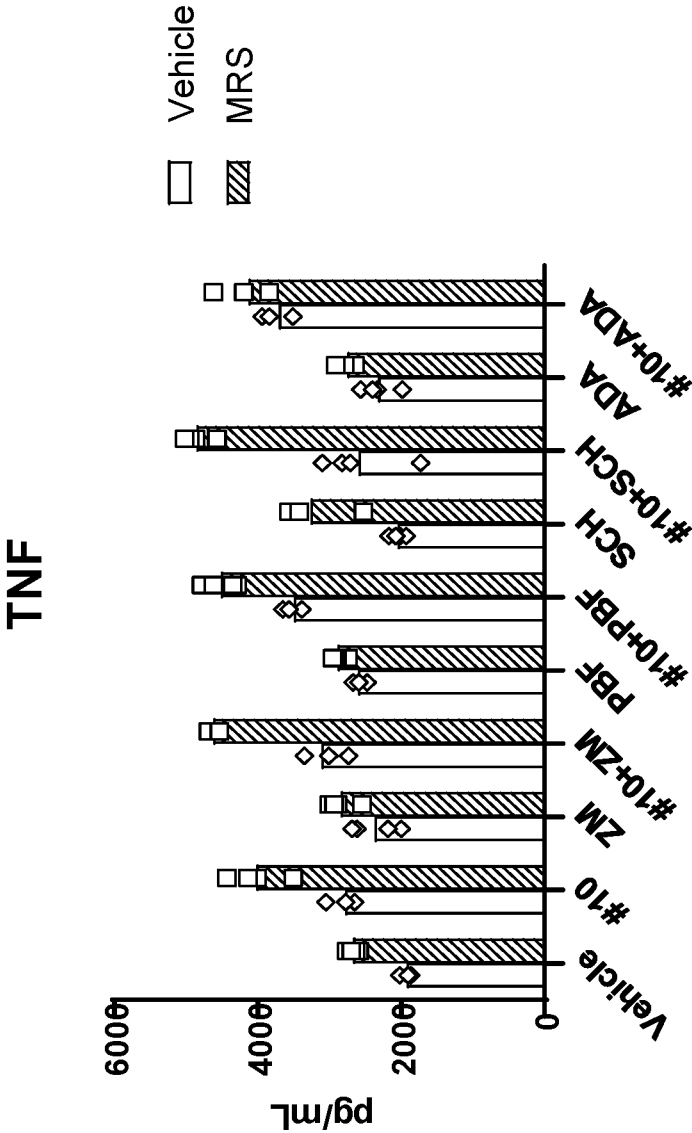


FIG. 54C

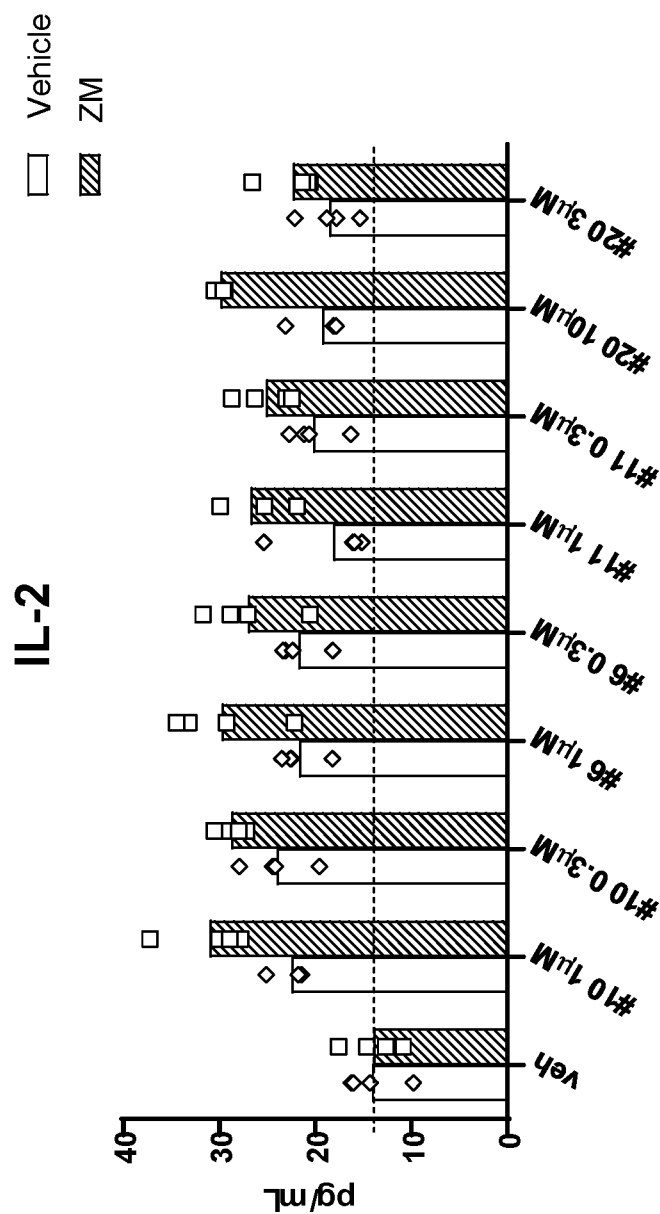


FIG. 55A

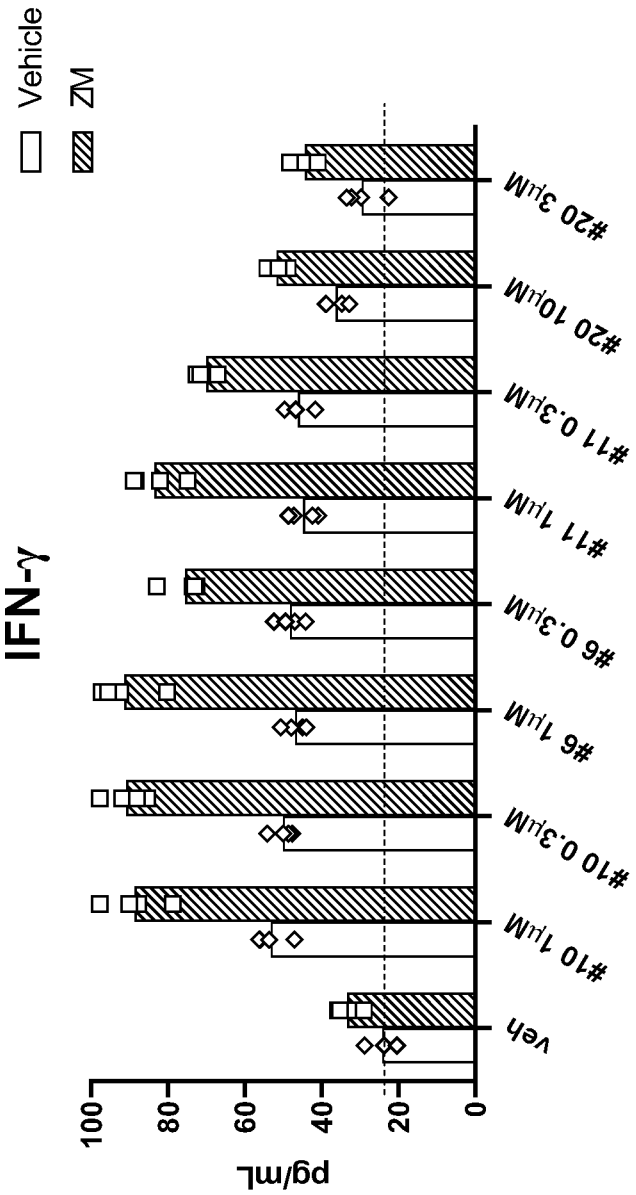


FIG. 55B

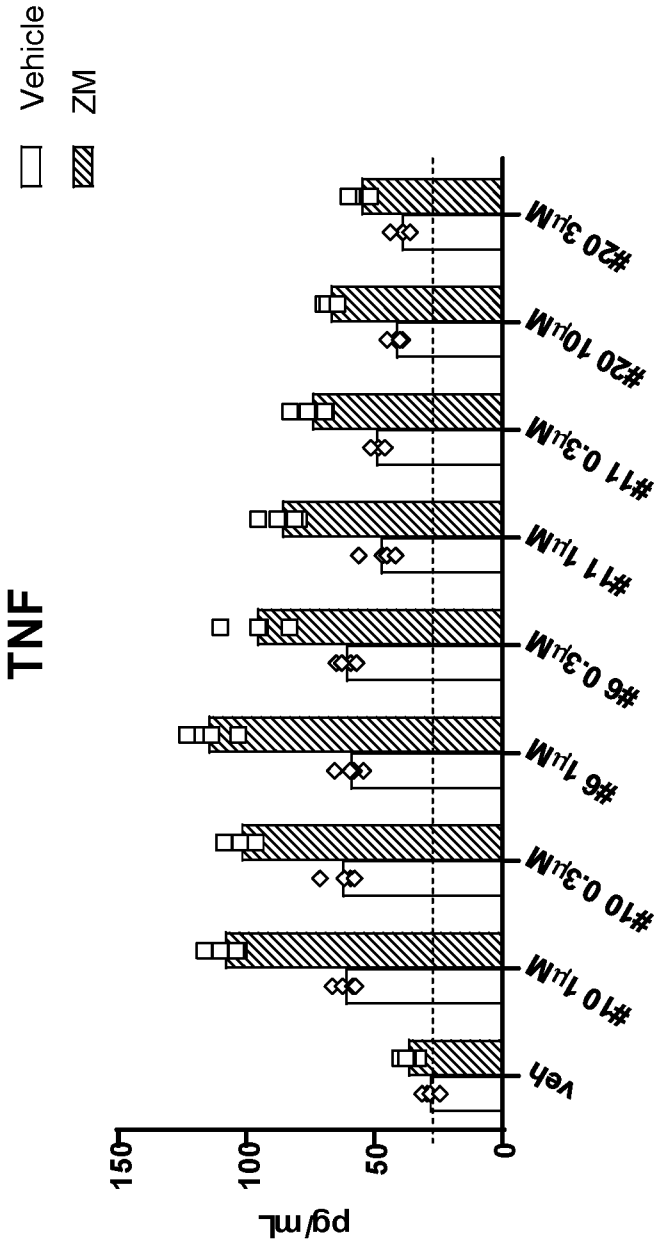


FIG. 55C

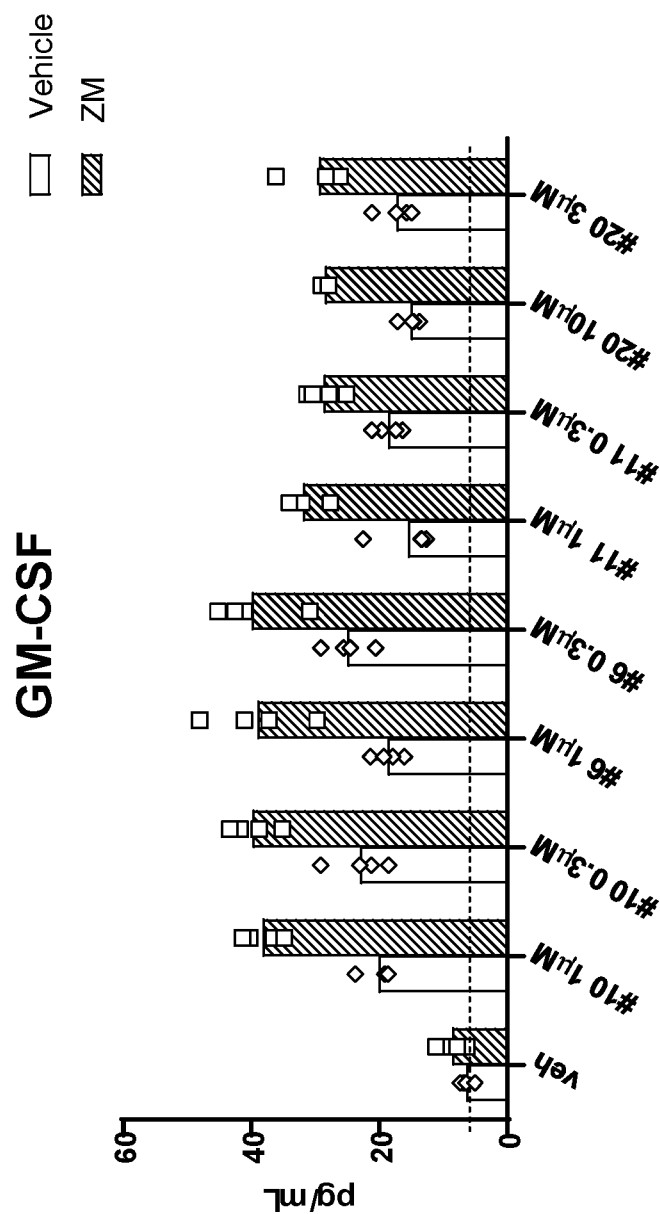


