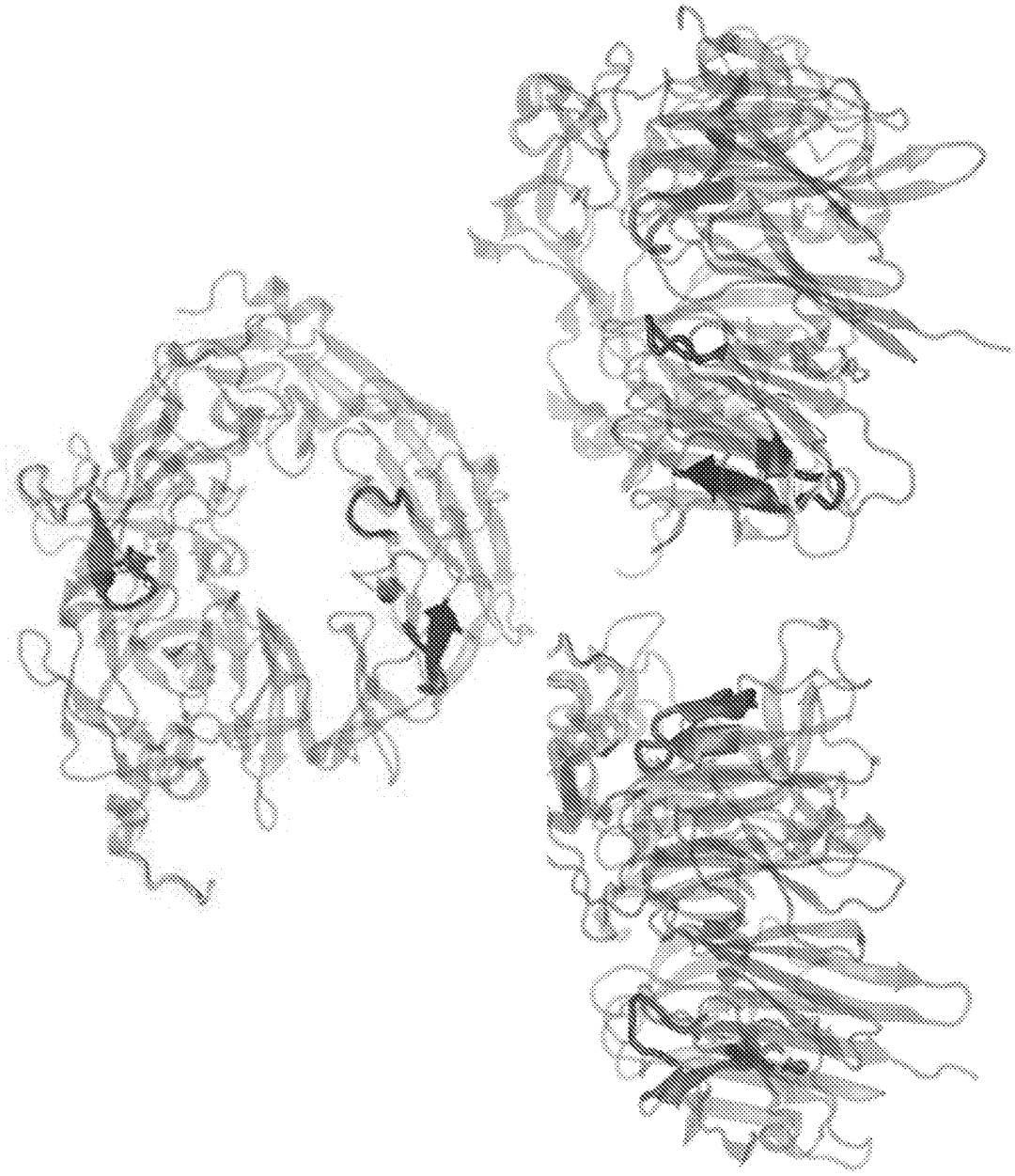


FIG. 1

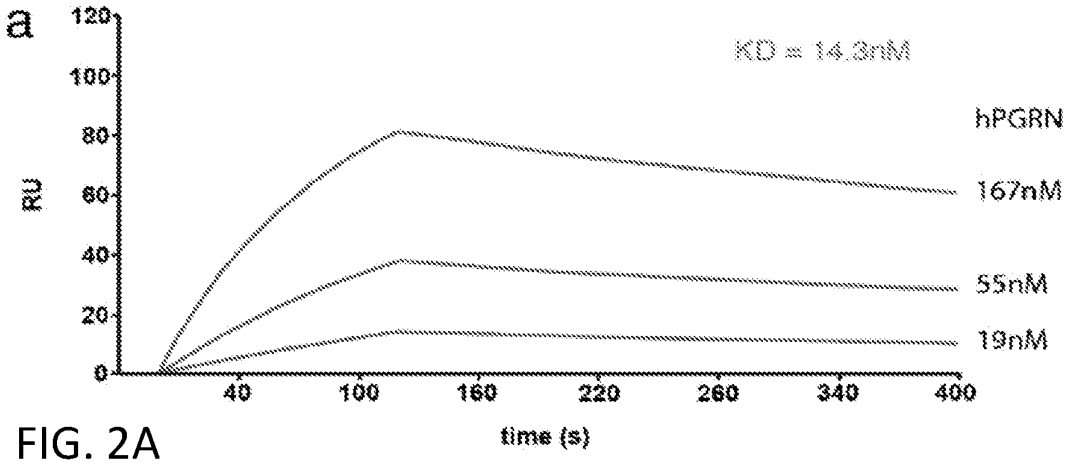


FIG. 2A

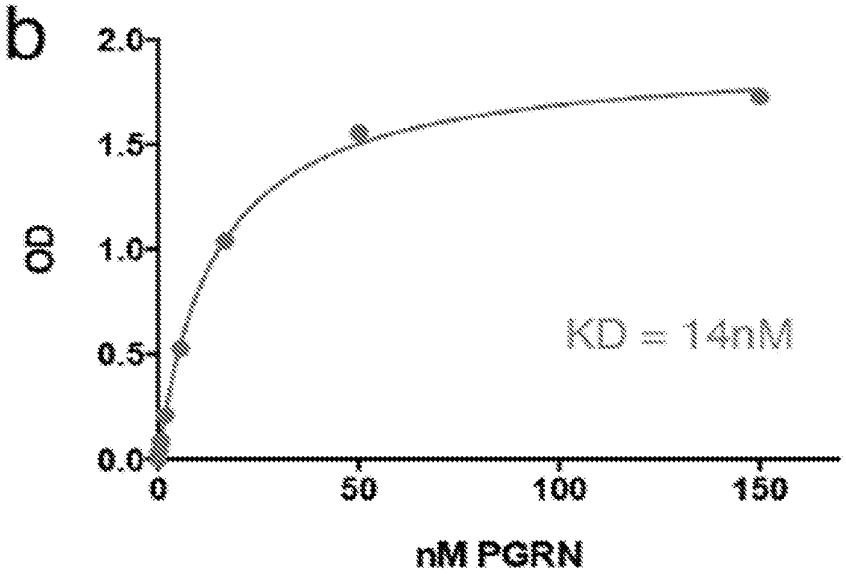


FIG. 2B

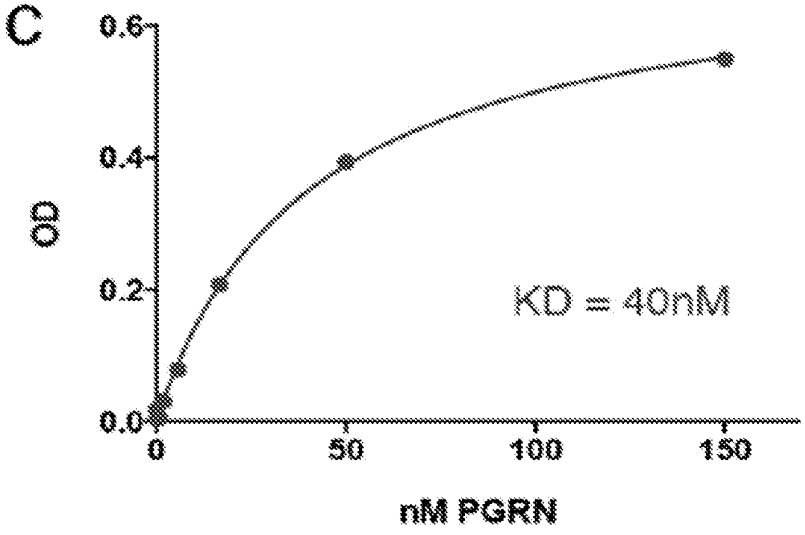


FIG. 2C

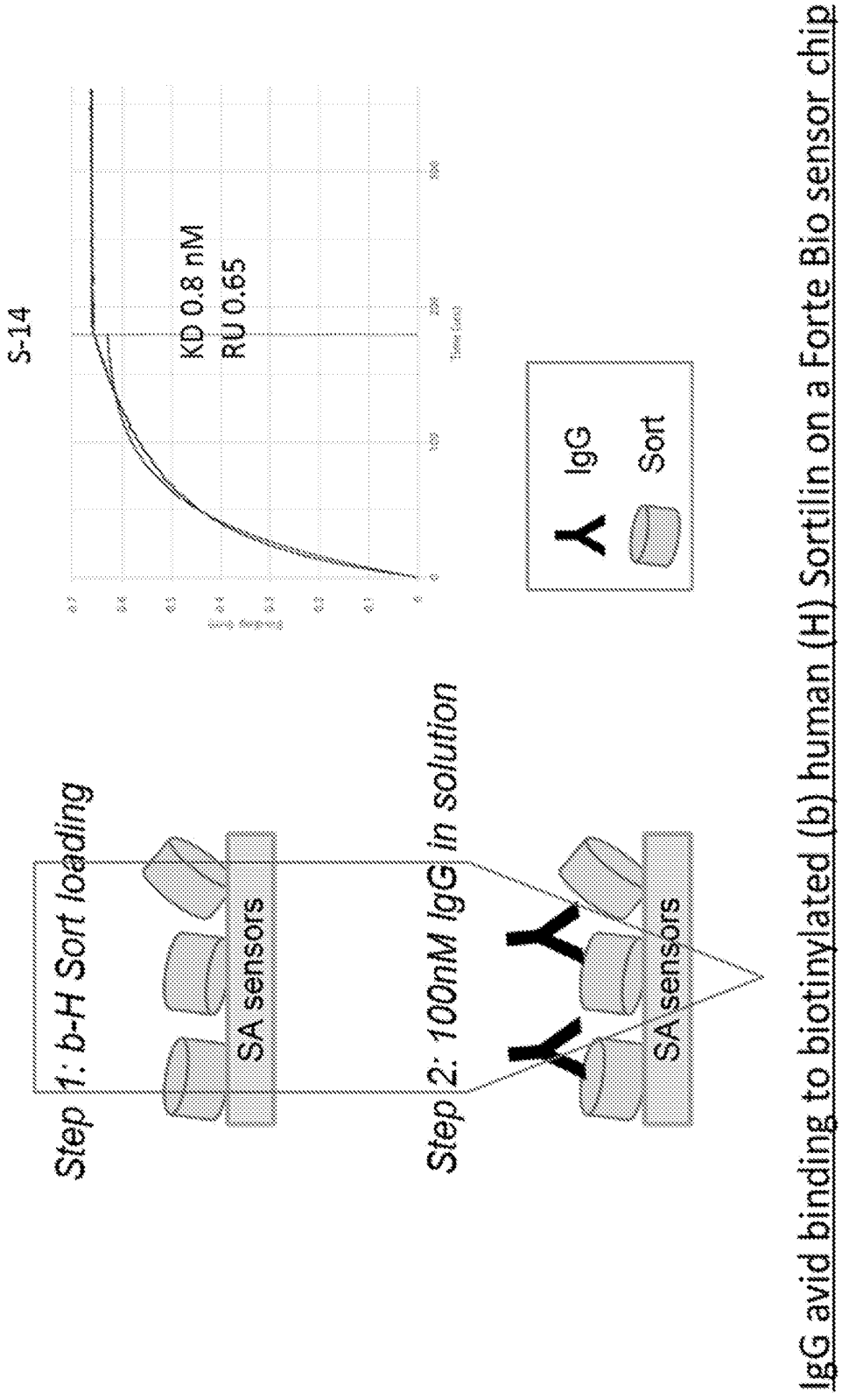

IgG avid binding to biotinylated (b) human (H) Sortilin on a Forte Bio sensor chip
Step 1: b-H Sort loading
SA sensors
Step 2: 100nM IgG in solution
SA sensors
IgG
Sort
S-14
KD 0.8 nM
RU 0.65

FIG. 3A

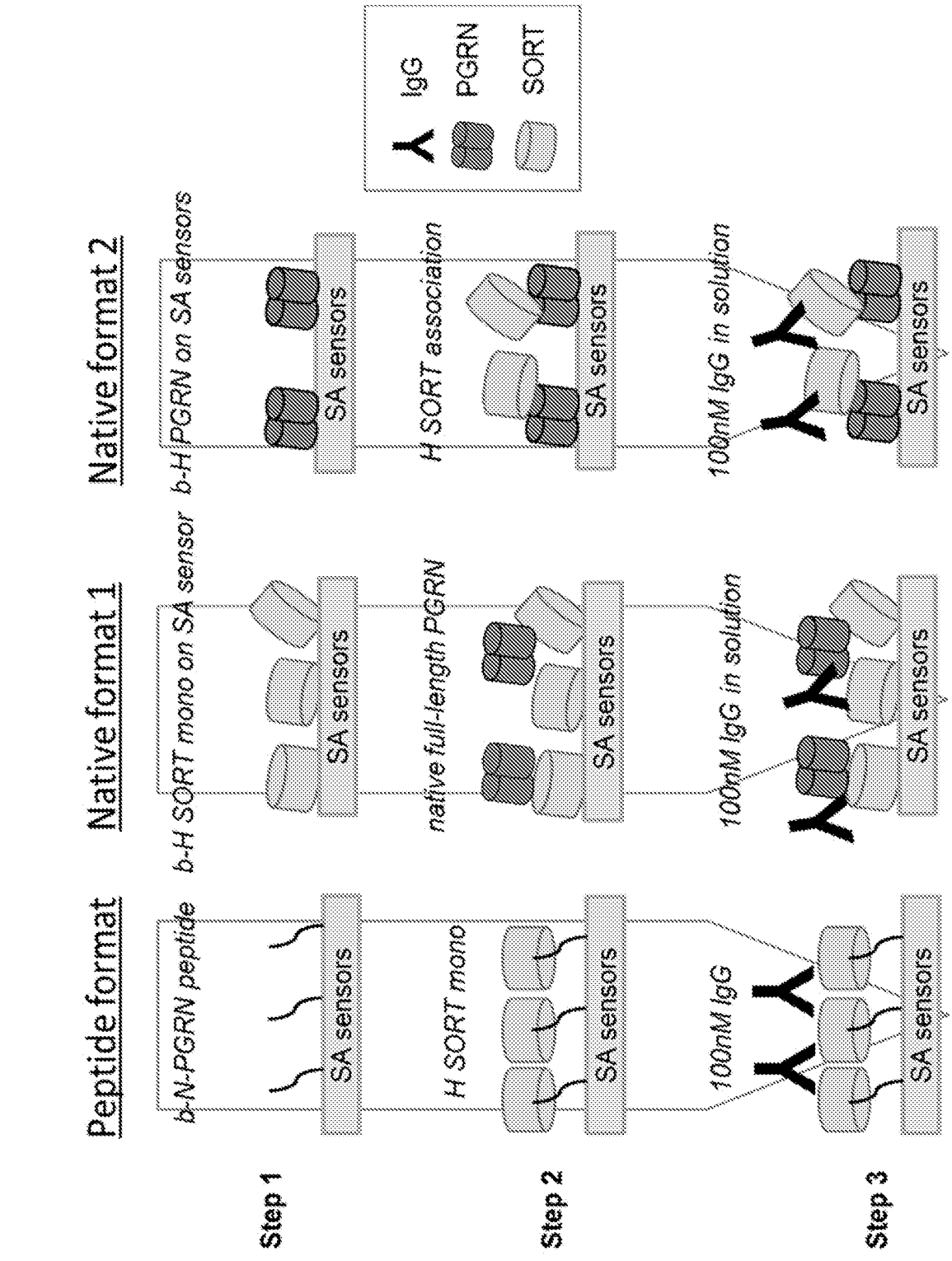

Peptide format
Native format 1
Native format 2
b-N-PGRN peptide
b-H SORT mono on SA sensor
b-H PGRN on SA sensors
IgG
PGRN
SORT
Step 1
SA sensors
H SORT mono
native full-length PGRN
H SORT association
Step 2
100nM IgG
100nM IgG in solution
100nM IgG in solution
Step 3

FIG. 3B

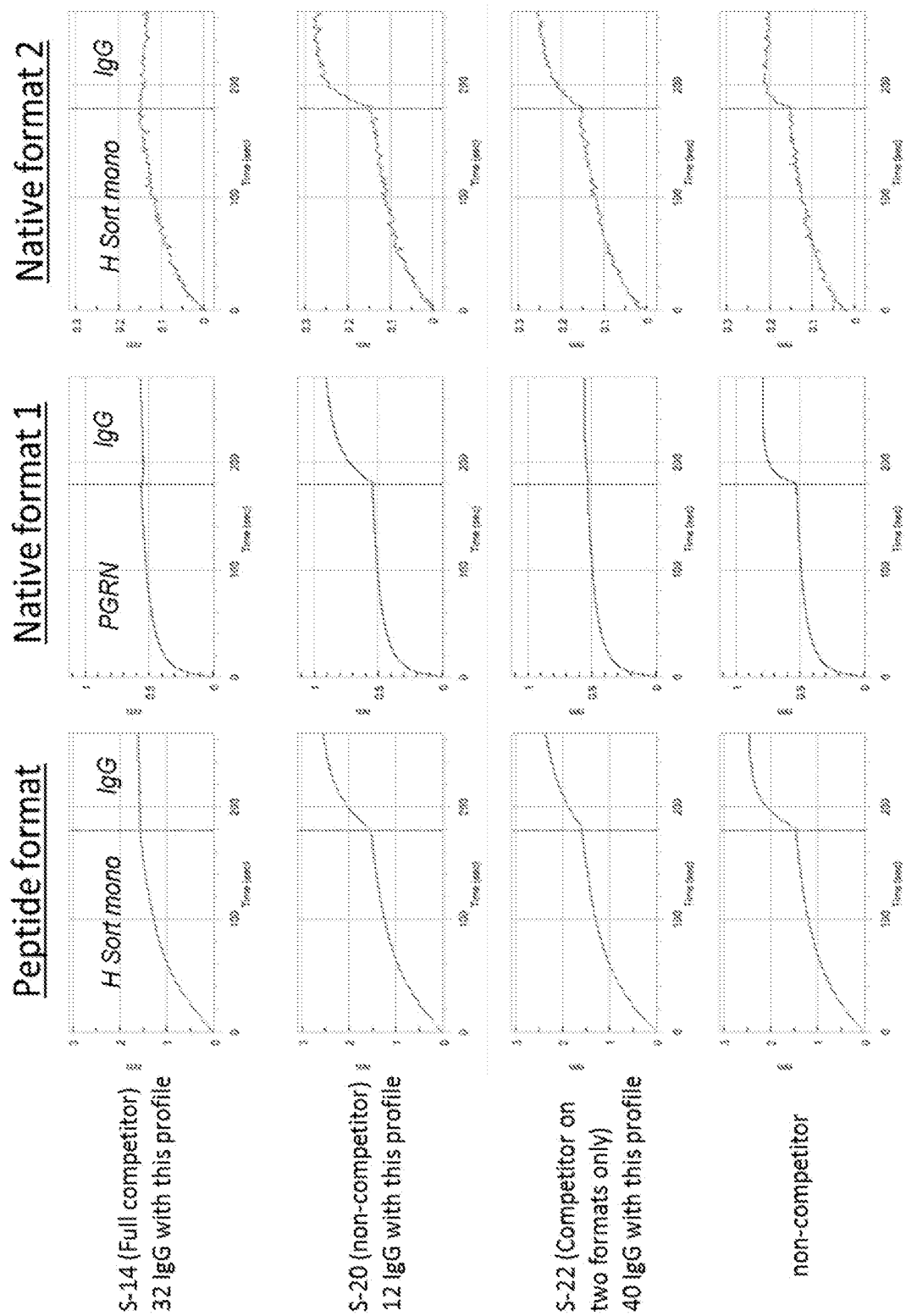

Peptide format
Native format 1
Native format 2
H Sort mono
IgG
PGRN
IgG
H Sort mono
IgG
S-14 (Full competitor)
32 IgG with this profile
S-20 (non-competitor)
12 IgG with this profile
S-22 (Competitor on
two formats only)
40 IgG with this profile
non-competitor

FIG. 4A

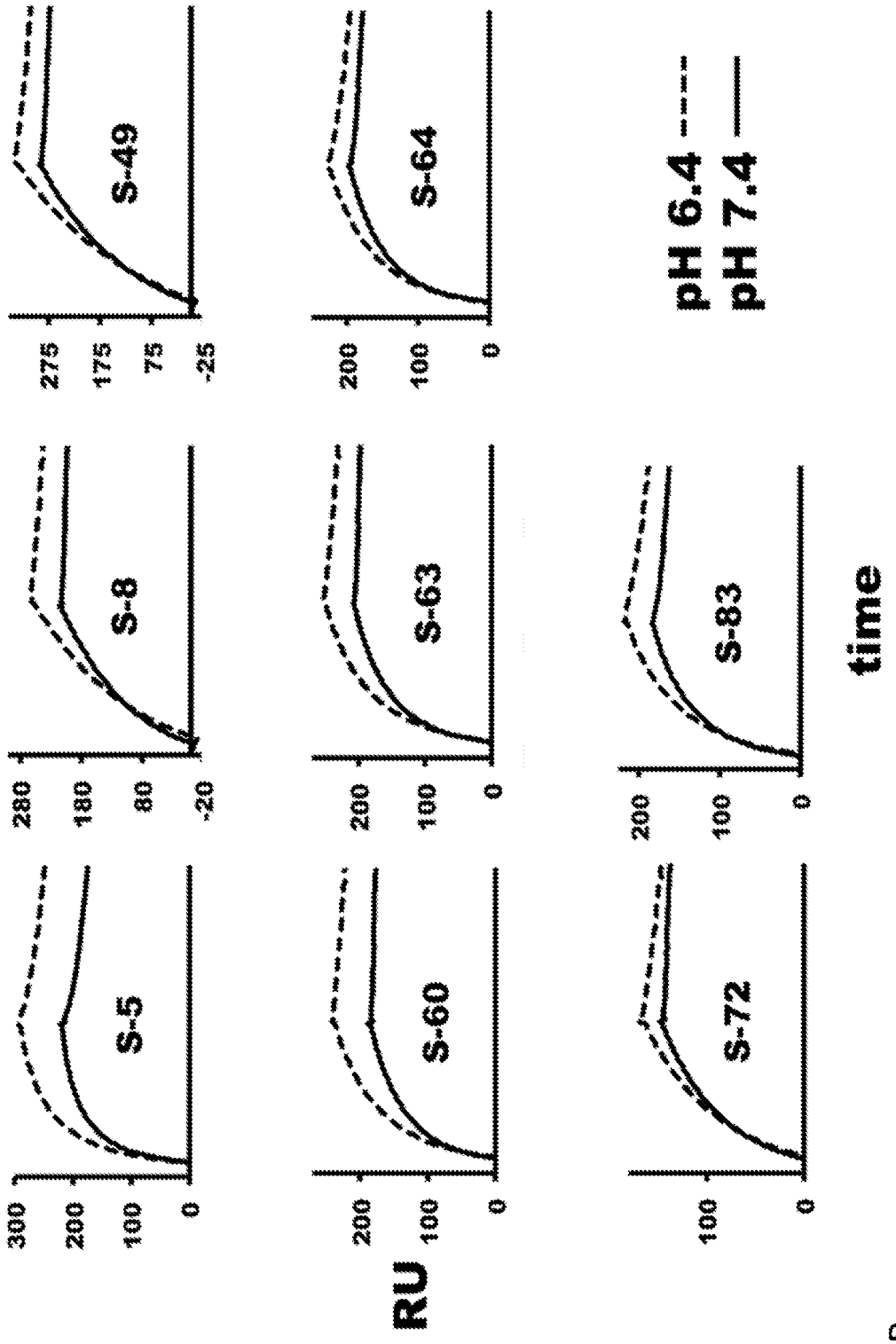


FIG. 4B

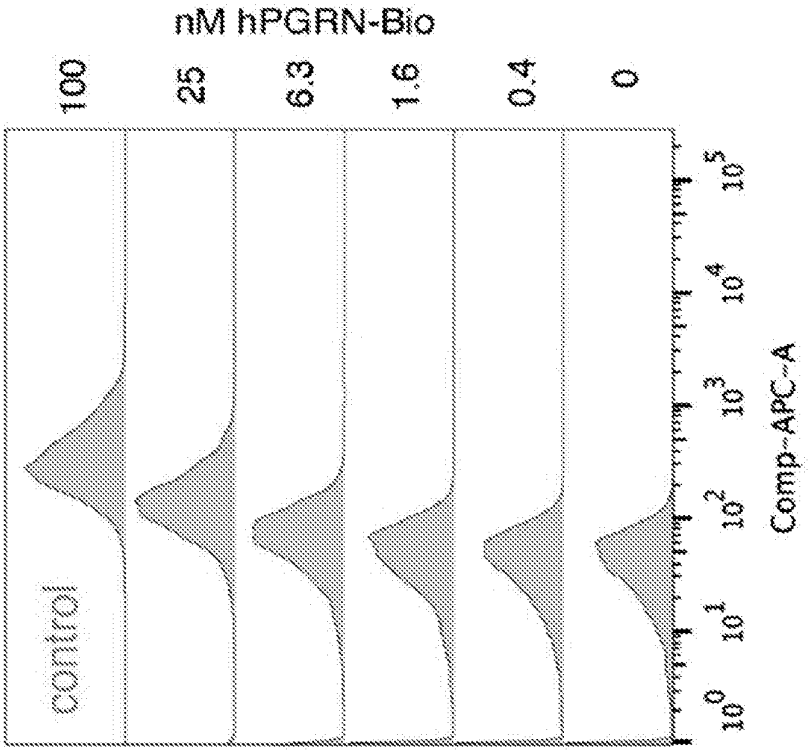

nM hPGRN-Bio
100
25
6.3
1.6
0.4
0
control
10^0 10^1 10^2 10^3 10^4 10^5
Comp-APC-A