FIG. 55D

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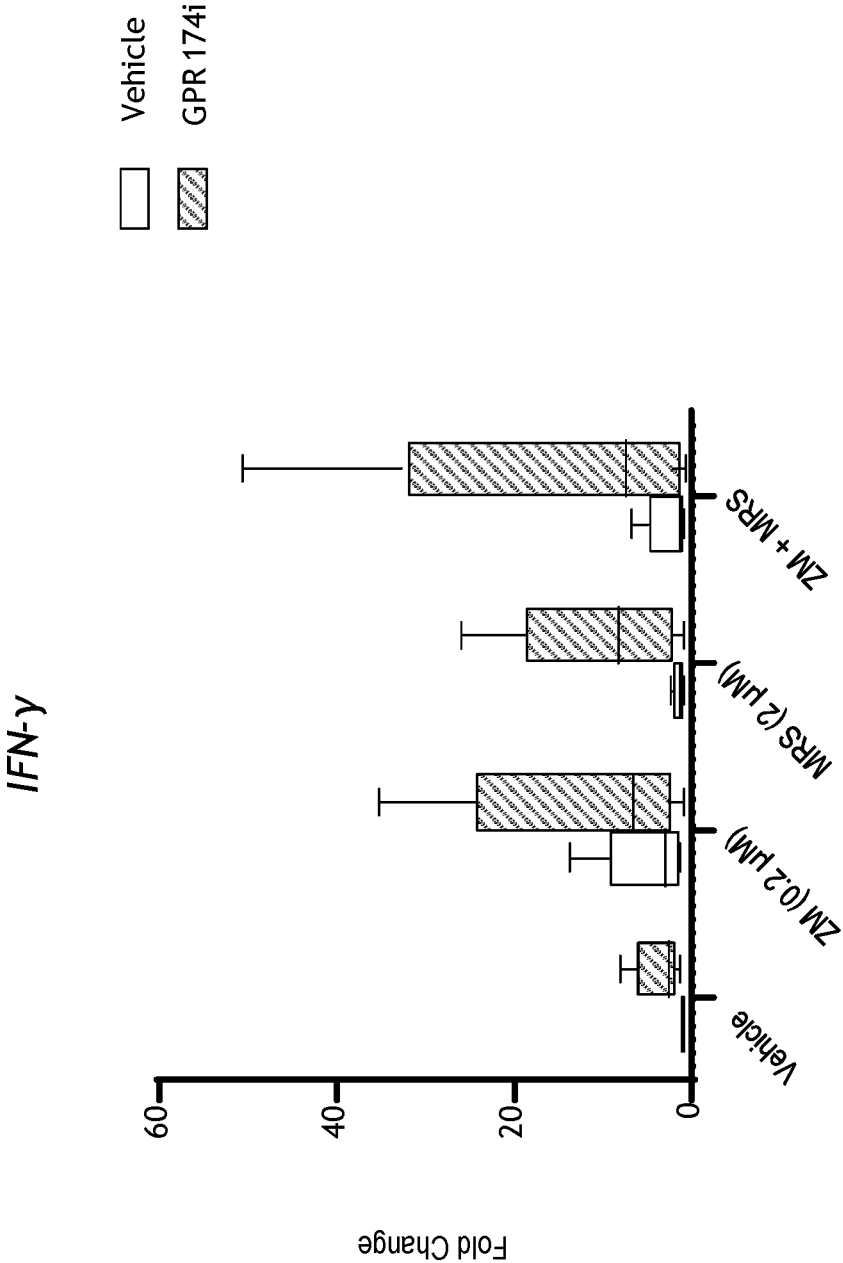


FIG. 56A

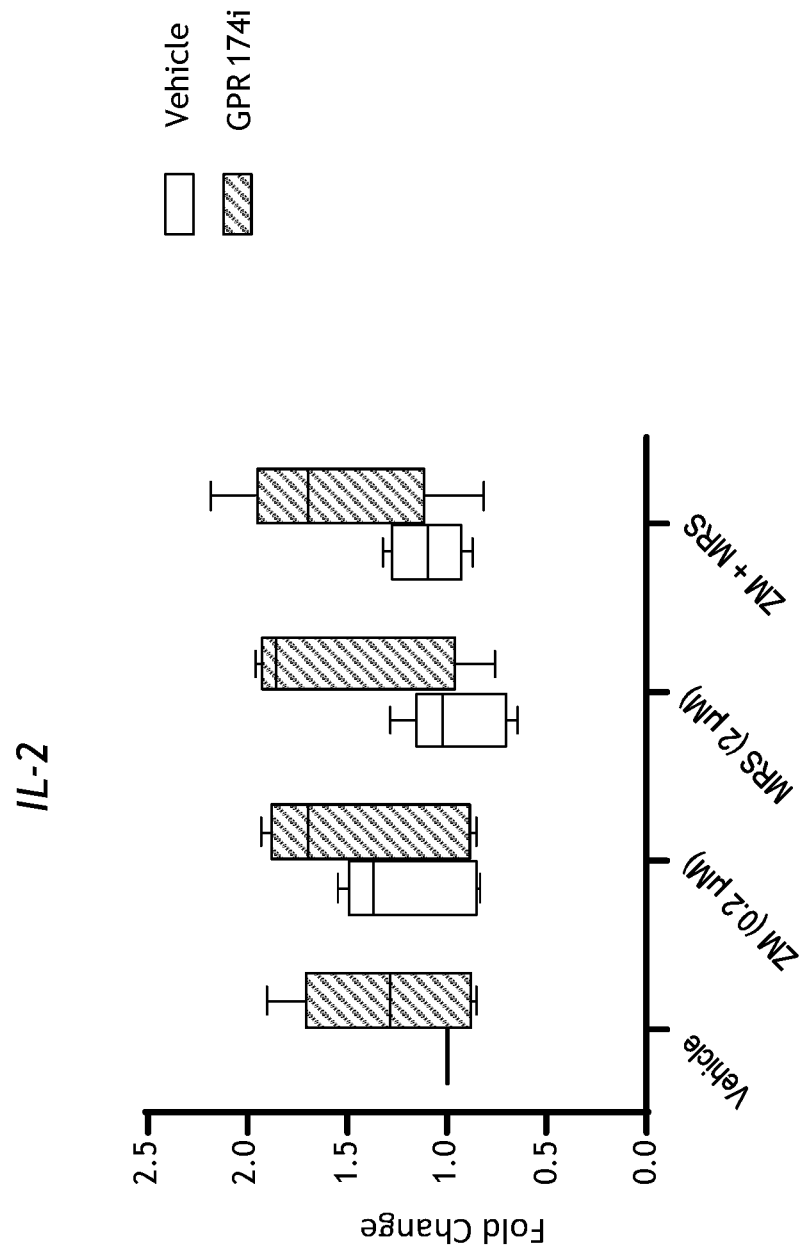


FIG. 56B

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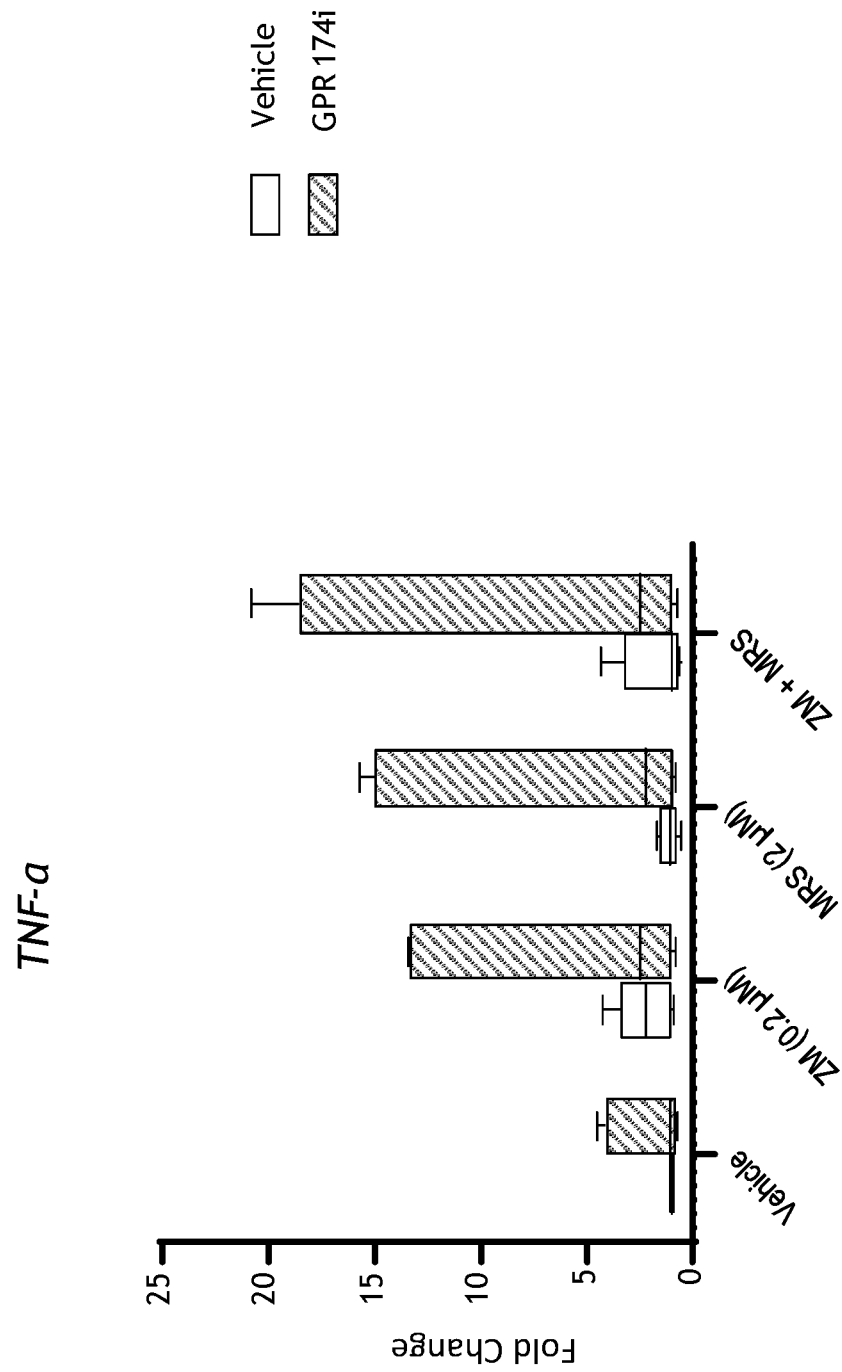