FIG. 5B

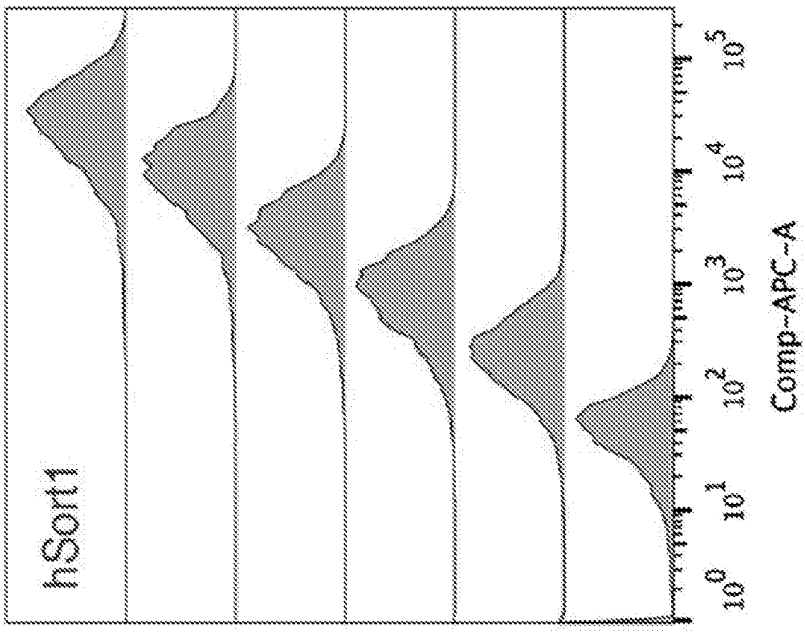

hSort1
10^0 10^1 10^2 10^3 10^4 10^5
Comp-APC-A

FIG. 5A

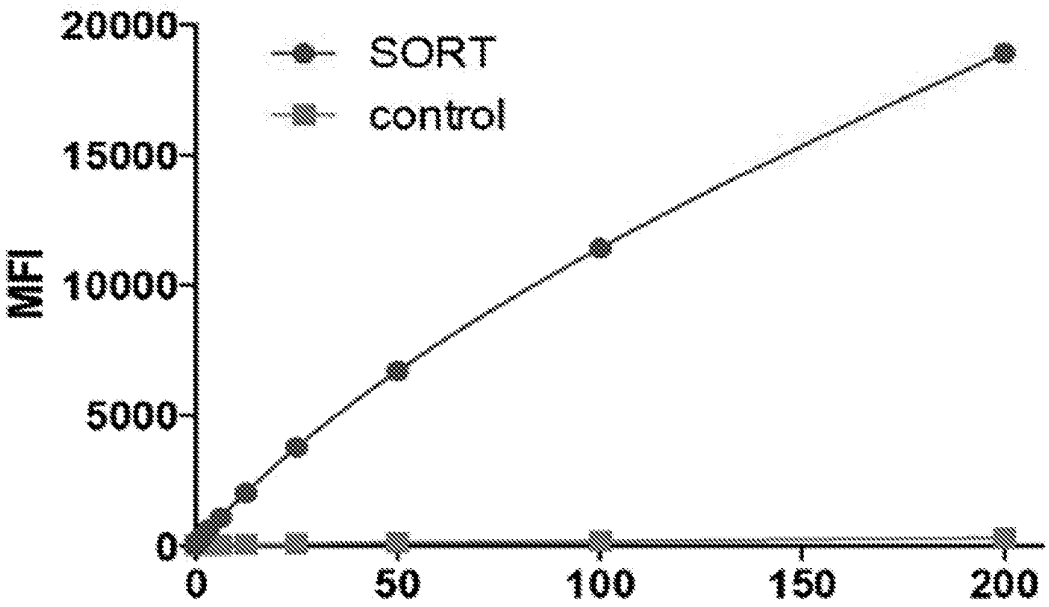

20000
15000
10000
5000
0
MFI
SORT
control
0
50
100
150
200
nM PGRN

FIG. 5C

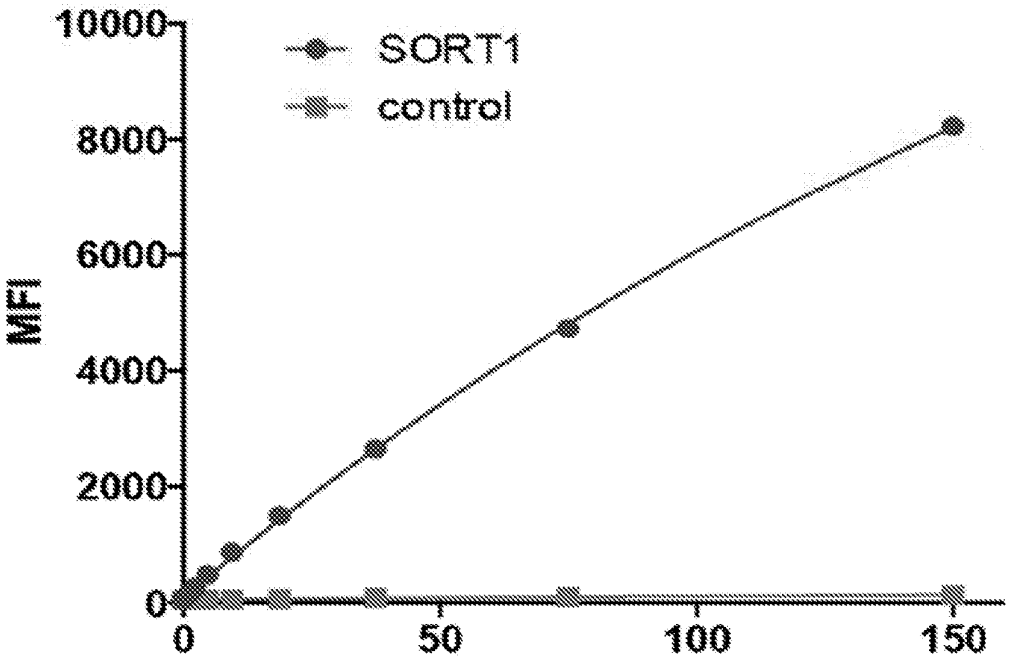

10000
8000
6000
4000
2000
0
MFI
SORT1
control
0
50
100
150
nM msPGRN-Bio

FIG. 5D

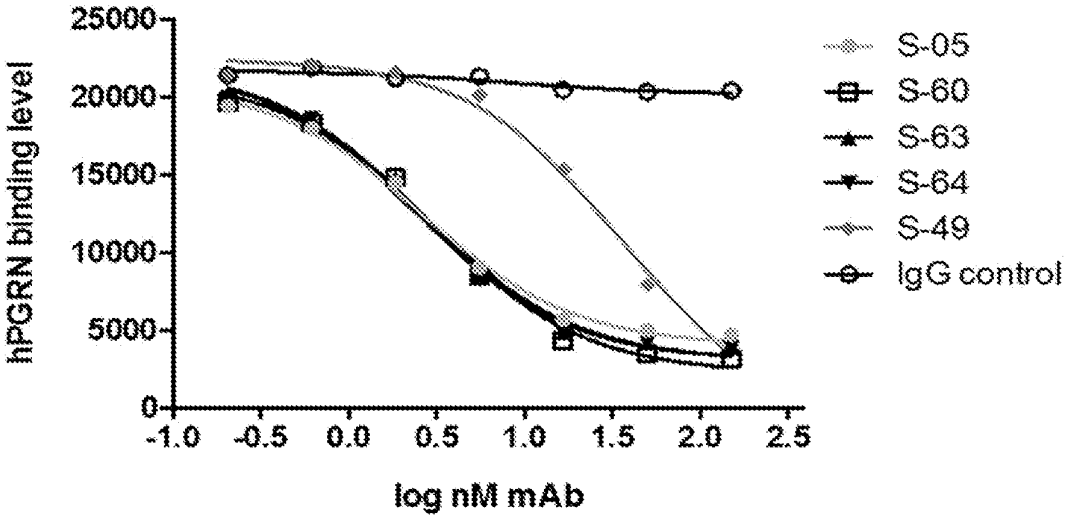

hPGRN binding level
25000
20000
15000
10000
5000
0
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
log nM mAb
S-05
S-60
S-63
S-64
S-49
IgG control

FIG. 6A

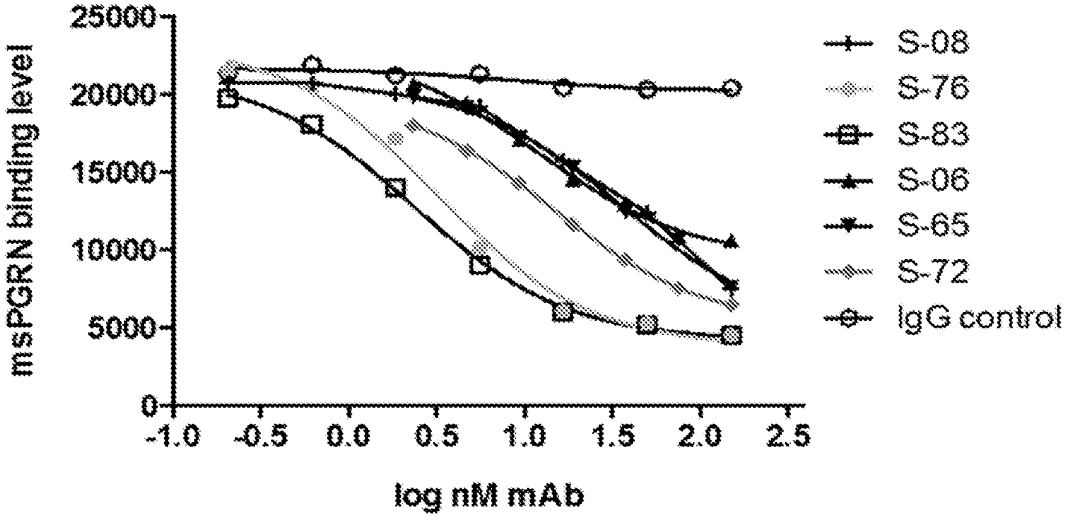

msPGRN binding level
25000
20000
15000
10000
5000
0
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
log nM mAb
S-08
S-76
S-83
S-06
S-65
S-72
IgG control

FIG. 6B

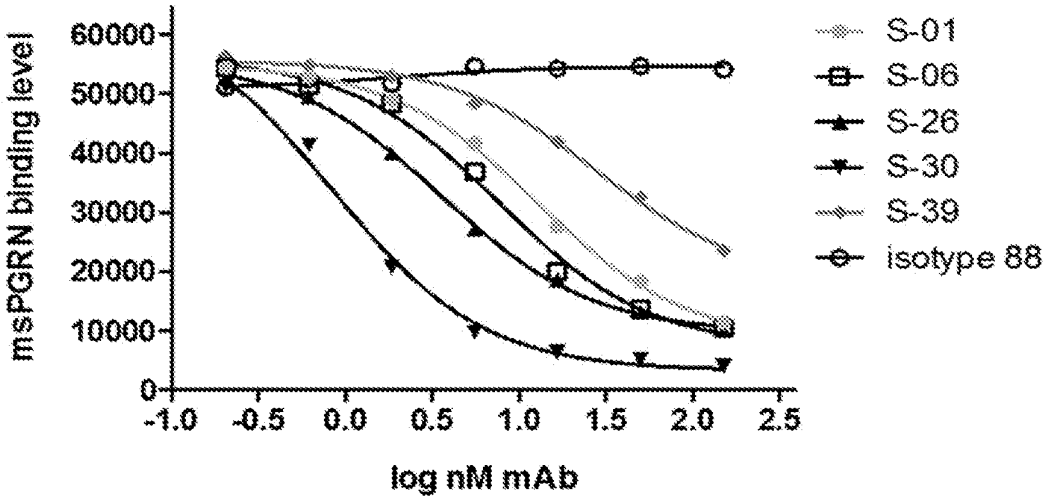

msPGRN binding level
60000
50000
40000
30000
20000
10000
0
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
log nM mAb
S-01
S-06
S-26
S-30
S-39
isotype 88

FIG. 6C

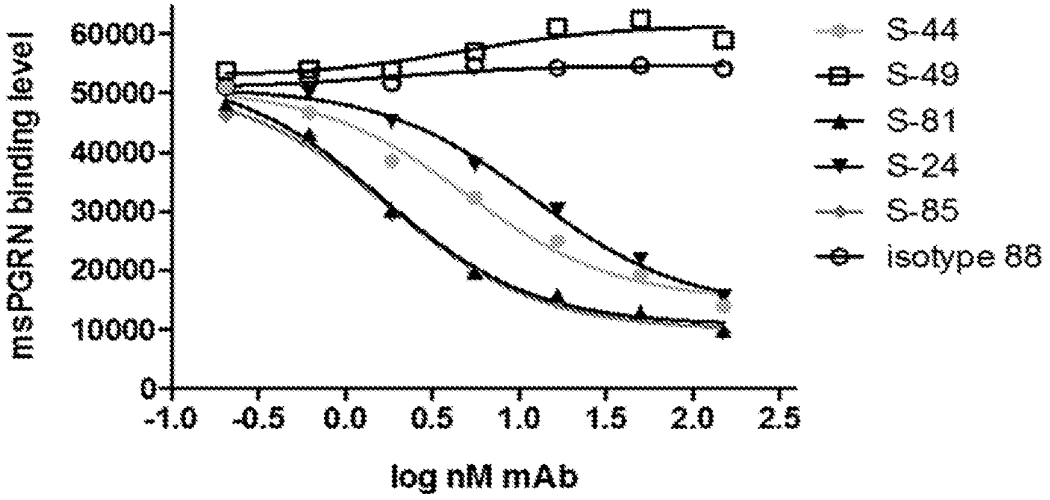

msPGRN binding level
60000
50000
40000
30000
20000
10000
0
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
log nM mAb
S-44
S-49
S-81
S-24
S-85
isotype 88

FIG. 6D

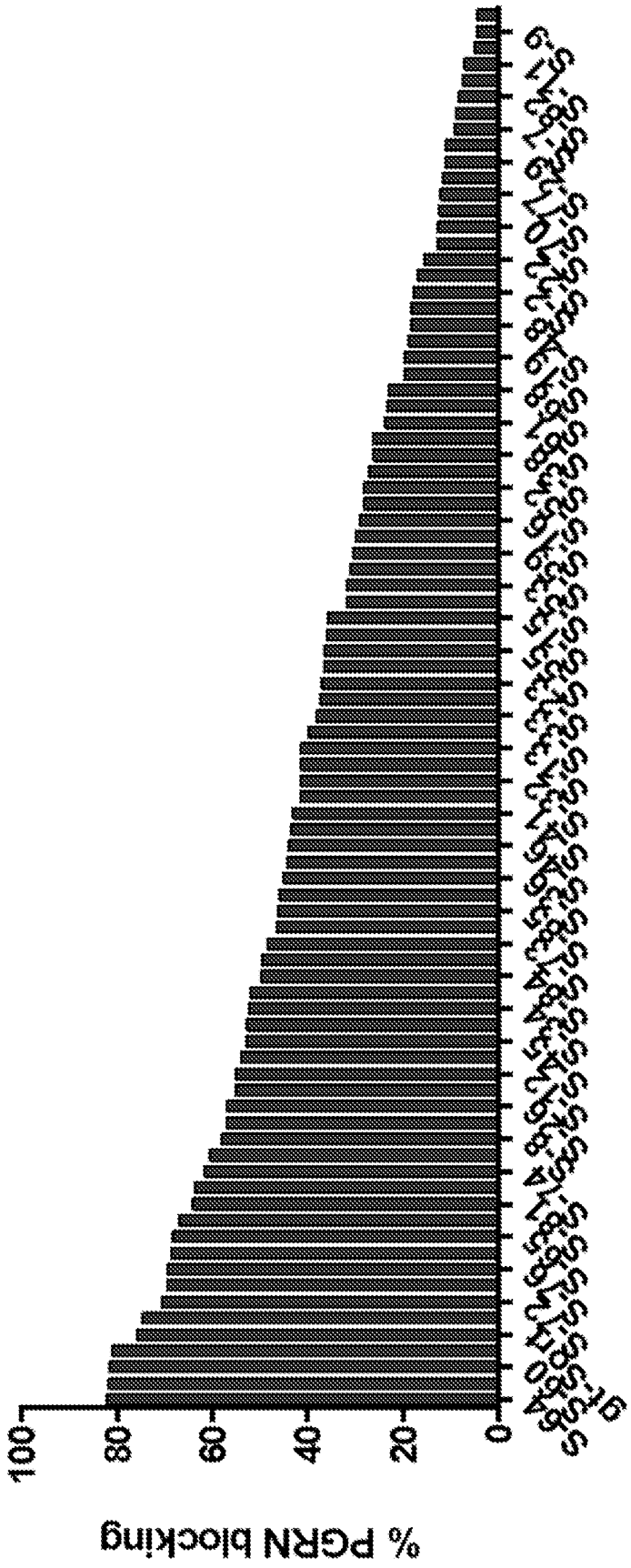


FIG. 6E

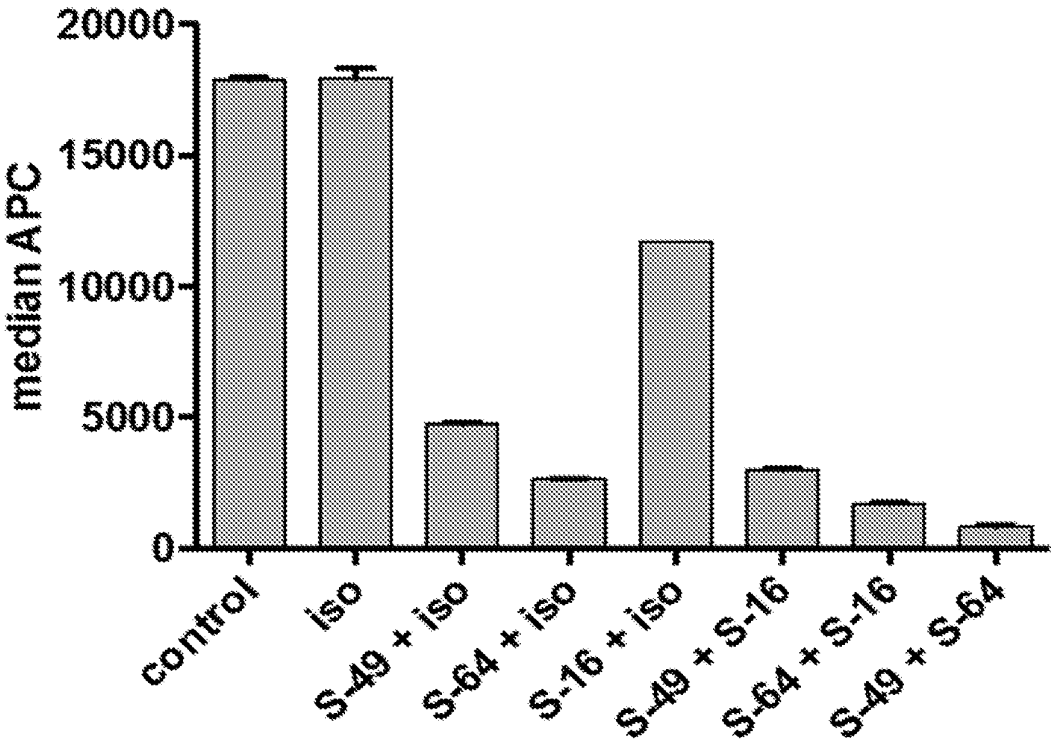

20000
15000
10000
5000
0
median APC
control
iso
S-49 + iso
S-64 + iso
S-16 + iso
S-49 + S-16
S-64 + S-16
S-49 + S-64

FIG. 7

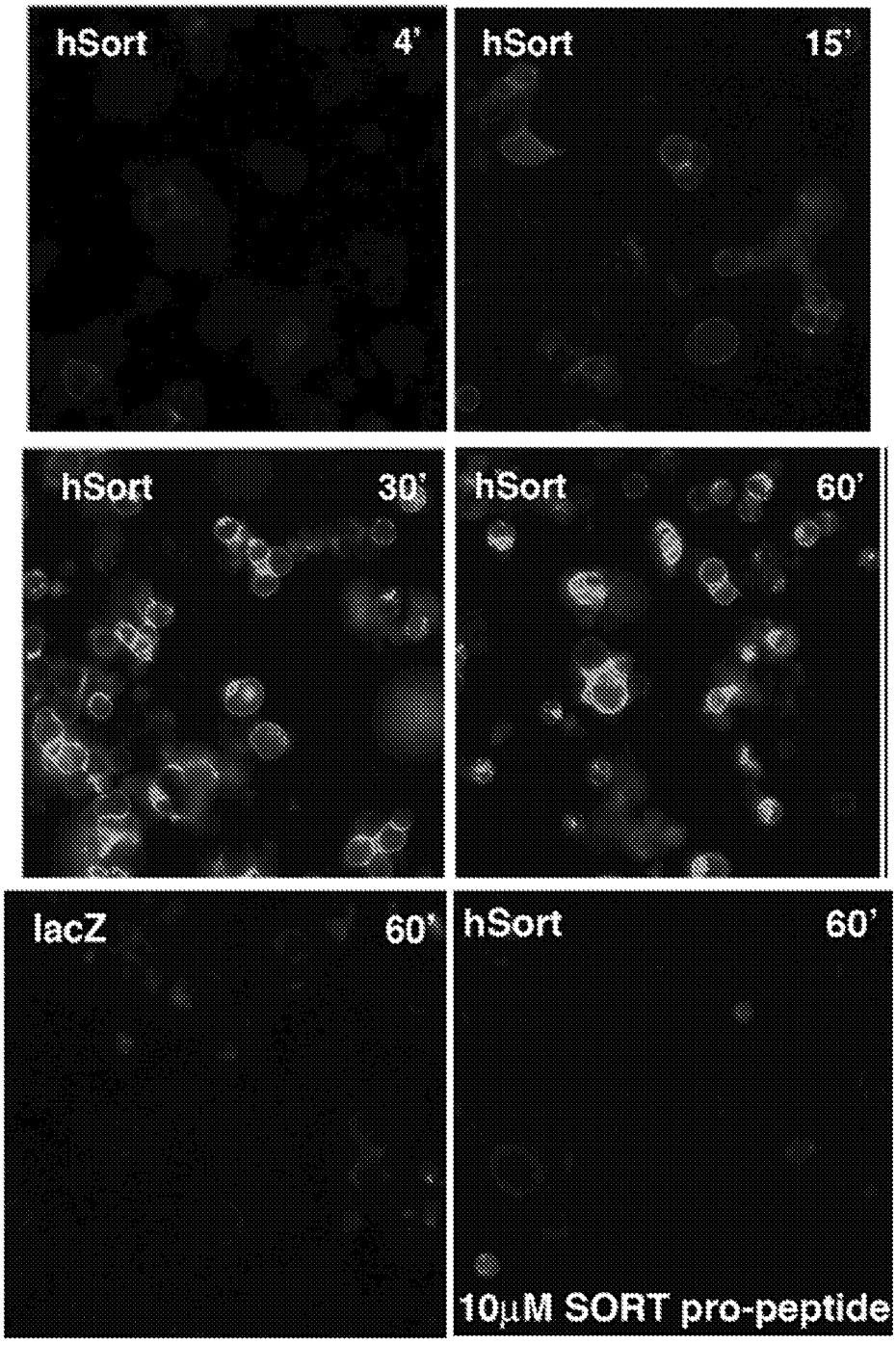

hSort 4'
hSort 15'
hSort 30'
hSort 60'
lacZ 60'
hSort 60'
10μM SORT pro-peptide

FIG. 8A

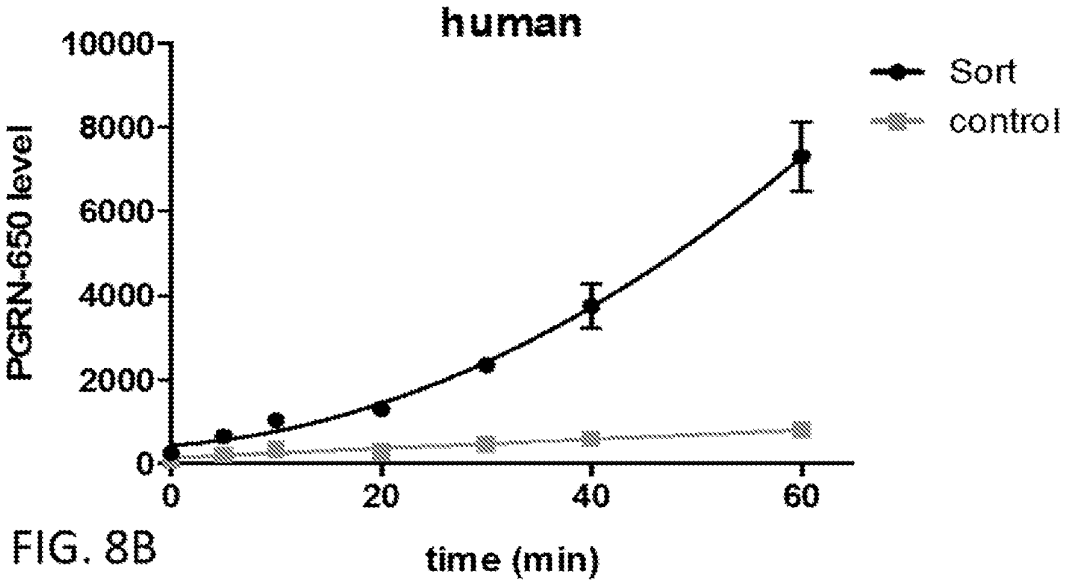

human
PGRN-650 level
10000
8000
6000
4000
2000
0
0
20
40
60
time (min)
Sort
control

FIG. 8B

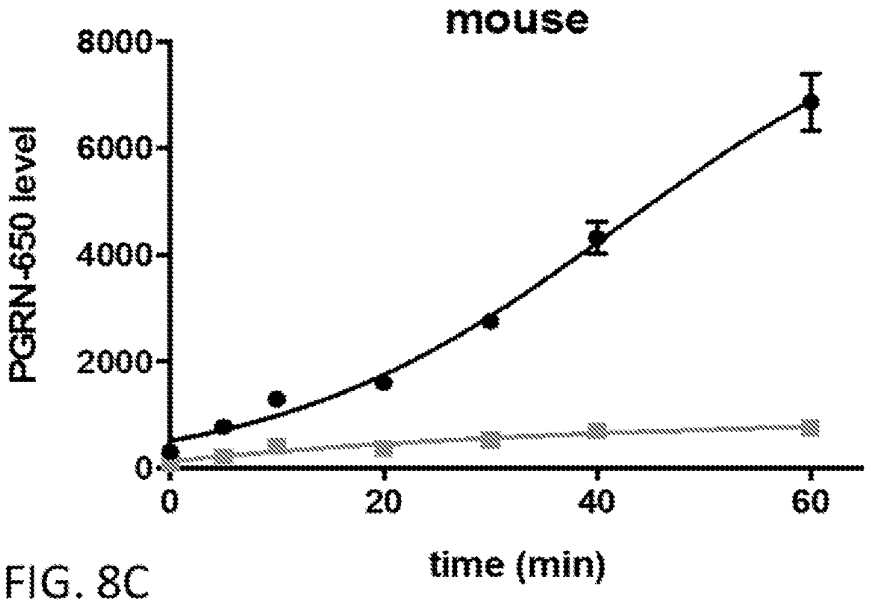

mouse
PGRN-650 level
8000
6000
4000
2000
0
0
20
40
60
time (min)

FIG. 8C

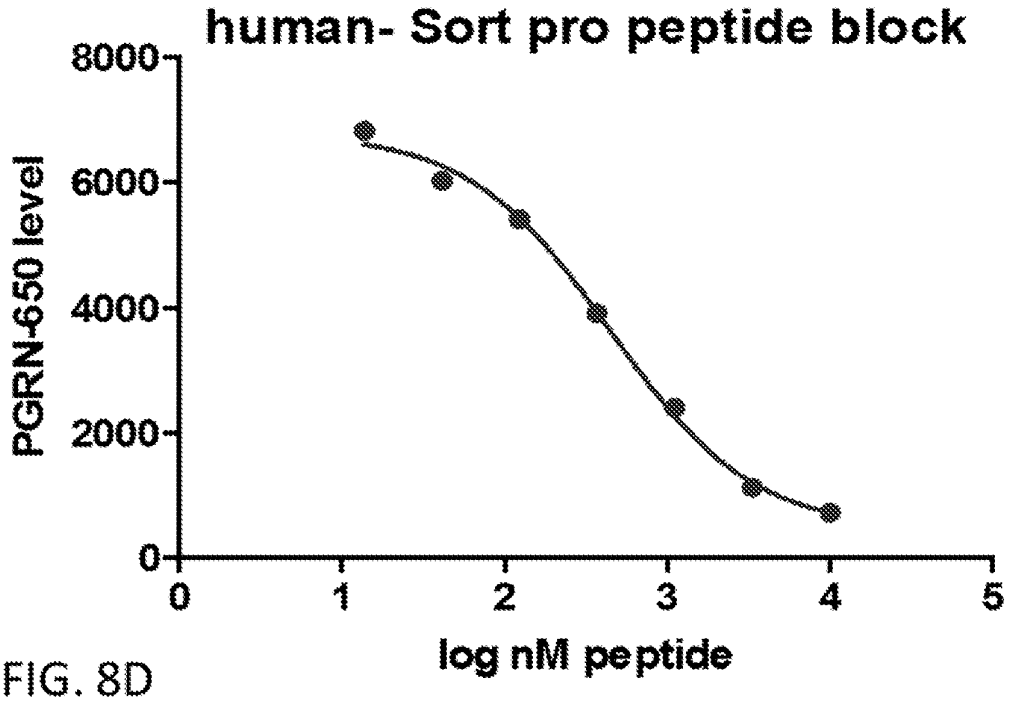

human- Sort pro peptide block
PGRN-650 level
8000
6000
4000
2000
0
0
1
2
3
4
5
log nM peptide

FIG. 8D

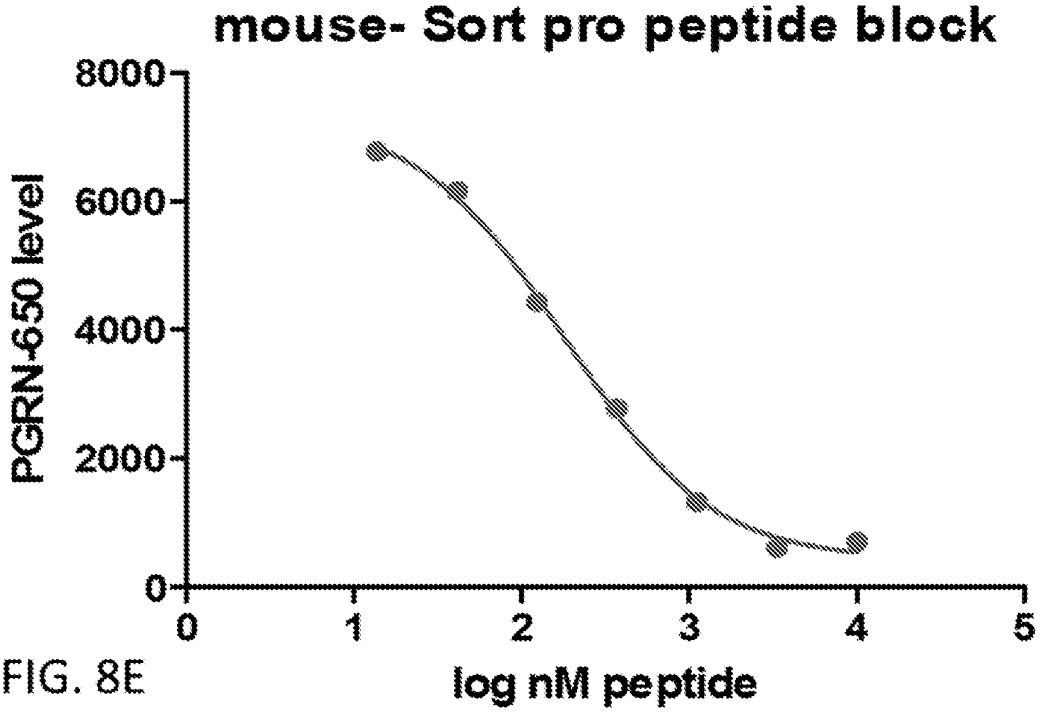

mouse- Sort pro peptide block
PGRN-650 level
8000
6000
4000
2000
0
0
1
2
3
4
5
log nM peptide

FIG. 8E

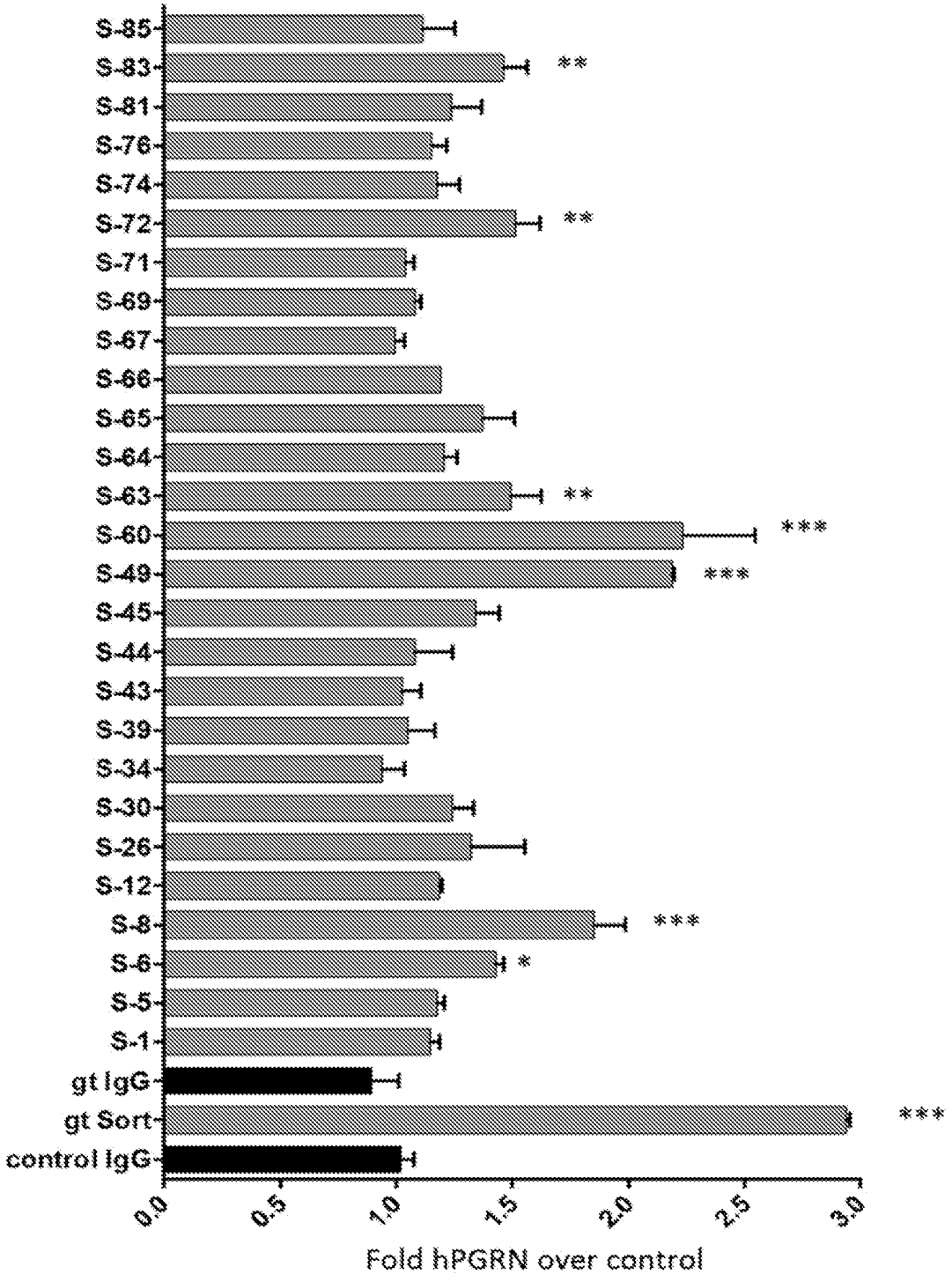

S-85
S-83
S-81
S-76
S-74
S-72
S-71
S-69
S-67
S-66
S-65
S-64
S-63
S-60
S-49
S-45
S-44
S-43
S-39
S-34
S-30
S-26
S-12
S-8
S-6
S-5
S-1
gt IgG
gt Sort
control IgG
**
**
**
***
***
***
*
***
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Fold hPGRN over control