FIG. 56C

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Activated CD4+ T cells

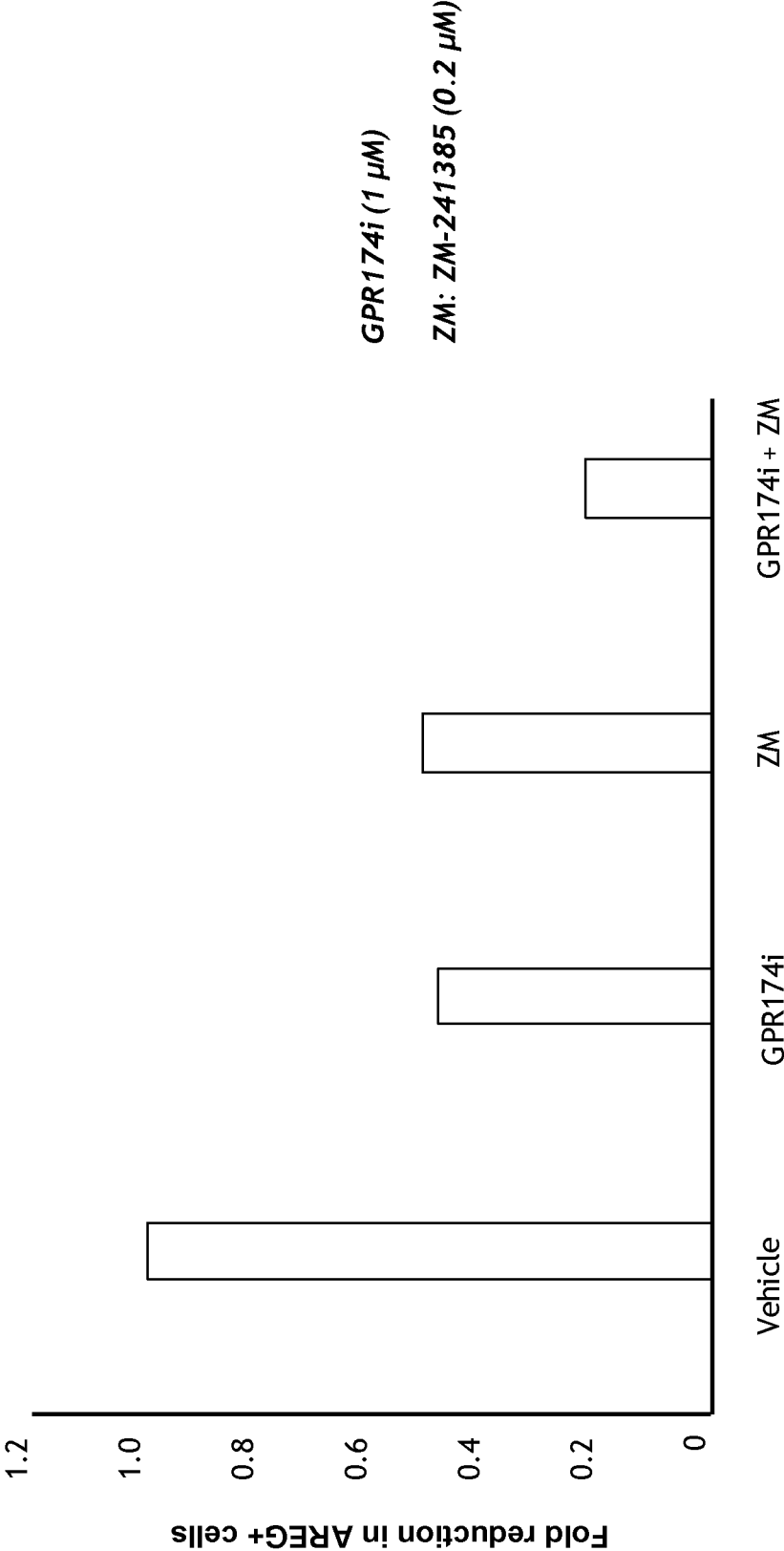


FIG. 57

Both GPR174 and Adenosine Receptors
Respond to Products of Cell Stress & Death

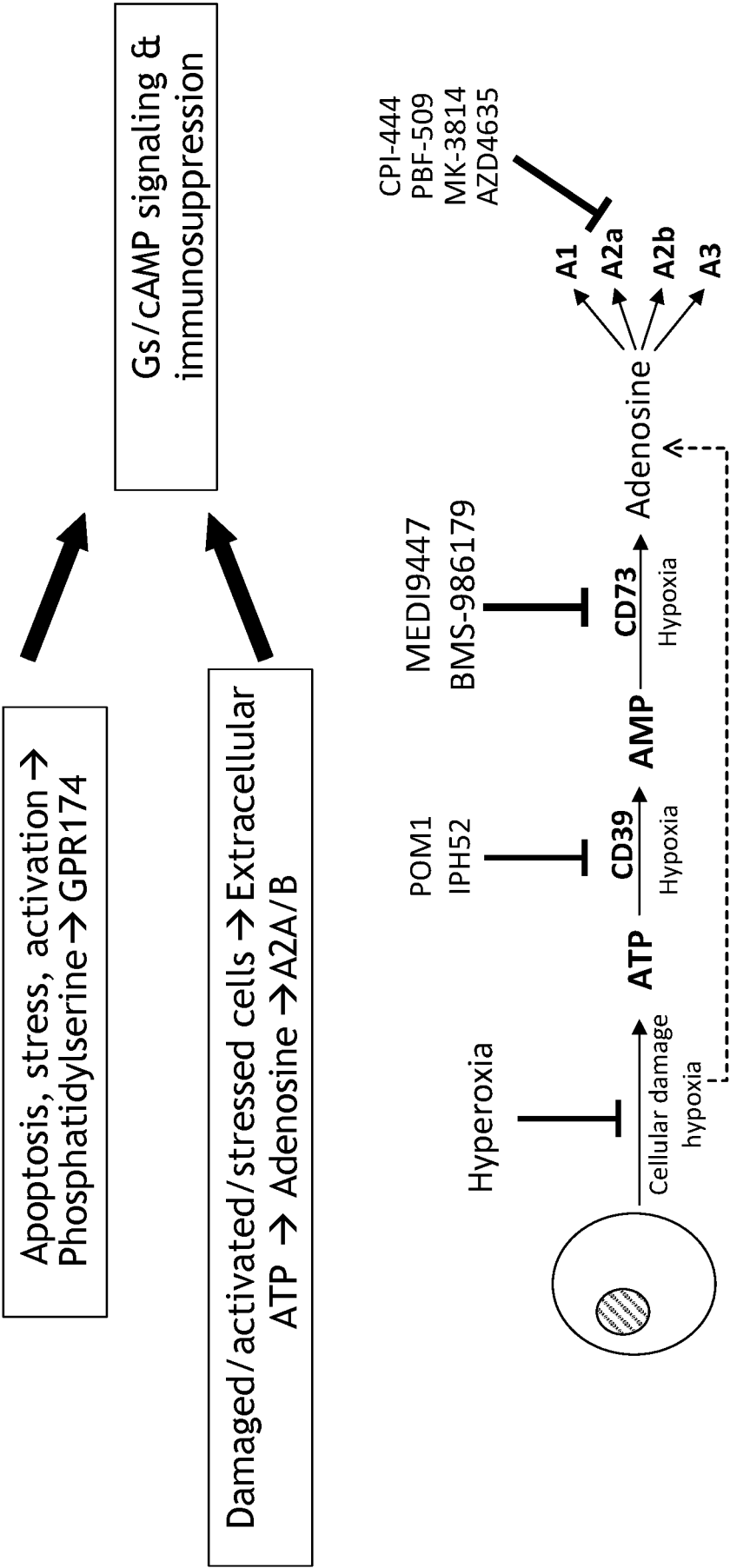


FIG. 58

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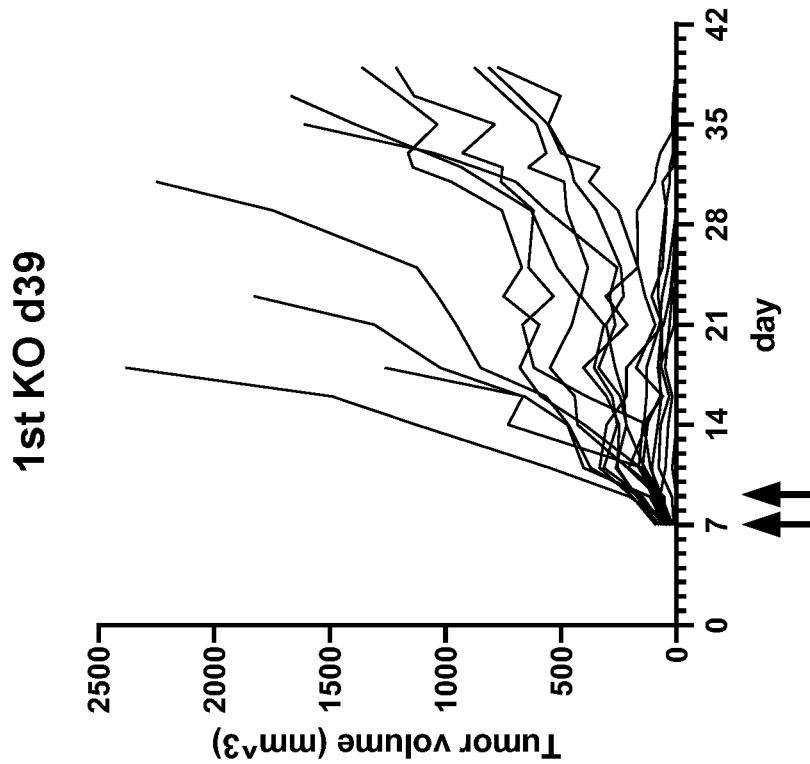