FIG. 9A

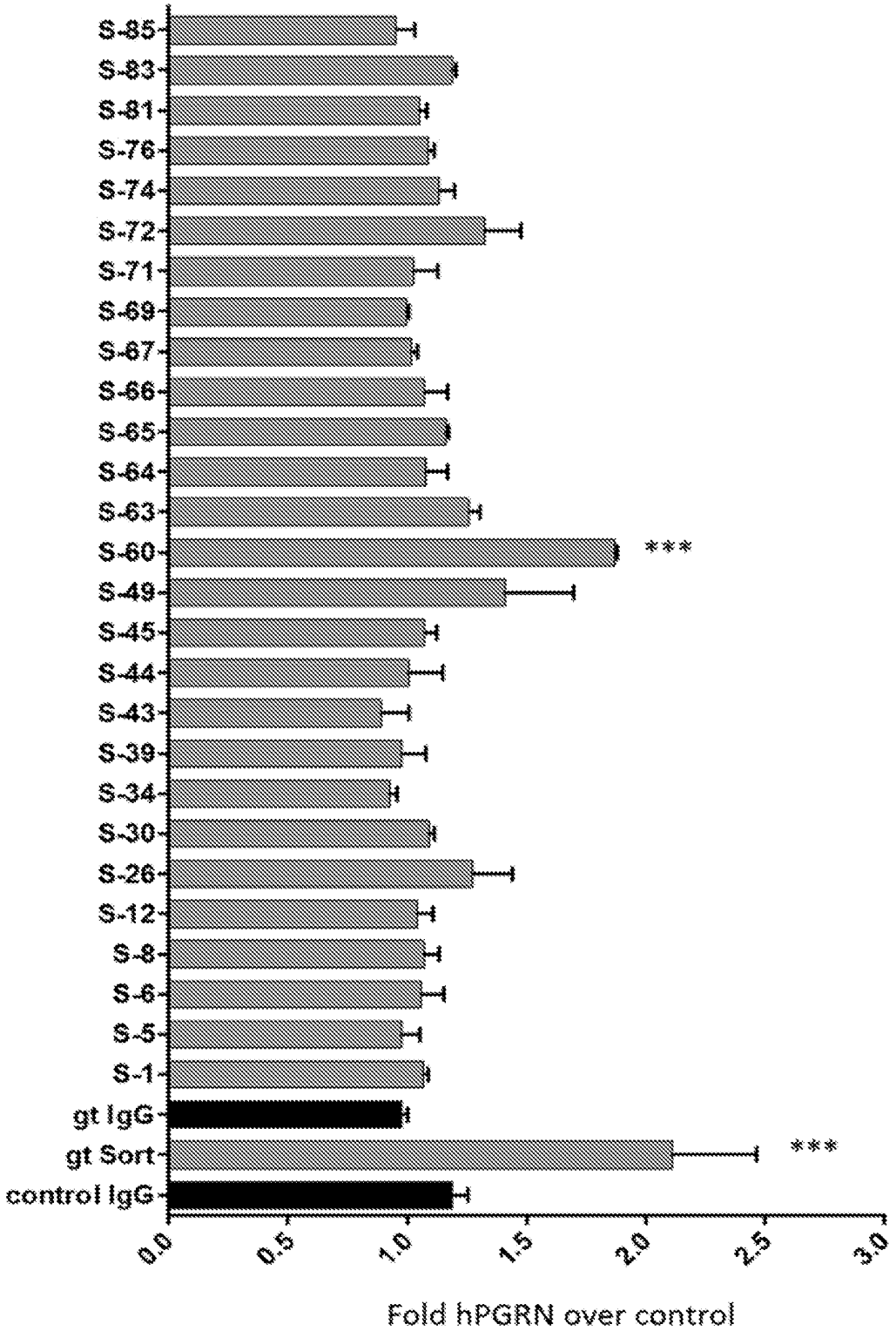

S-85
S-83
S-81
S-76
S-74
S-72
S-71
S-69
S-67
S-66
S-65
S-64
S-63
S-60
S-49
S-45
S-44
S-43
S-39
S-34
S-30
S-26
S-12
S-8
S-6
S-5
S-1
gt IgG
gt Sort
control IgG
***
***
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Fold hPGRN over control

FIG. 9B

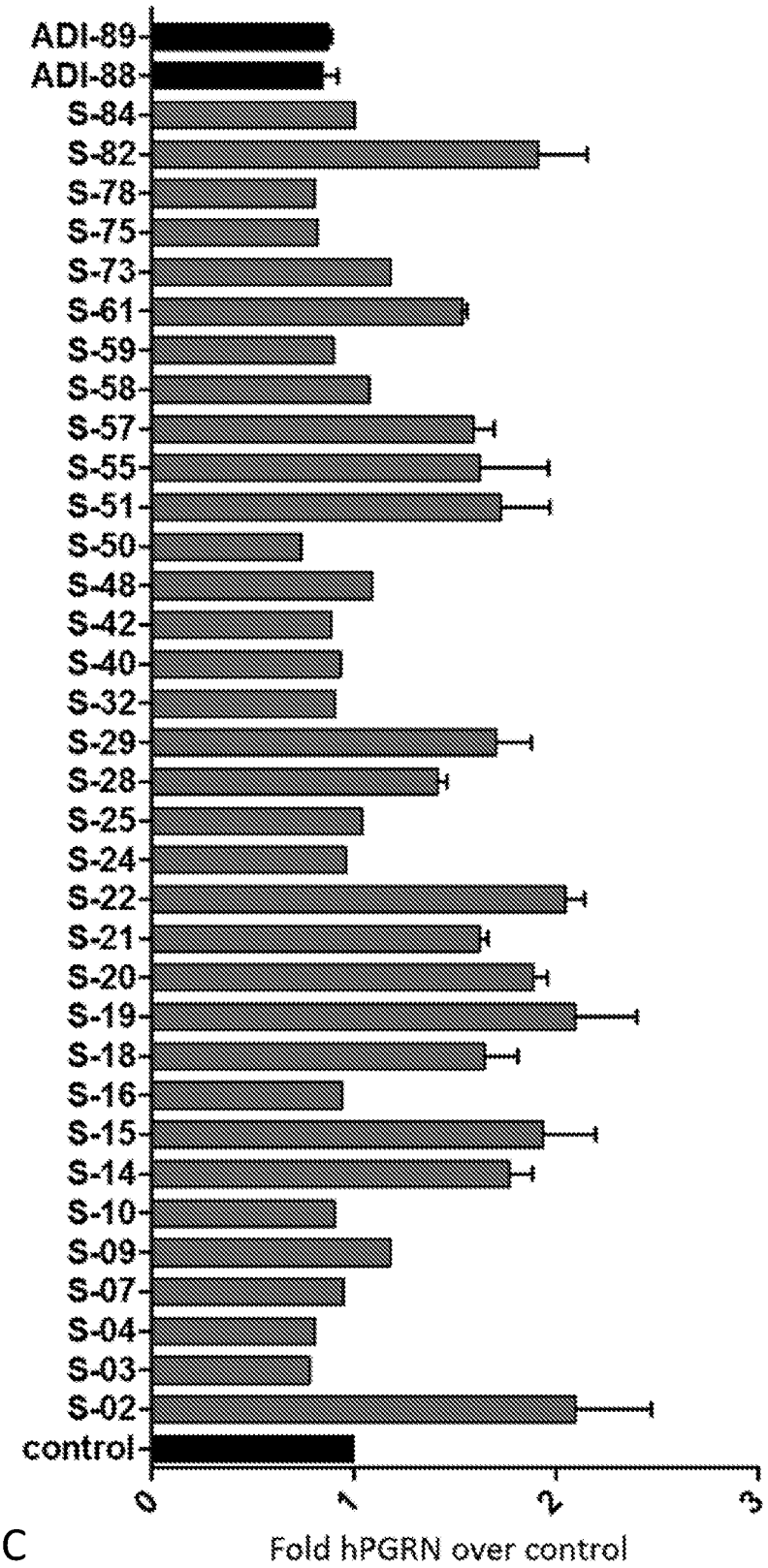

ADI-89
ADI-88
S-84
S-82
S-78
S-75
S-73
S-61
S-59
S-58
S-57
S-55
S-51
S-50
S-48
S-42
S-40
S-32
S-29
S-28
S-25
S-24
S-22
S-21
S-20
S-19
S-18
S-16
S-15
S-14
S-10
S-09
S-07
S-04
S-03
S-02
control
0
1
2
3
Fold hPGRN over control

FIG. 9C

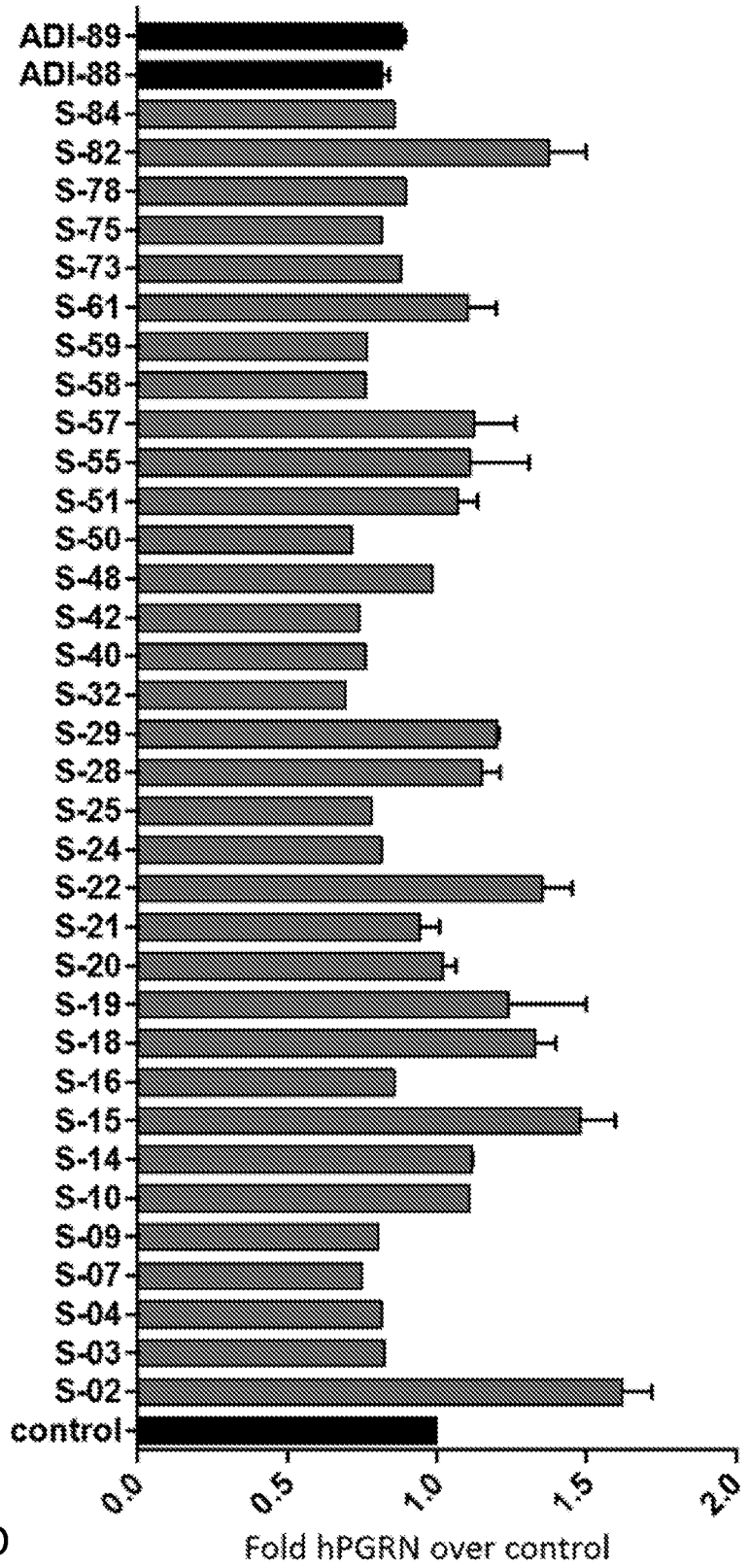

ADI-89
ADI-88
S-84
S-82
S-78
S-75
S-73
S-61
S-59
S-58
S-57
S-55
S-51
S-50
S-48
S-42
S-40
S-32
S-29
S-28
S-25
S-24
S-22
S-21
S-20
S-19
S-18
S-16
S-15
S-14
S-10
S-09
S-07
S-04
S-03
S-02
control
0.0
0.5
1.0
1.5
2.0
Fold hPGRN over control

FIG. 9D

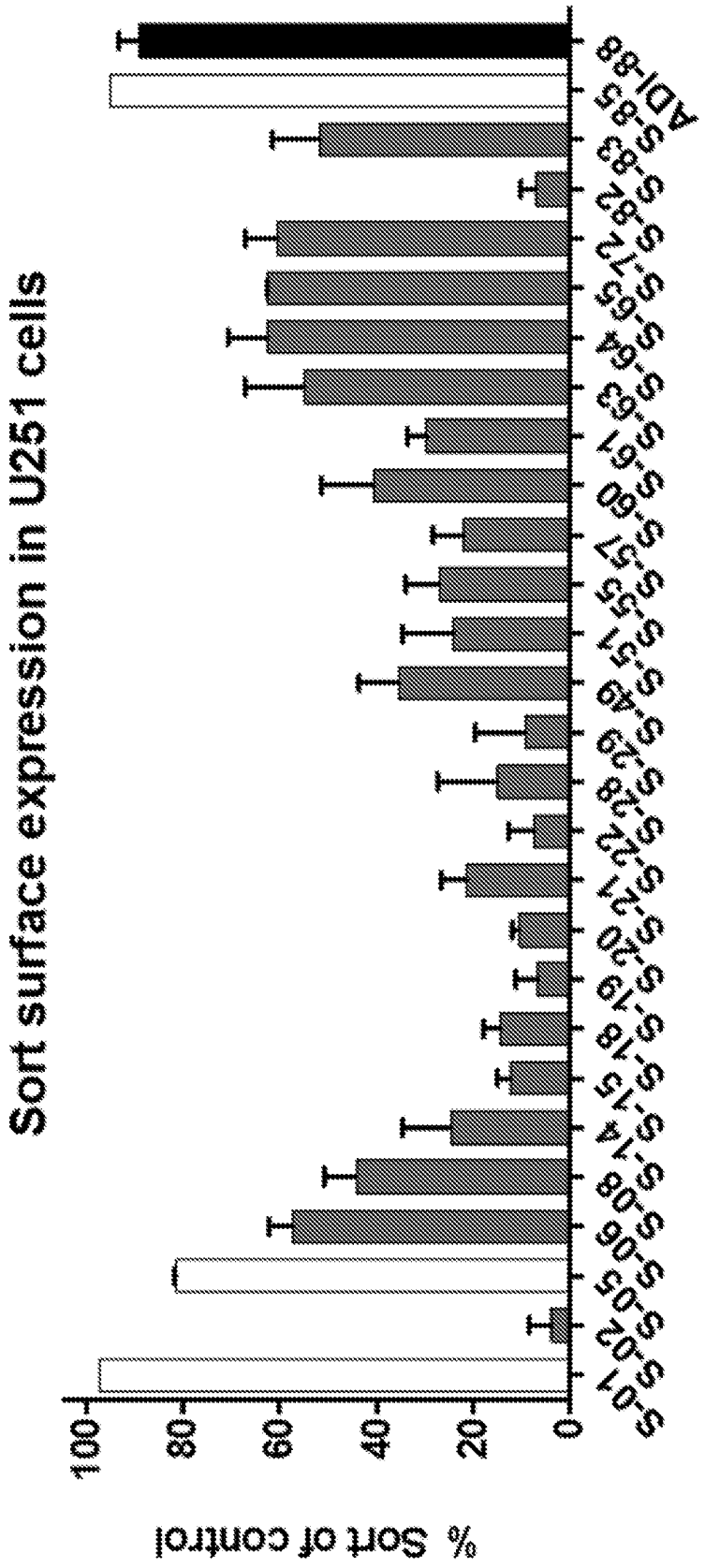

Sort surface expression in U251 cells
% Sort of control
100
80
60
40
20
0
S-01
S-02
S-05
S-06
S-08
S-14
S-15
S-18
S-19
S-20
S-21
S-22
S-28
S-29
S-49
S-51
S-55
S-57
S-60
S-61
S-63
S-64
S-65
S-72
S-82
S-83
S-85
ADI-68