FIG. 59B

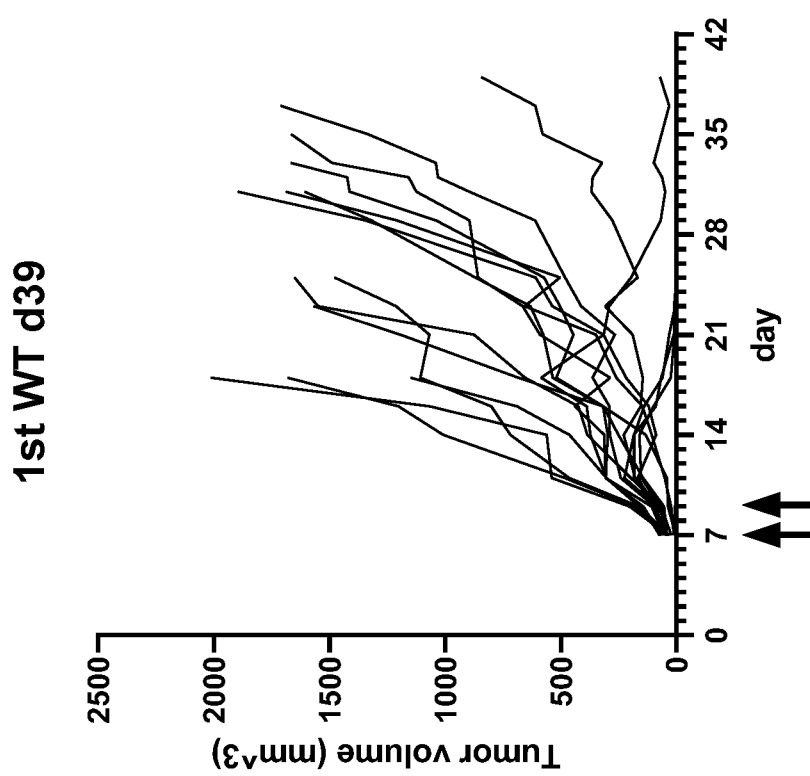


FIG. 59A

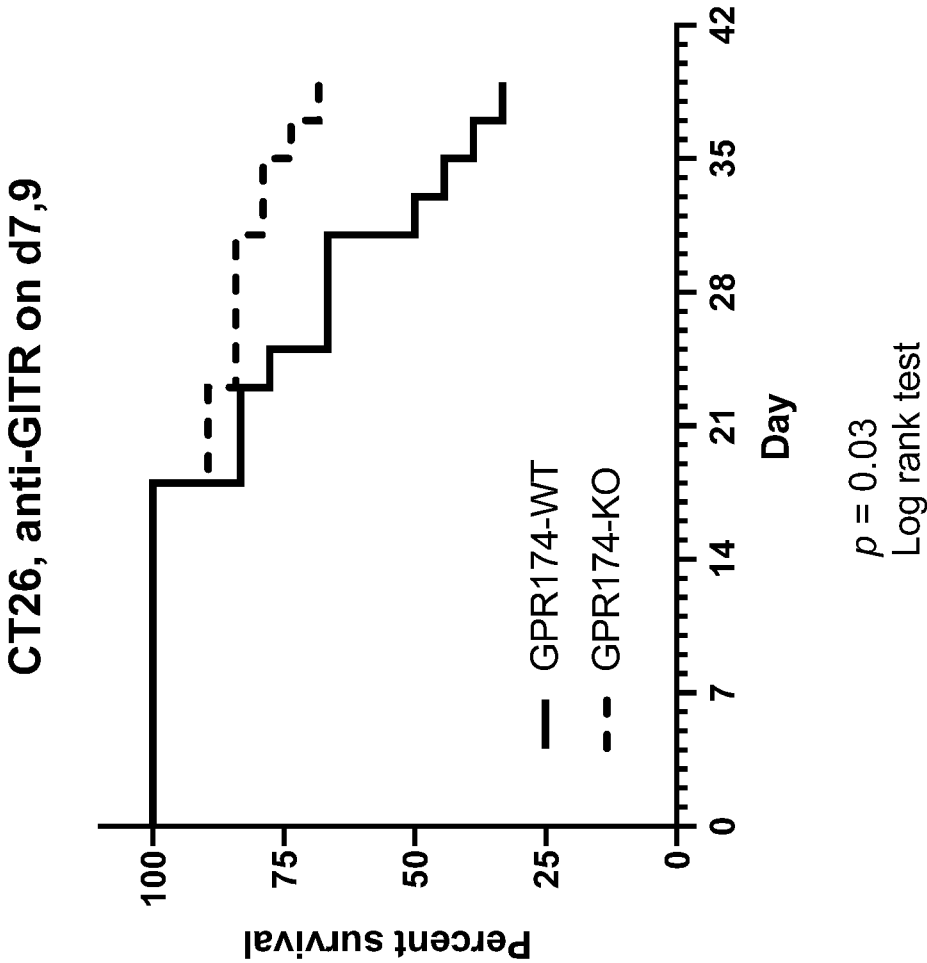


FIG. 60

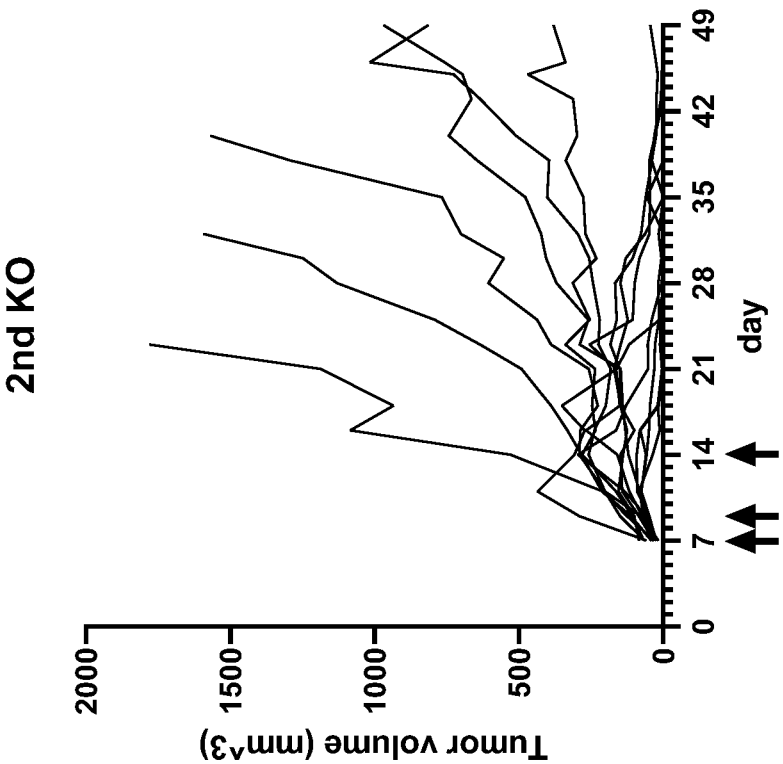


FIG. 61B

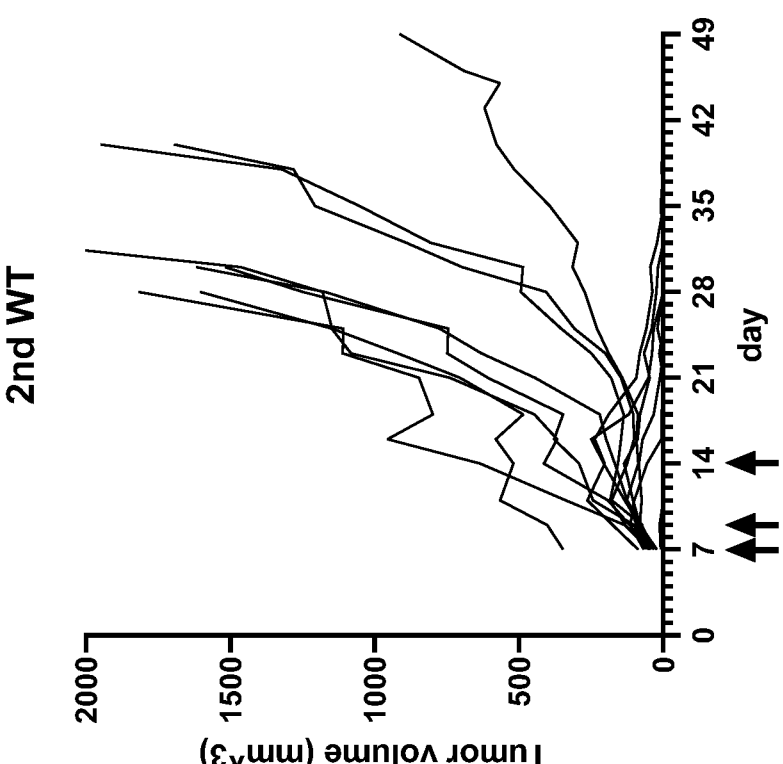


FIG. 61A

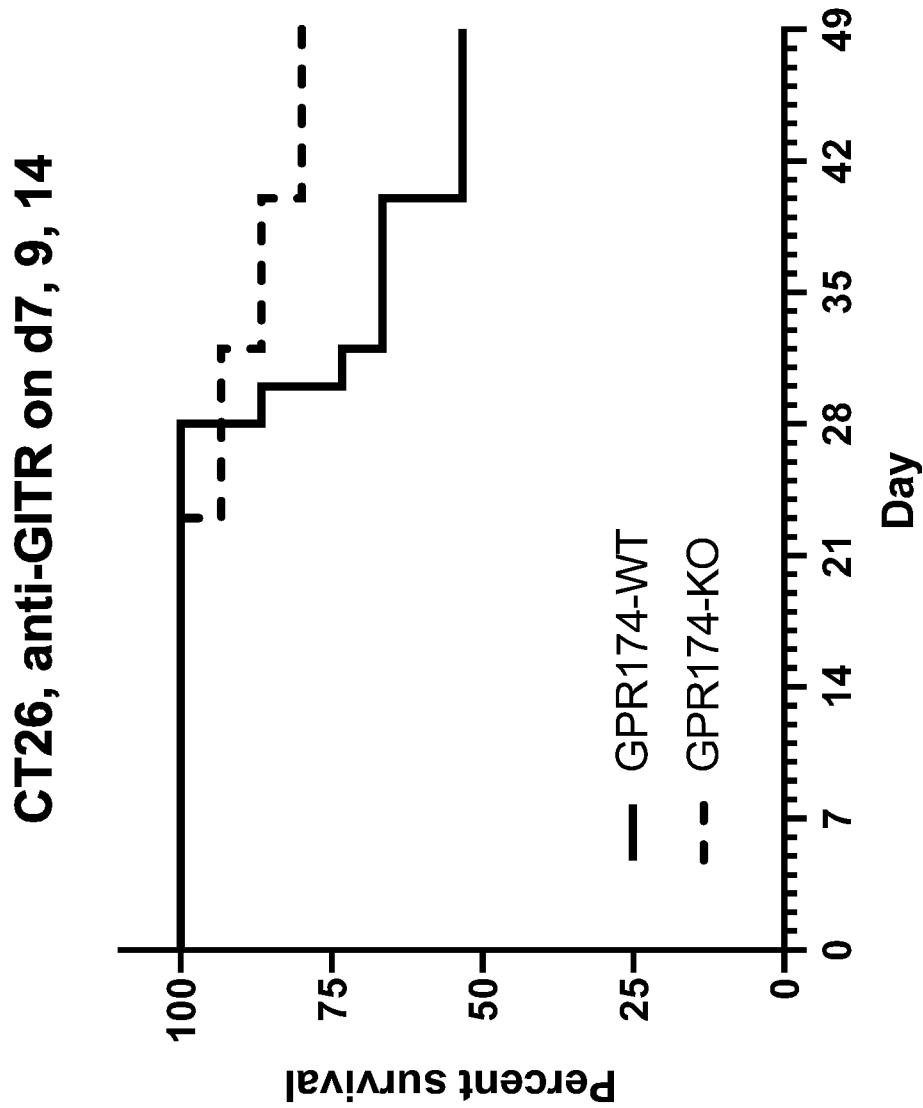


FIG. 62

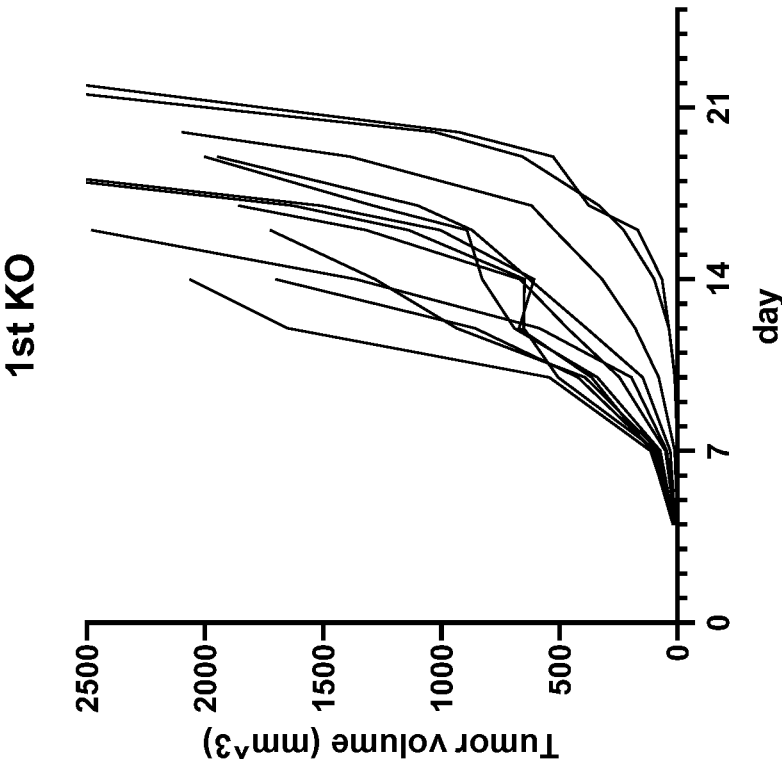


FIG. 63B

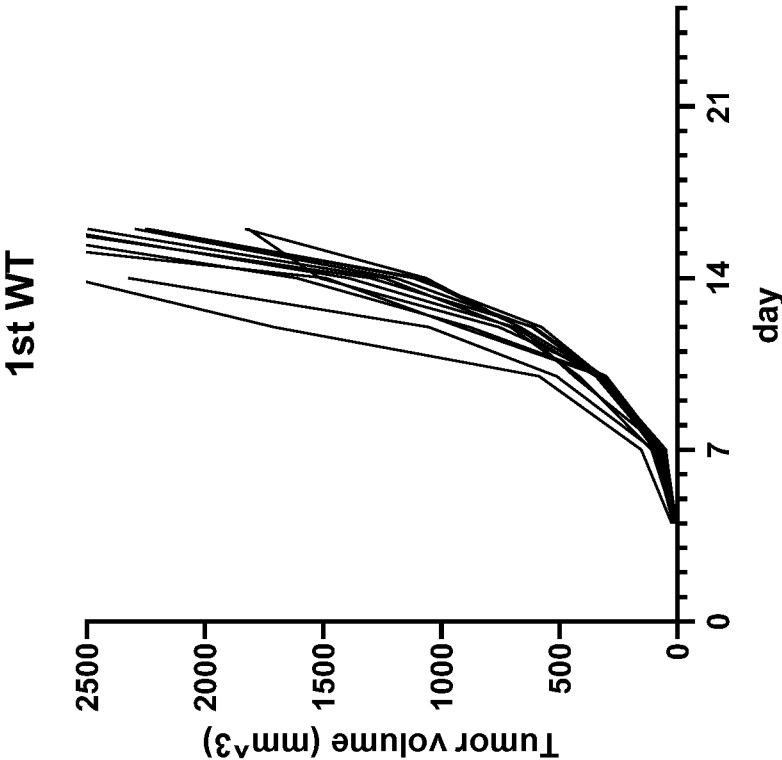


FIG. 63A

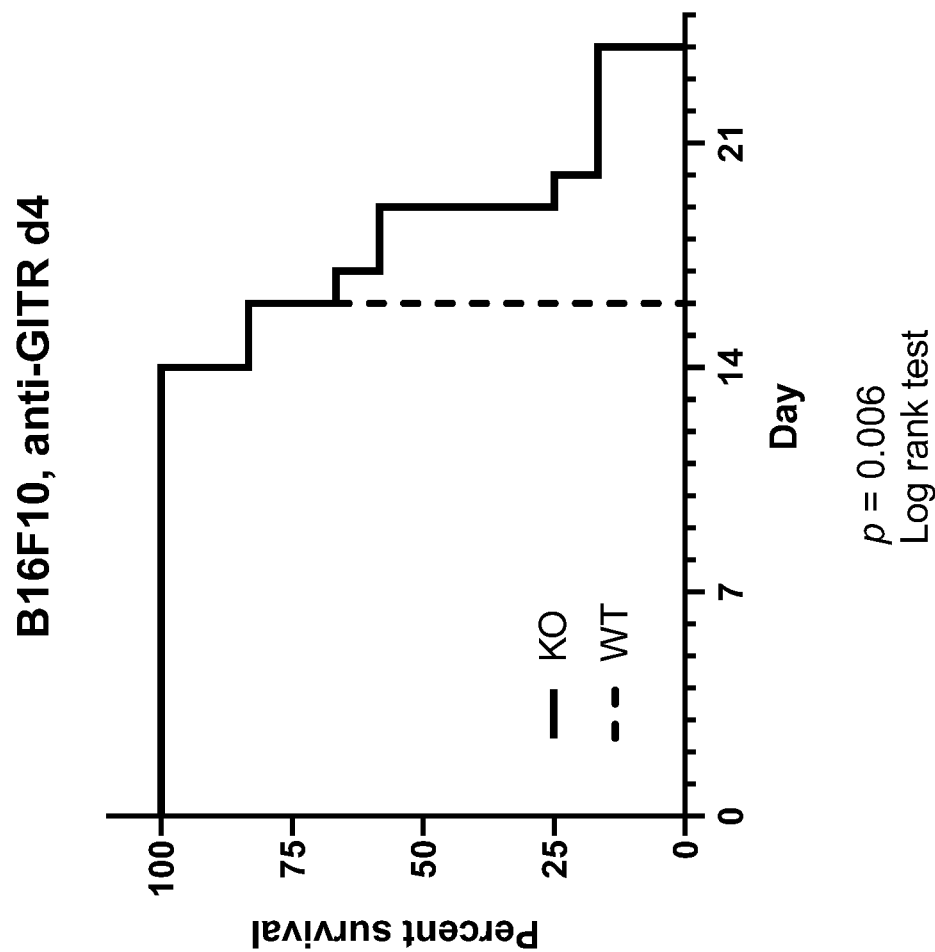