FIG. 10A

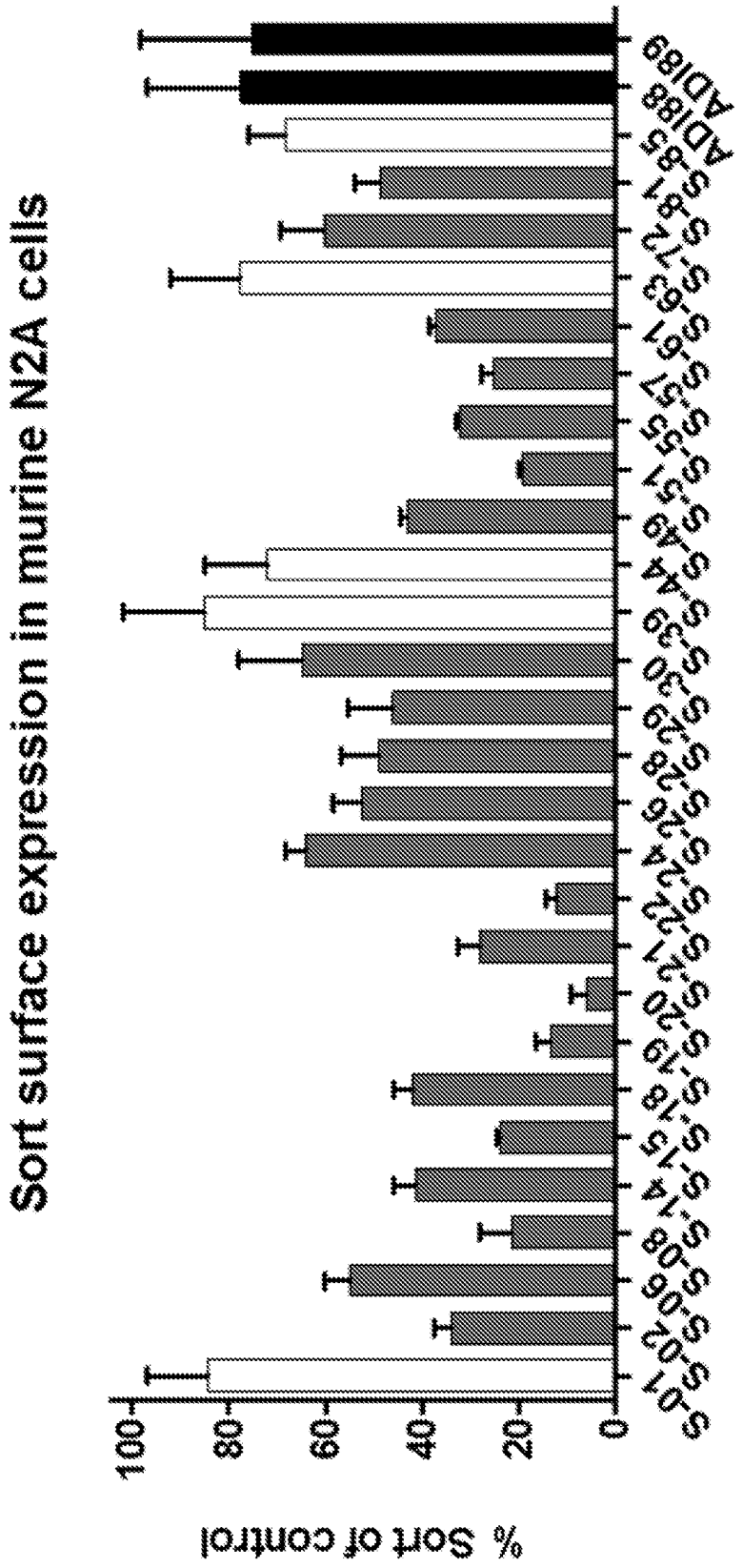

Sort surface expression in murine N2A cells
% Sort of control
100
80
60
40
20
0
S-10-S
S-20-S
S-06-S
S-08-S
S-14-S
S-15-S
S-18-S
S-19-S
S-20-S
S-21-S
S-22-S
S-24-S
S-26-S
S-28-S
S-29-S
S-30-S
S-39-S
S-44-S
S-49-S
S-54-S
S-55-S
S-57-S
S-61-S
S-63-S
S-72-S
S-81-S
S-85-S
ADI188
ADI189

FIG. 10B

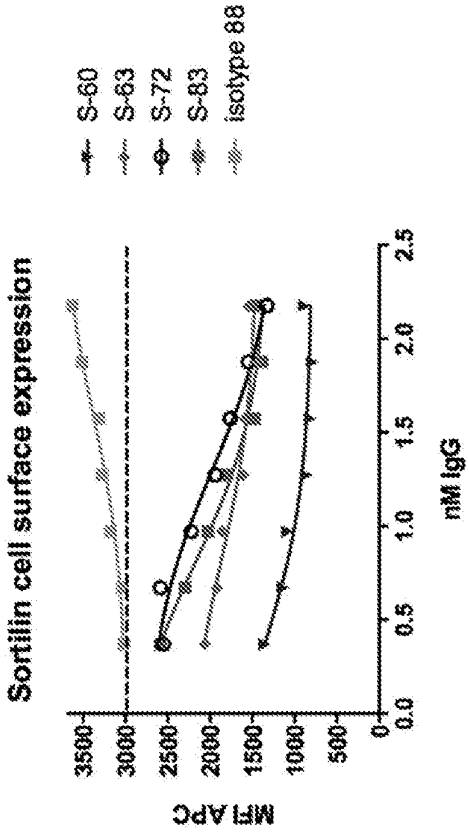


FIG. 10D

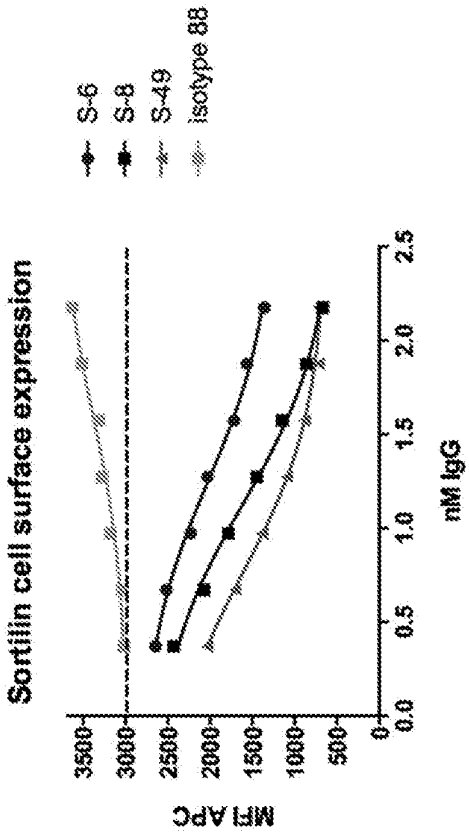


FIG. 10C

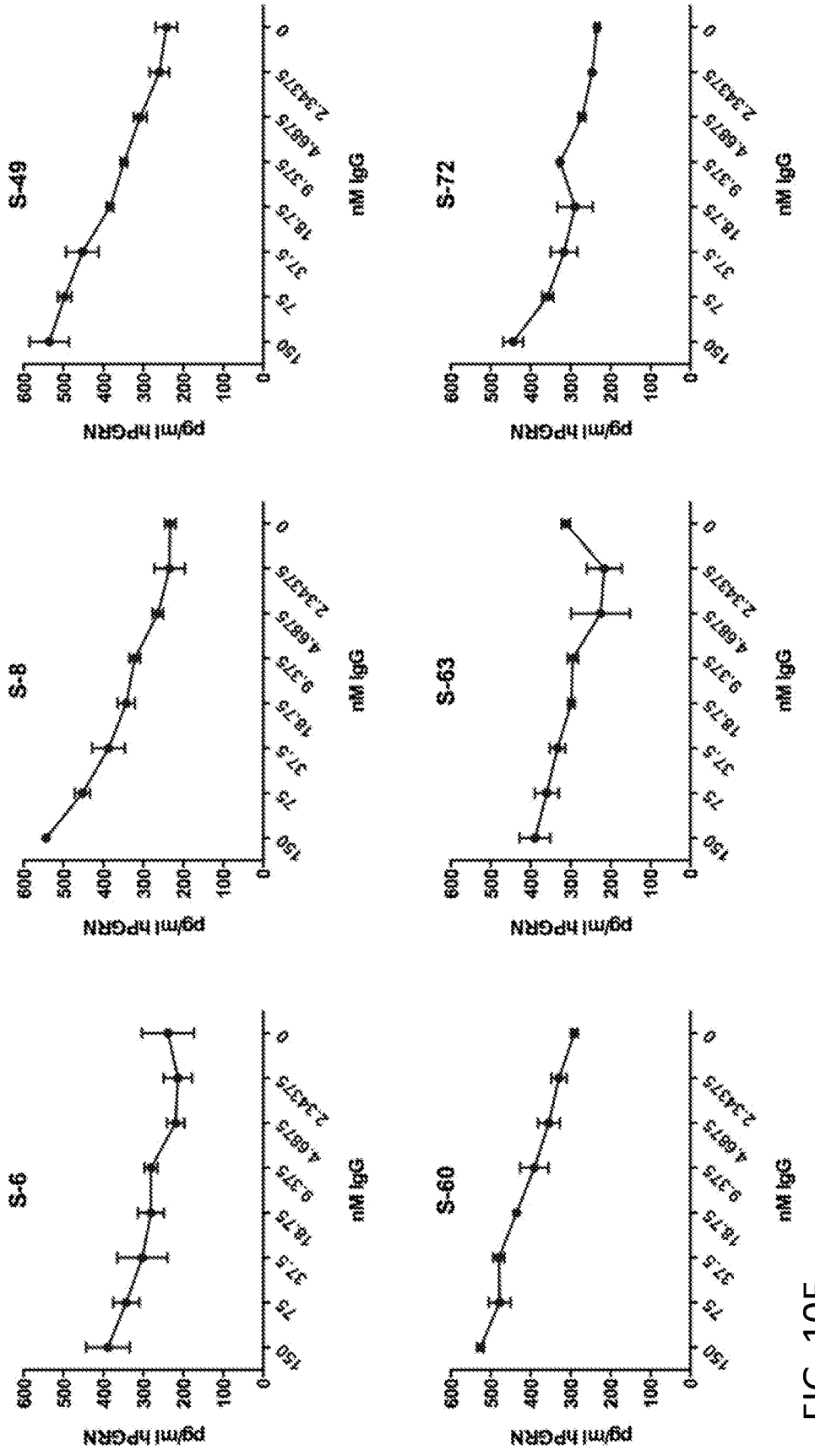

S-49
S-72
S-8
S-63
S-6
S-60
pg/ml hPGRN
nM IgG
600
500
400
300
200
100
0
150
75
37.5
18.75
9.375
4.6875
2.34375

FIG. 10E

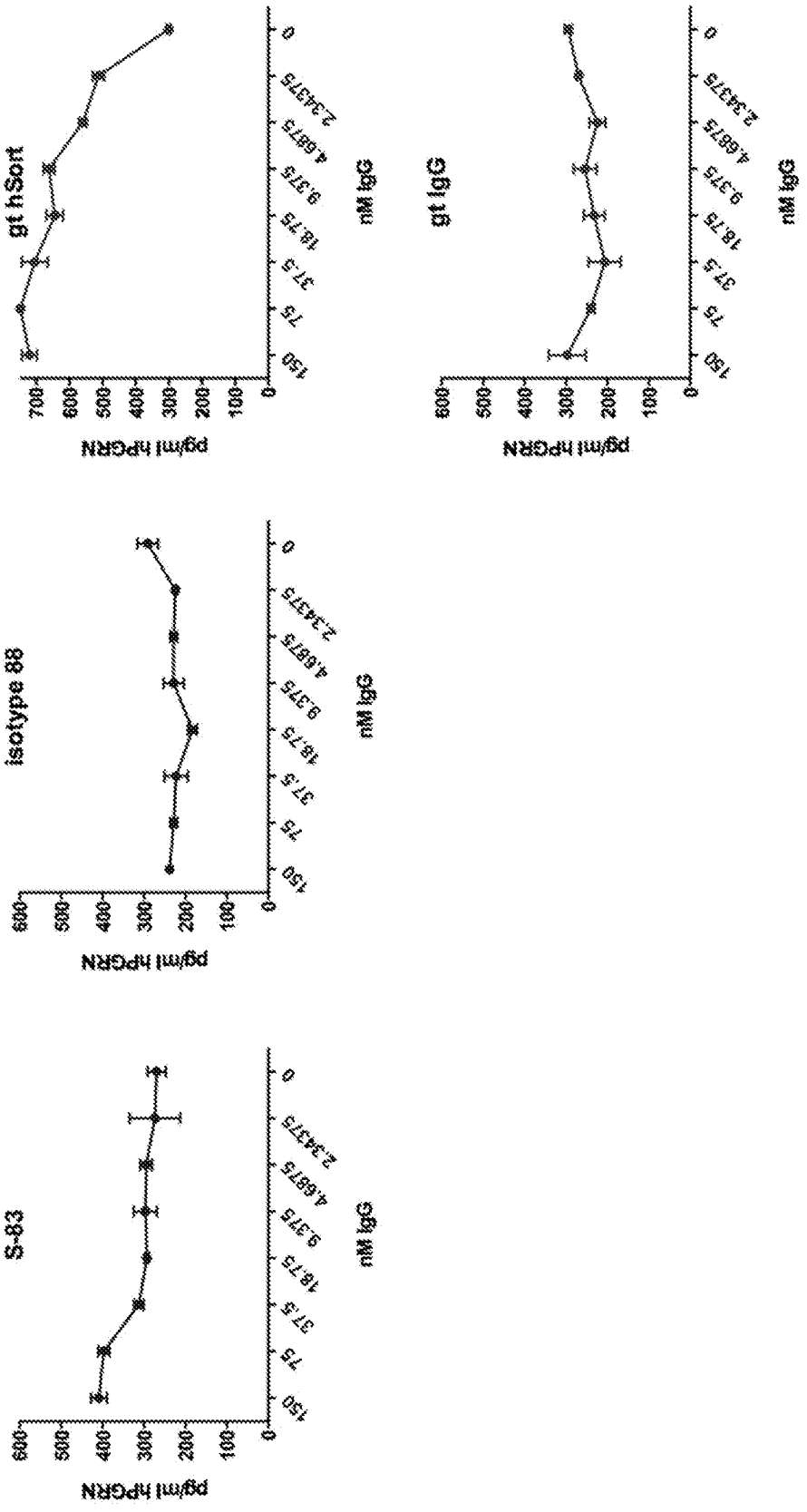

gt hSort
gt IgG
isotype 88
S-83
pg/ml hPGRN
nM IgG
0
2.34375
4.6875
9.375
18.75
37.5
75
150
100
200
300
400
500
600
700

FIG. 10E (Cont.)