FIG. 64

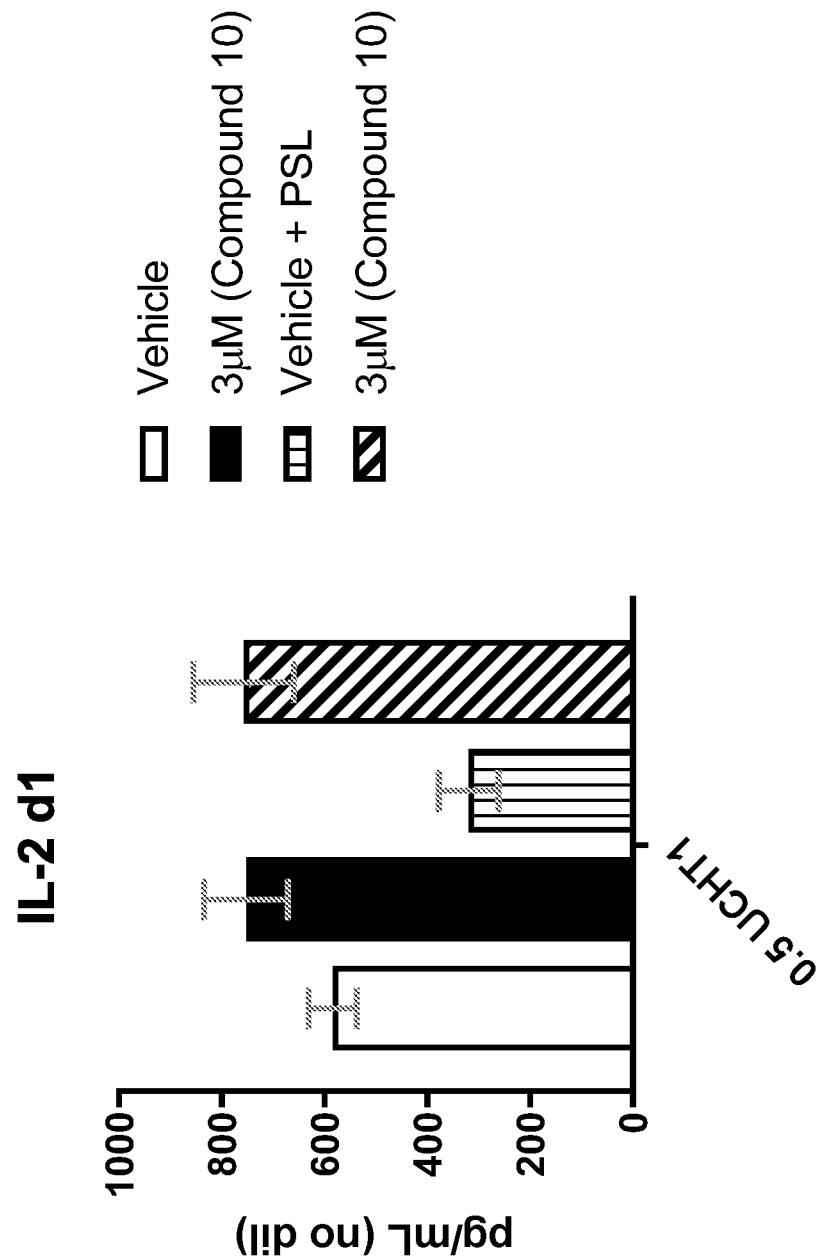


FIG. 65

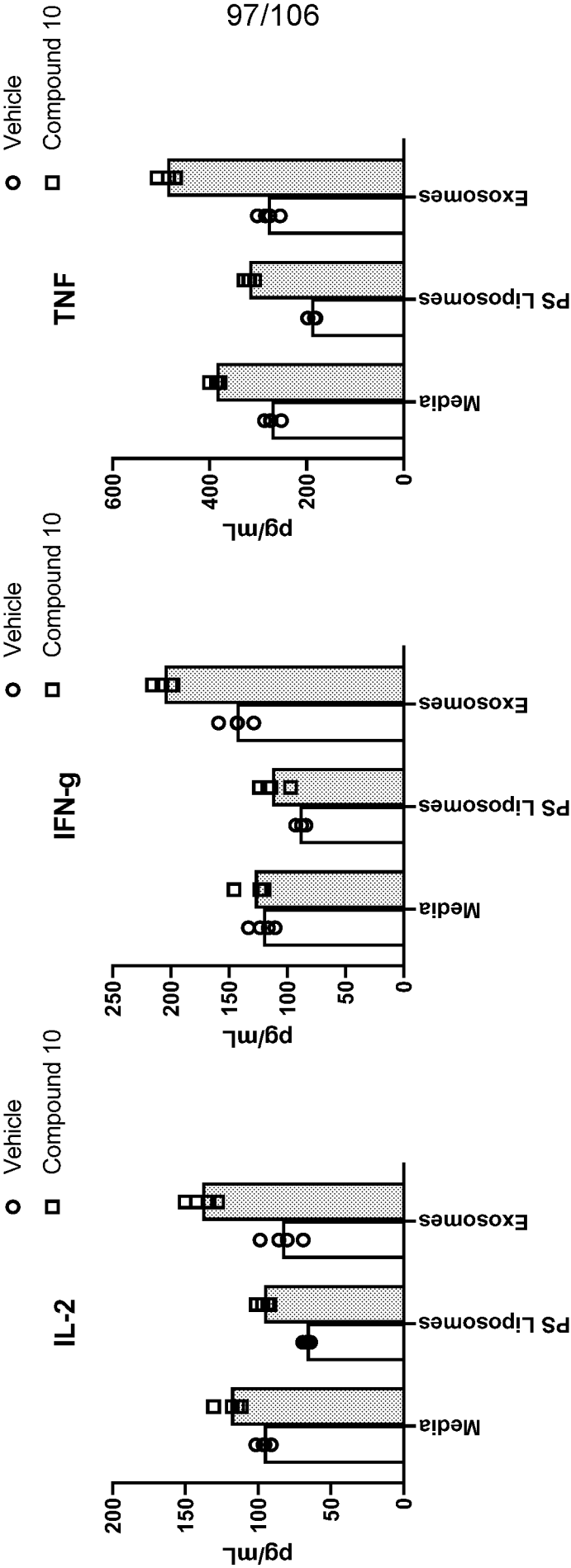


FIG. 66A

FIG. 66B

FIG. 66C

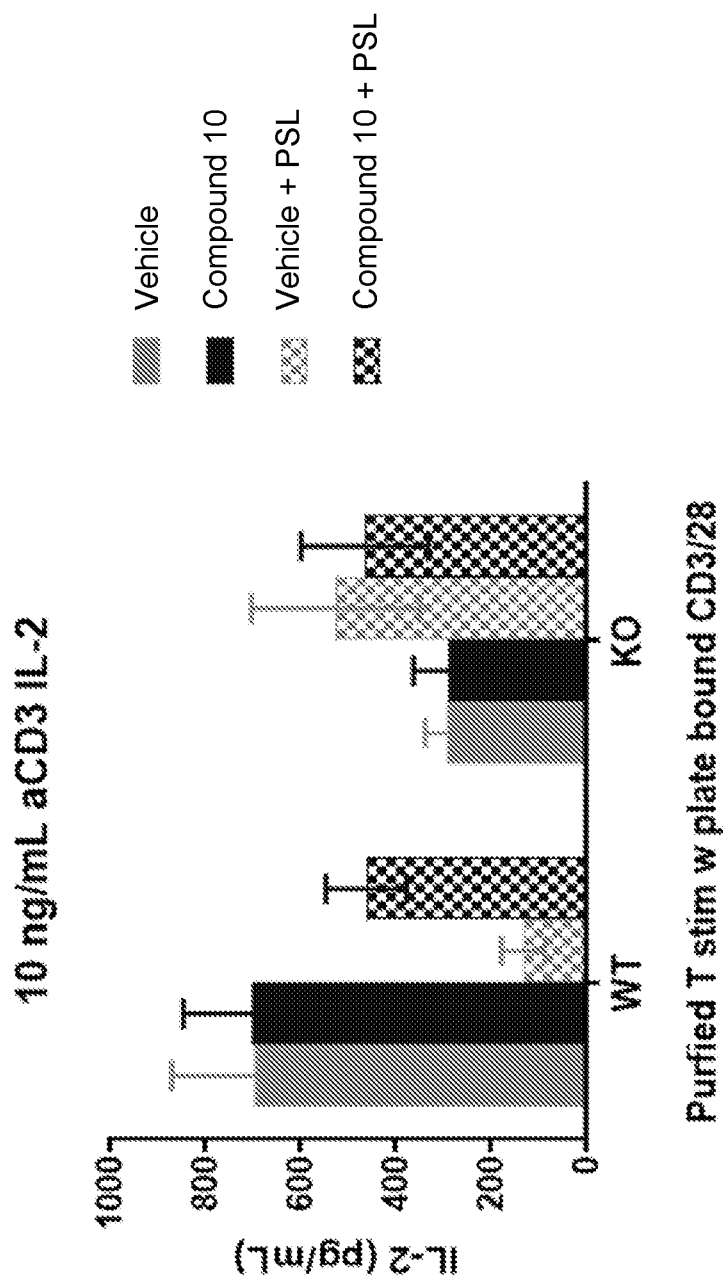


FIG. 67

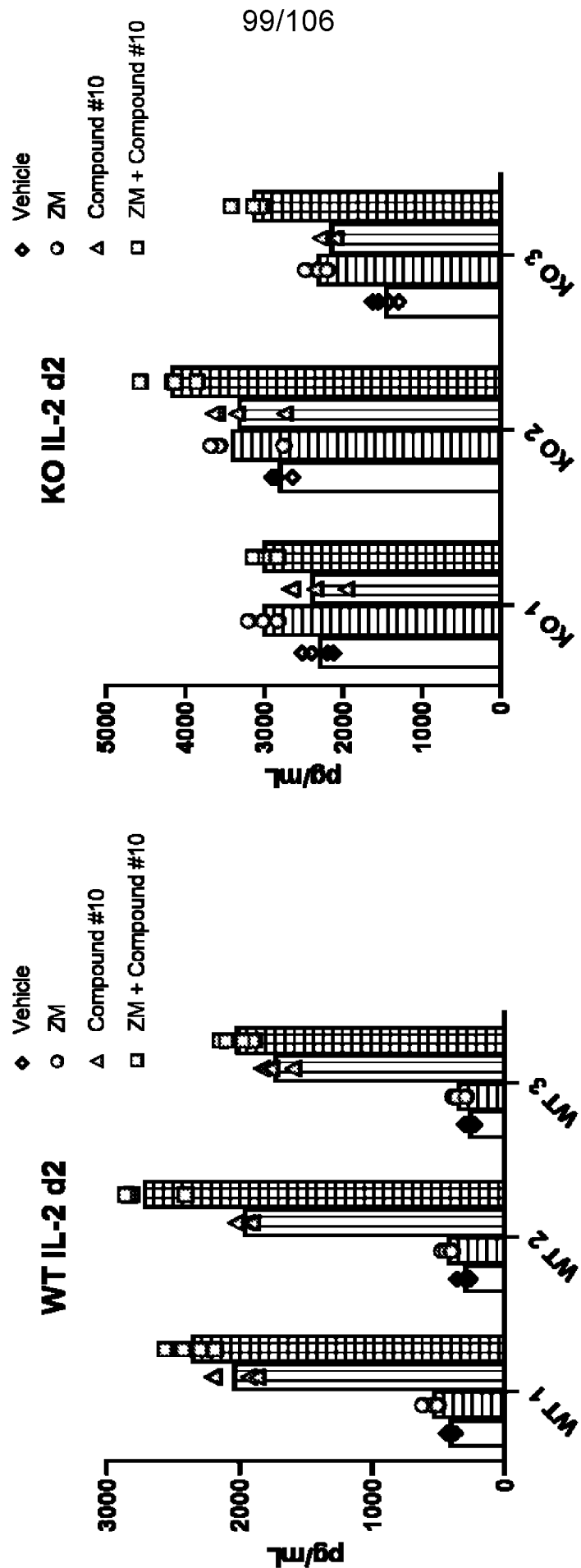


FIG. 68A

FIG. 68B

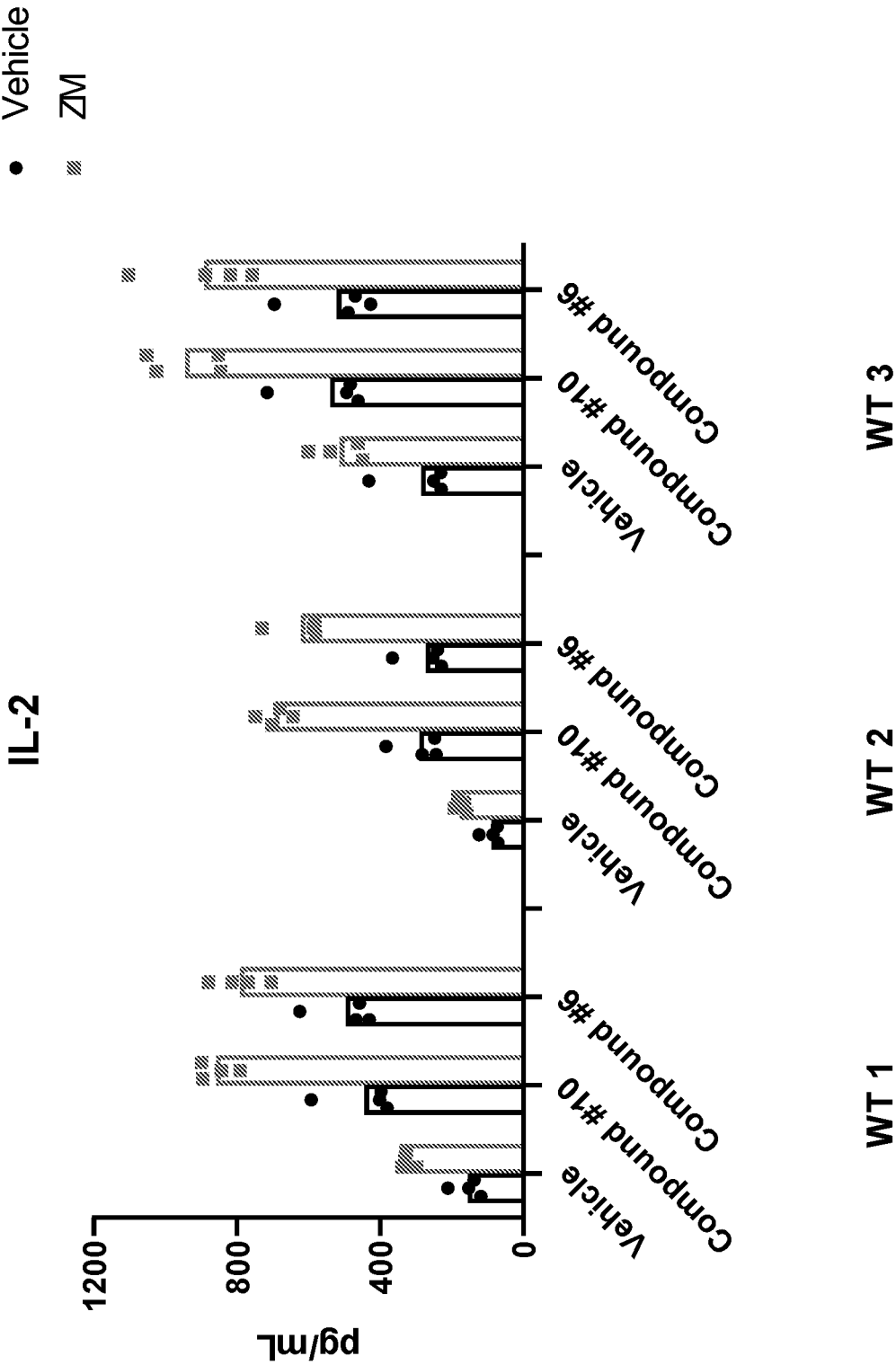


FIG. 69

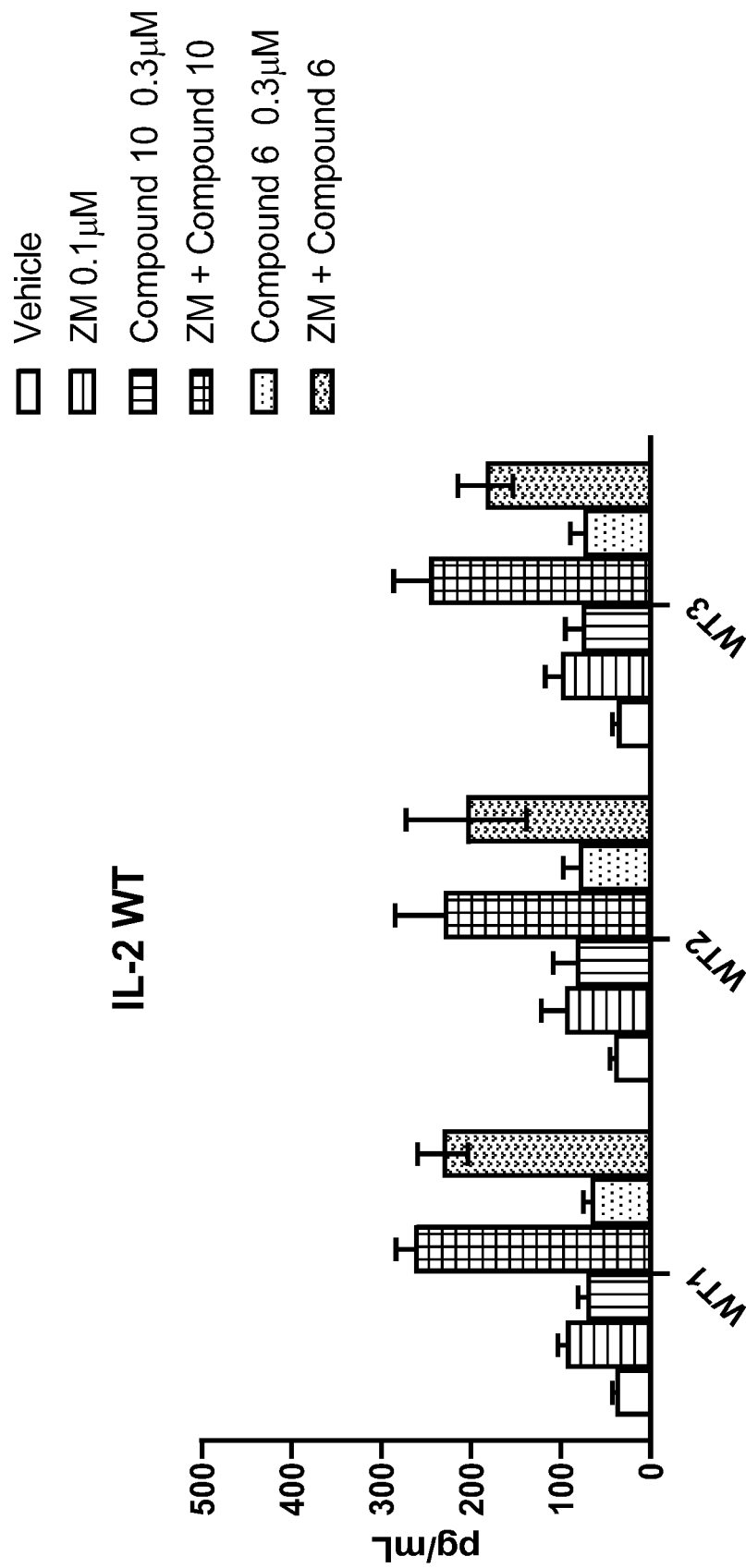


FIG. 70A

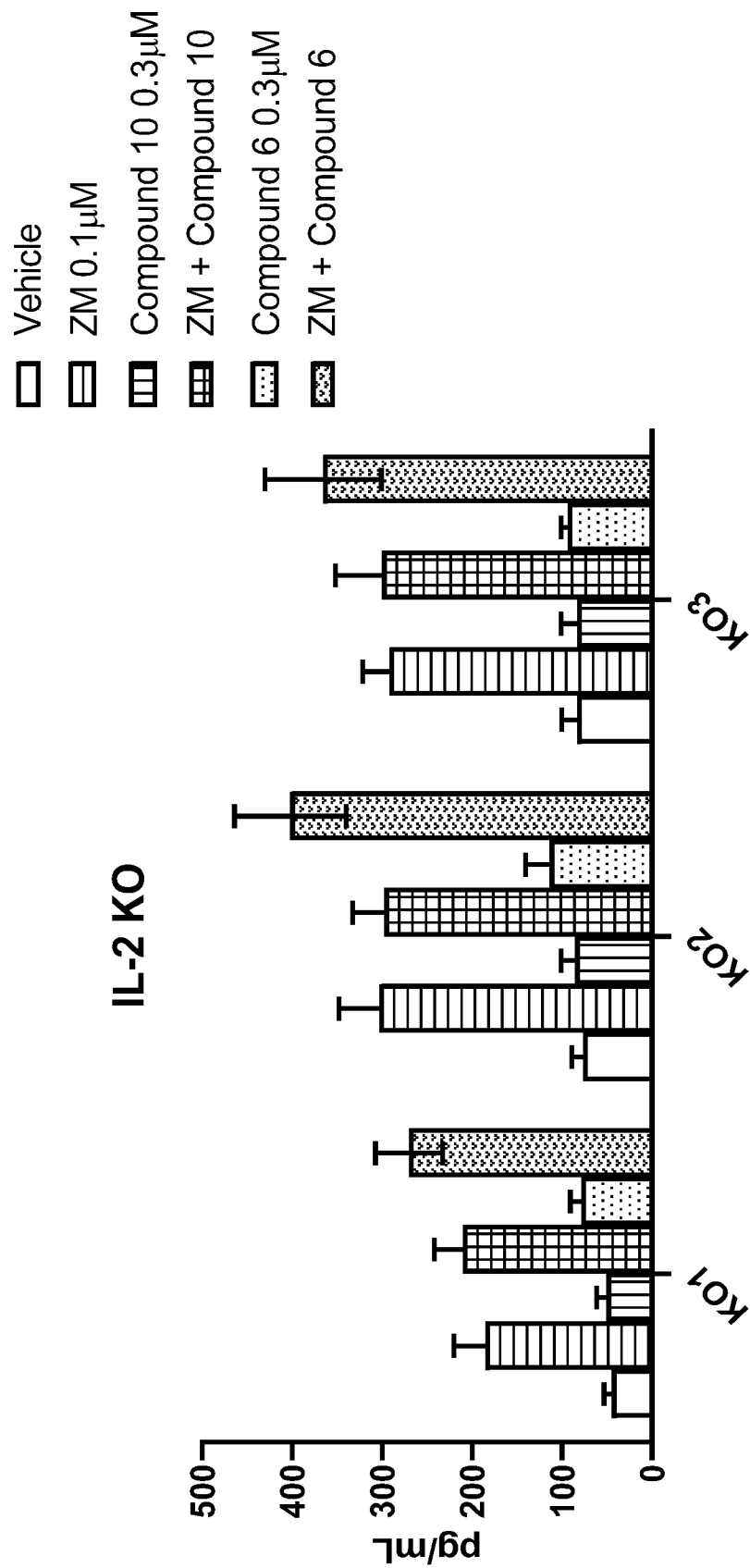


FIG. 70B