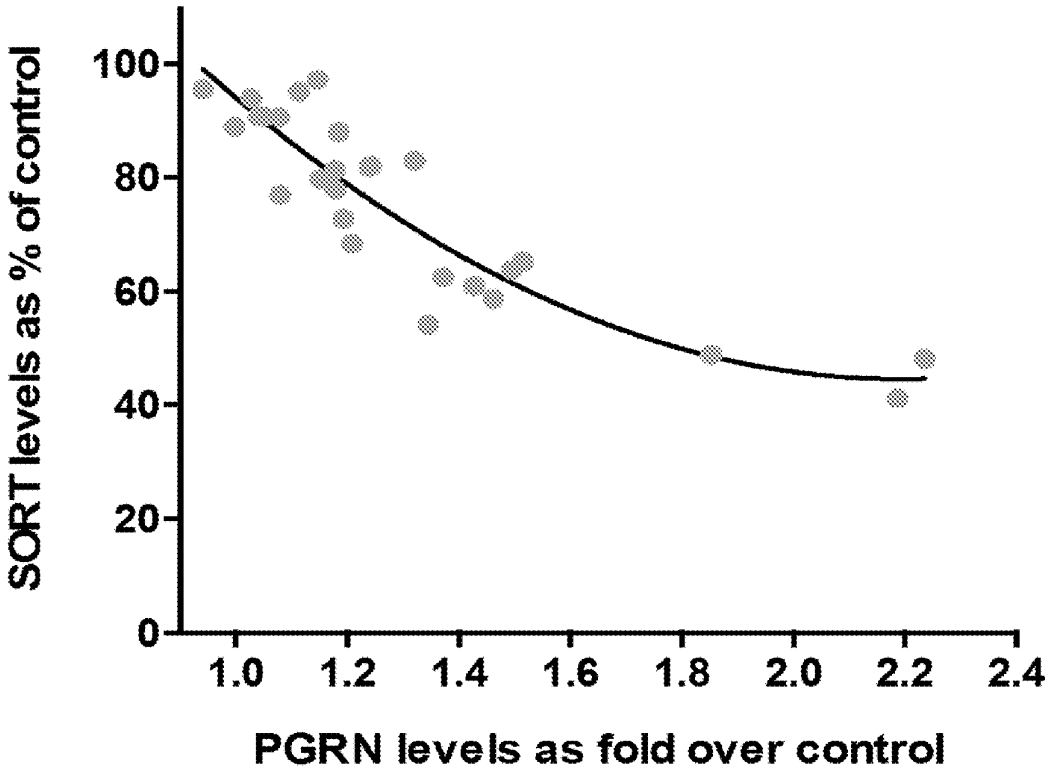

SORT levels as % of control
100
80
60
40
20
0
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
PGRN levels as fold over control