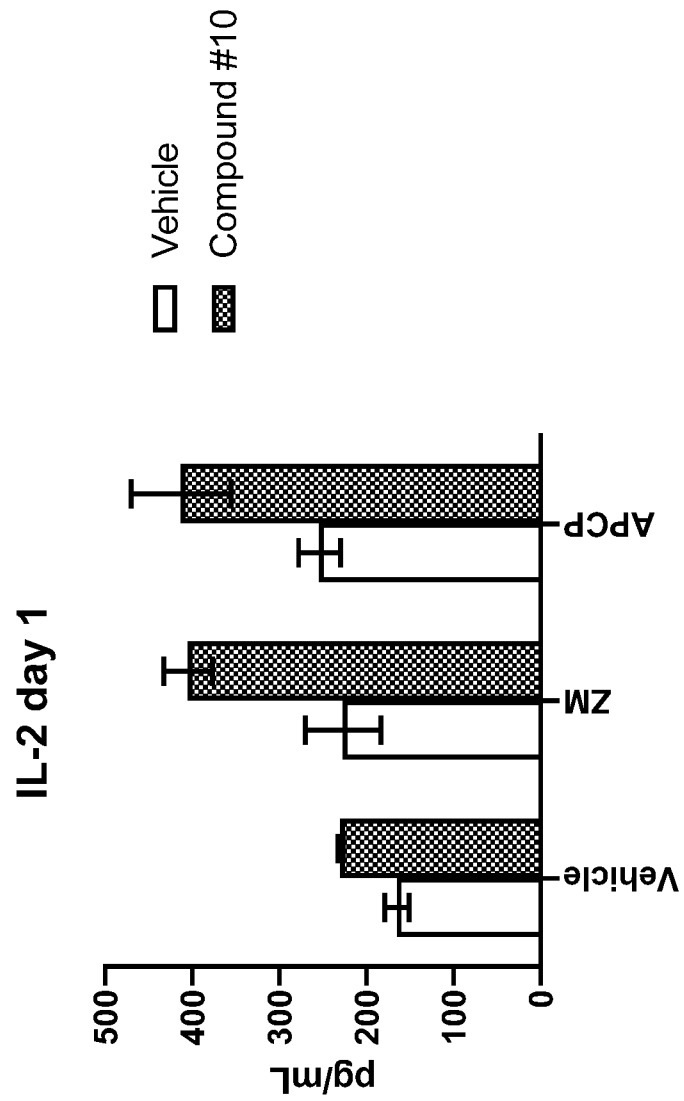


FIG. 71

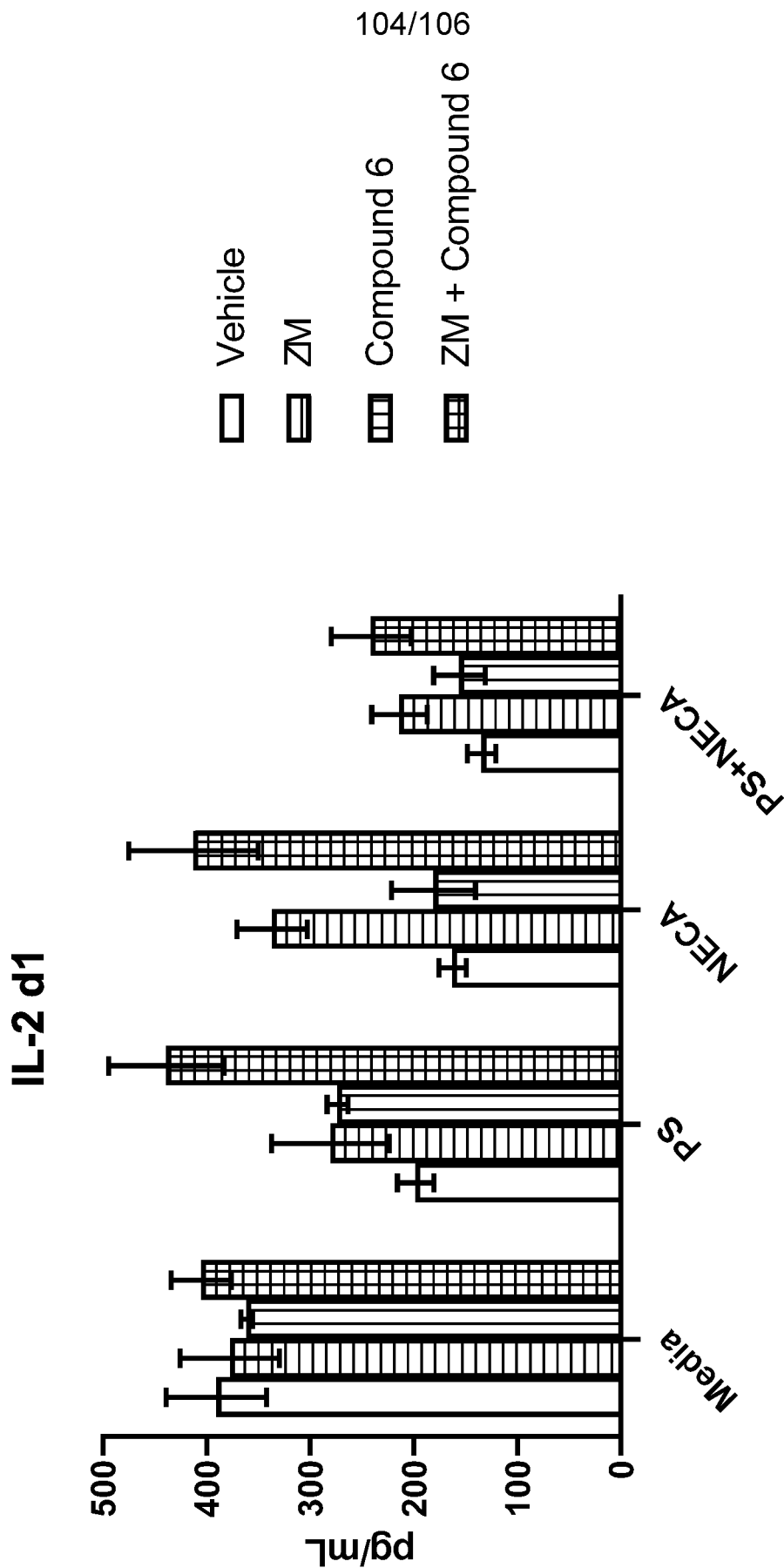


FIG. 72A

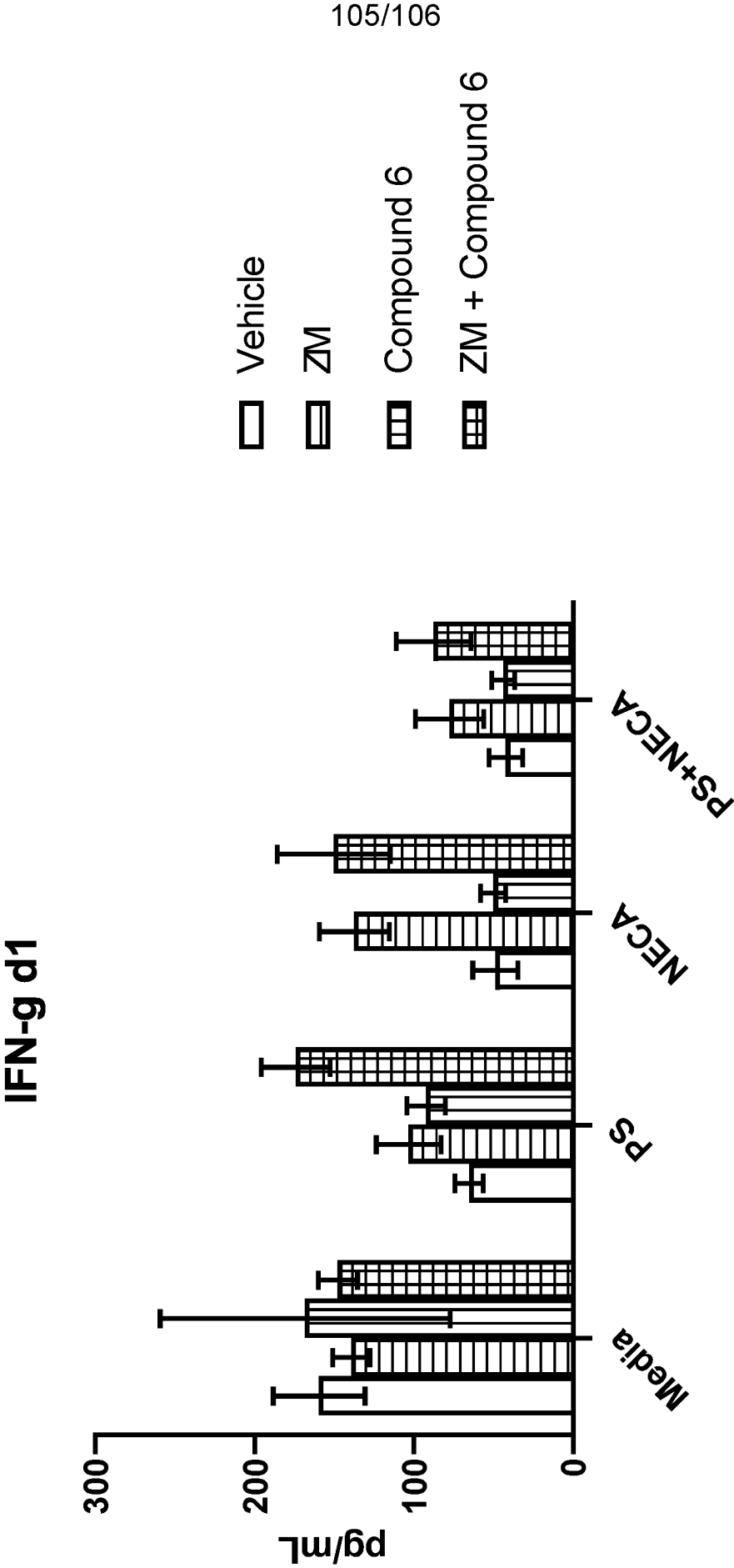


FIG. 72B

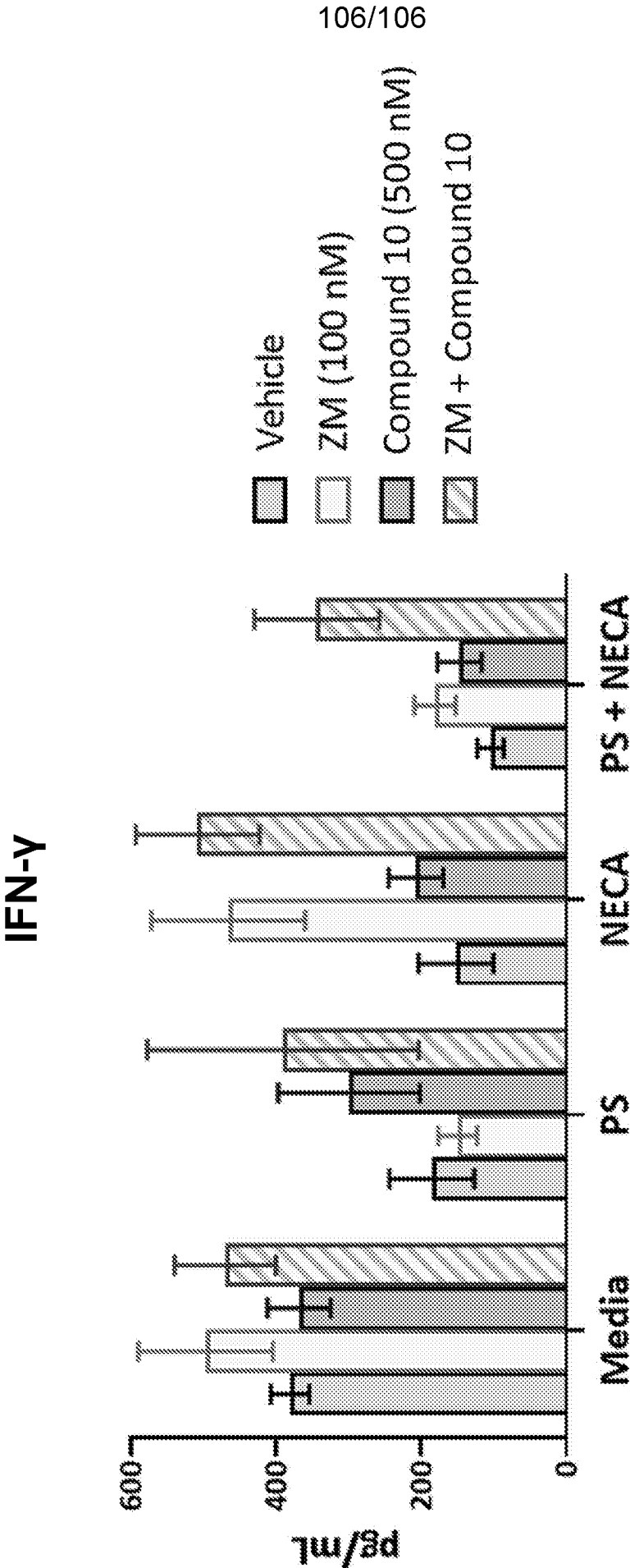


FIG. 72C