FIG. 10F

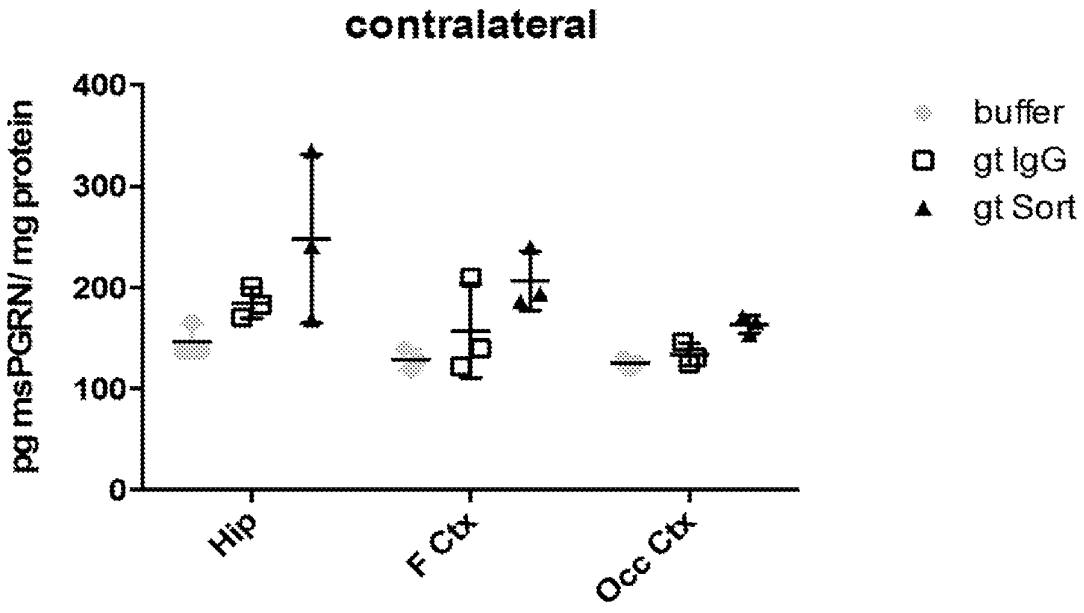


FIG. 11A

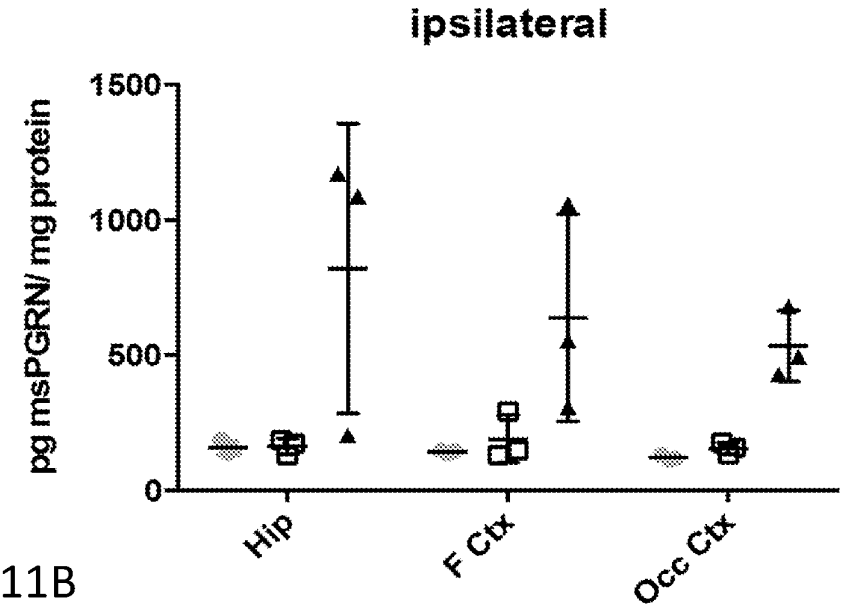


FIG. 11B

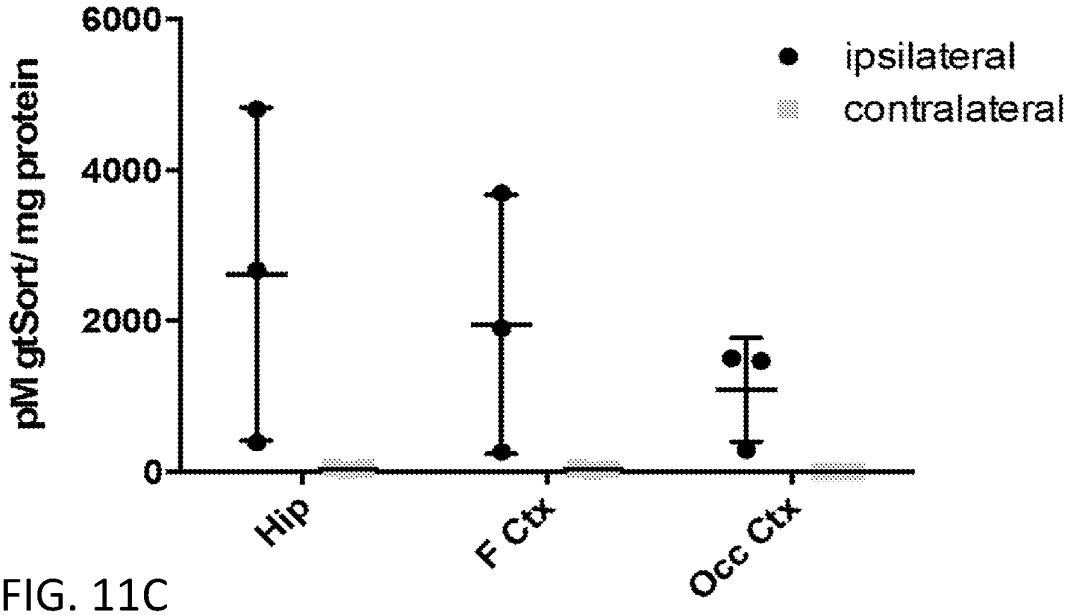


FIG. 11C

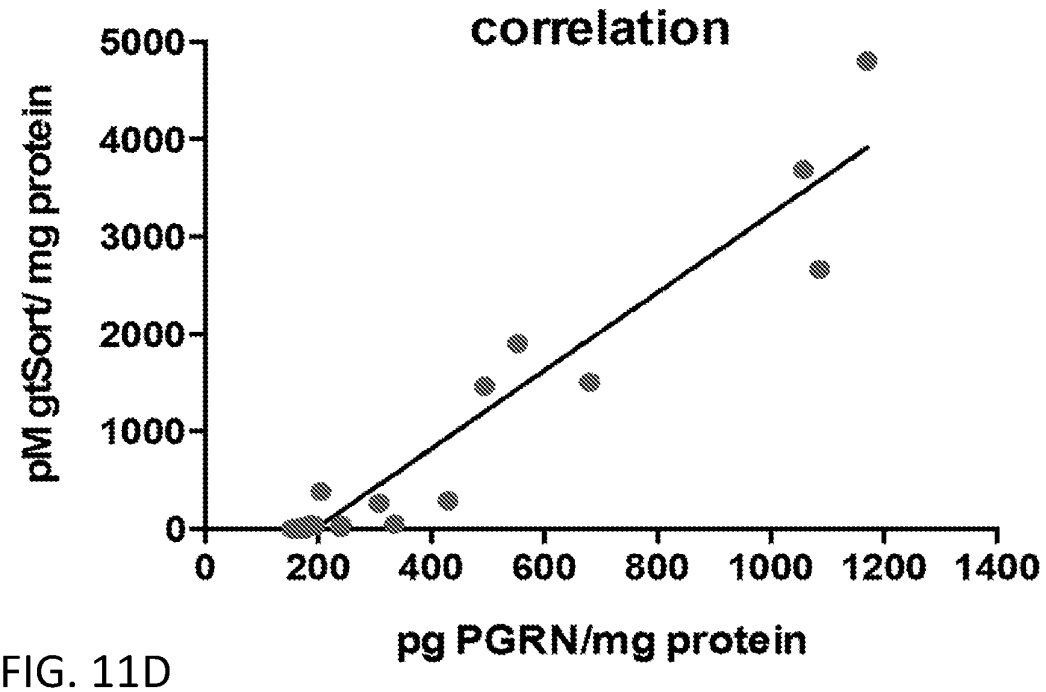


FIG. 11D

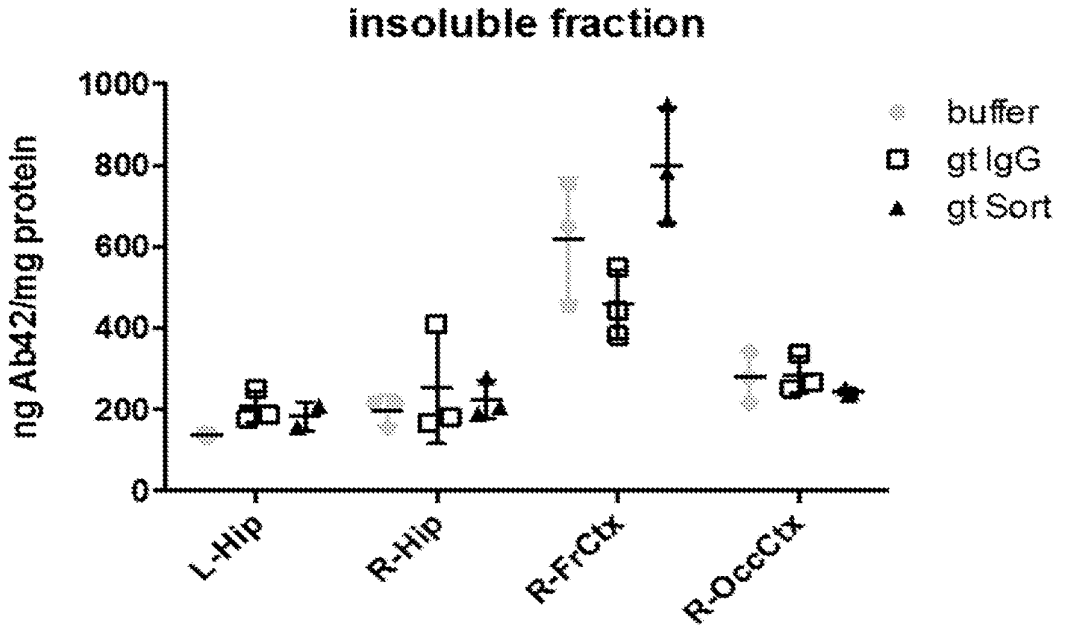


FIG. 11E

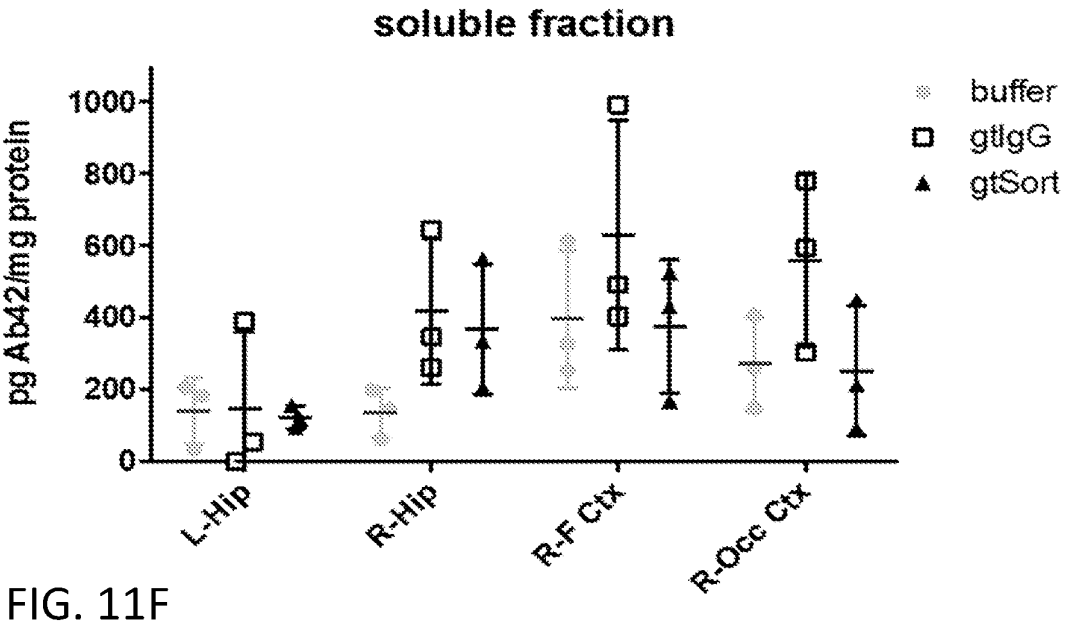


FIG. 11F

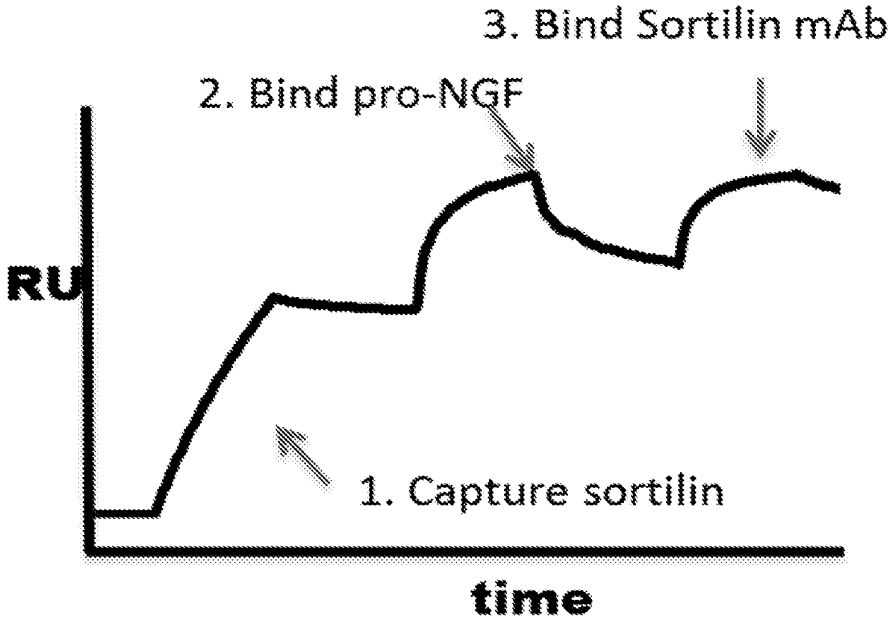


FIG. 12A

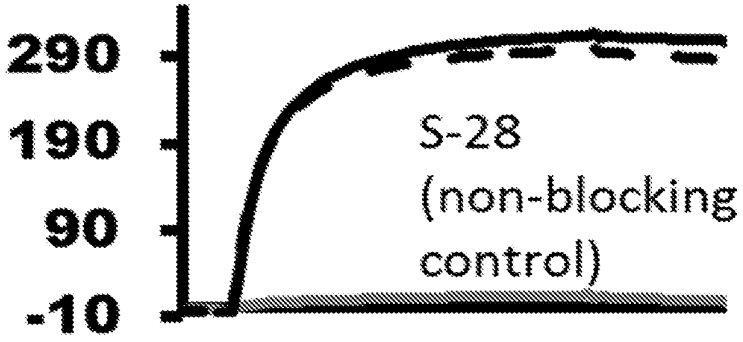


FIG. 12B

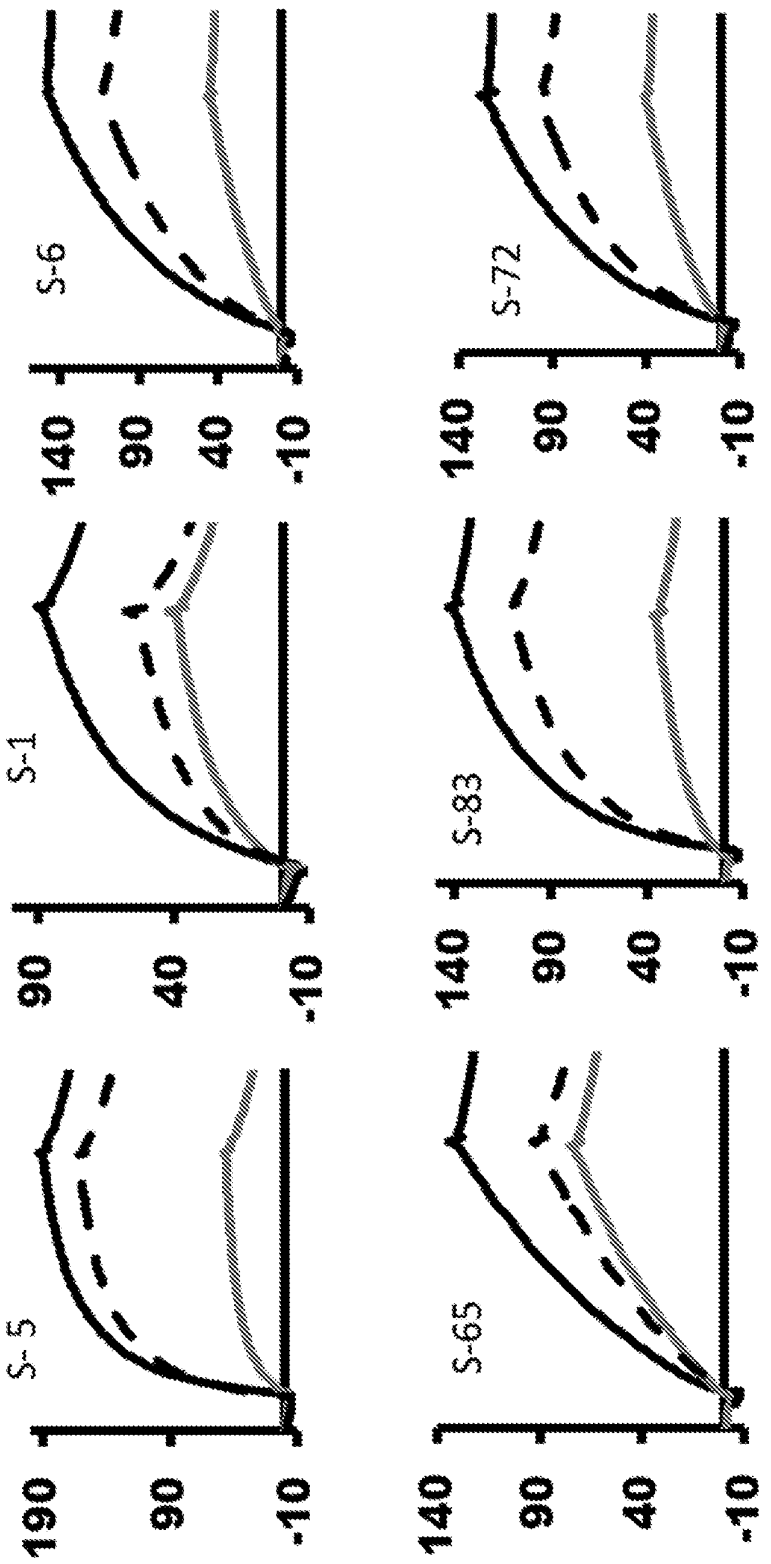

S-5
190
90
-10
S-1
90
40
-10
S-6
140
90
40
-10
S-65
140
90
40
-10
S-83
140
90
40
-10
S-72
140
90
40
-10

FIG. 12C

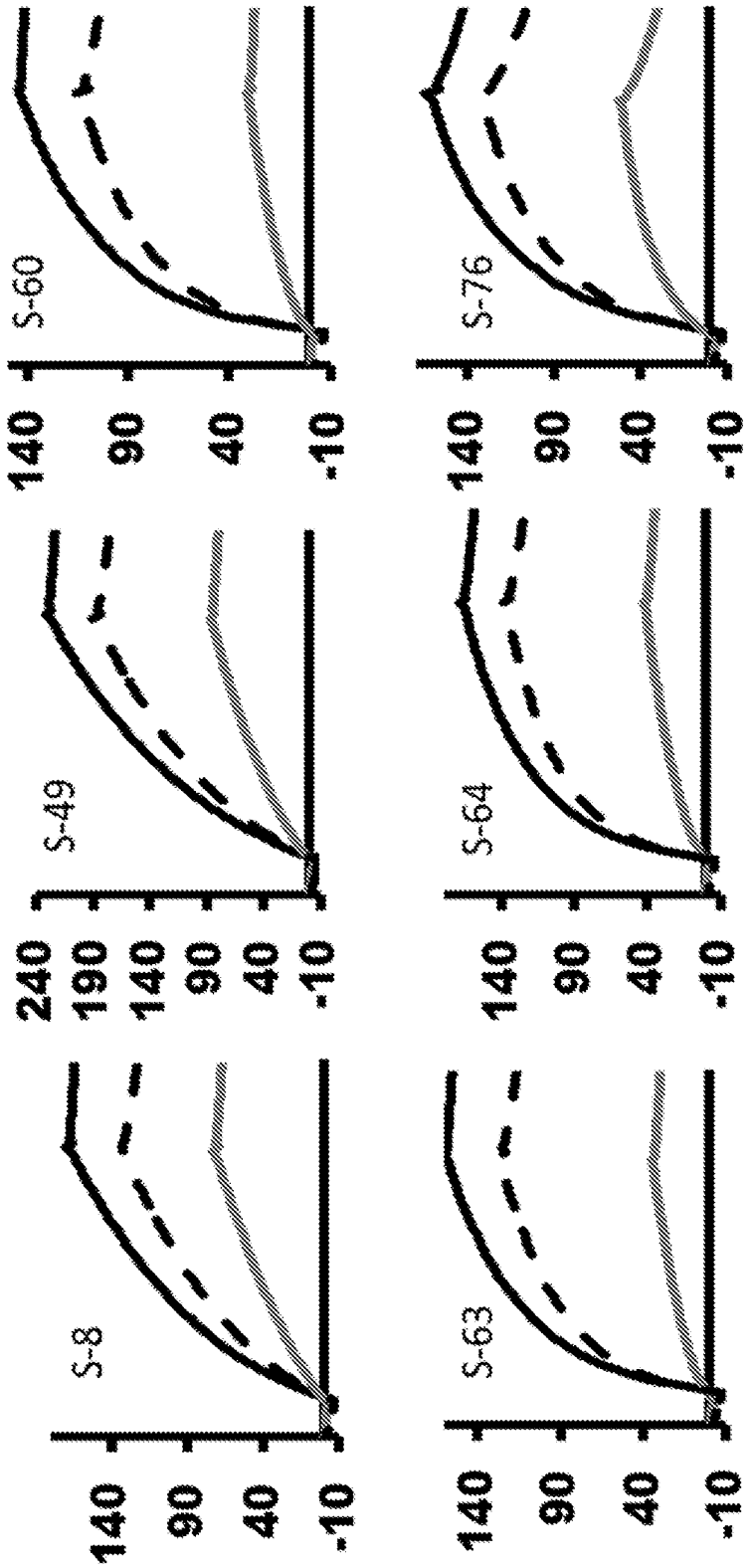


FIG. 12C (Cont.)

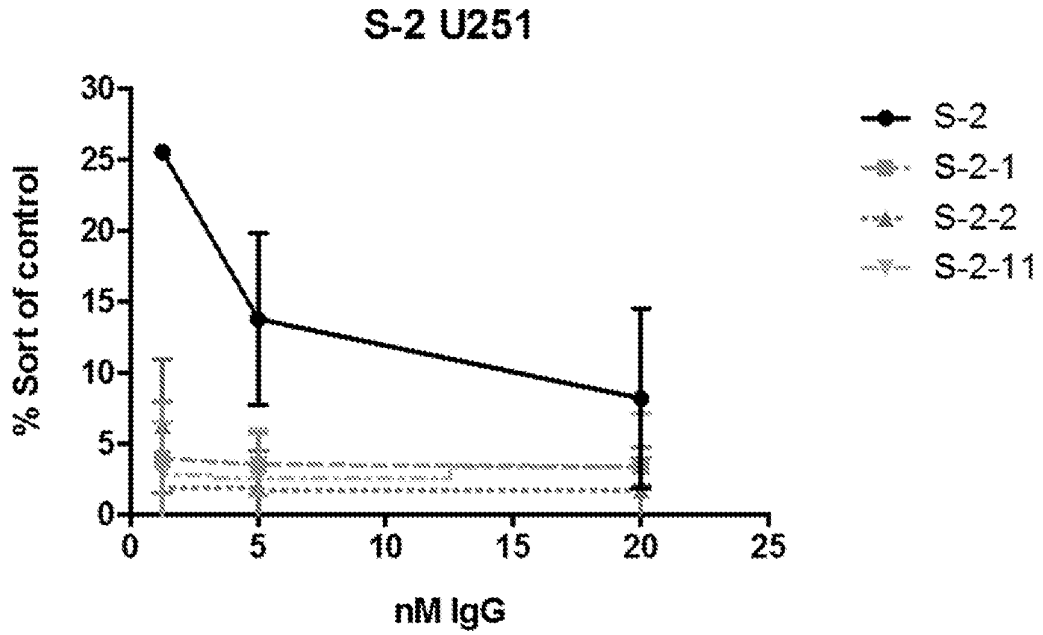


FIG. 13A

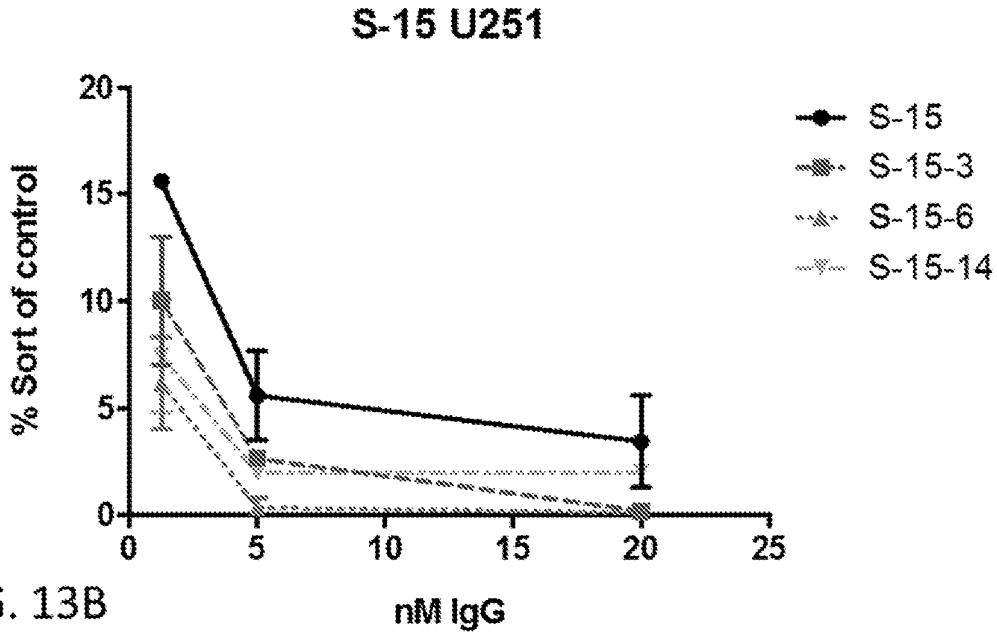


FIG. 13B

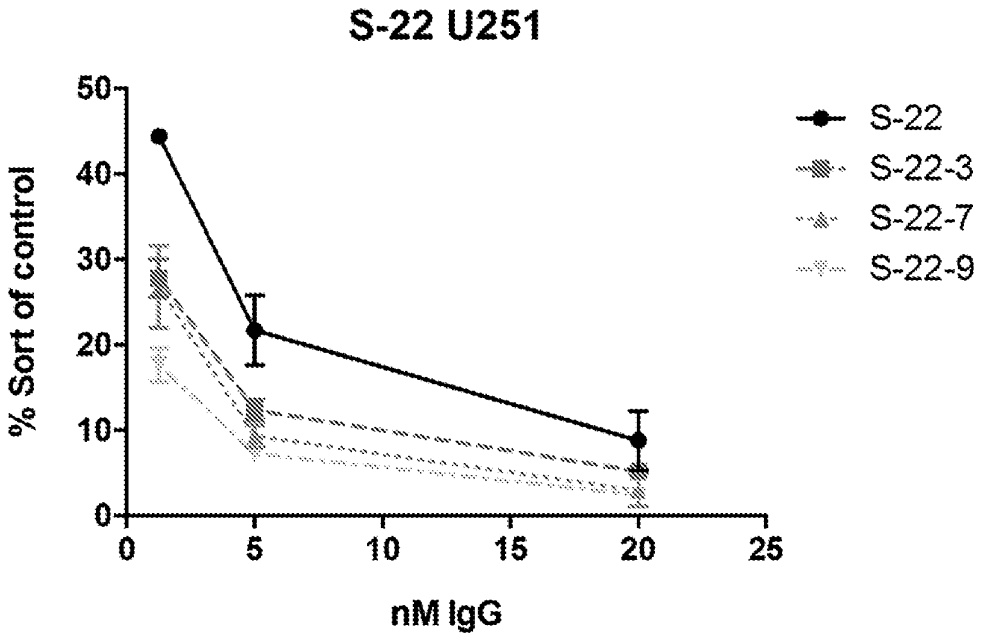


FIG. 13C

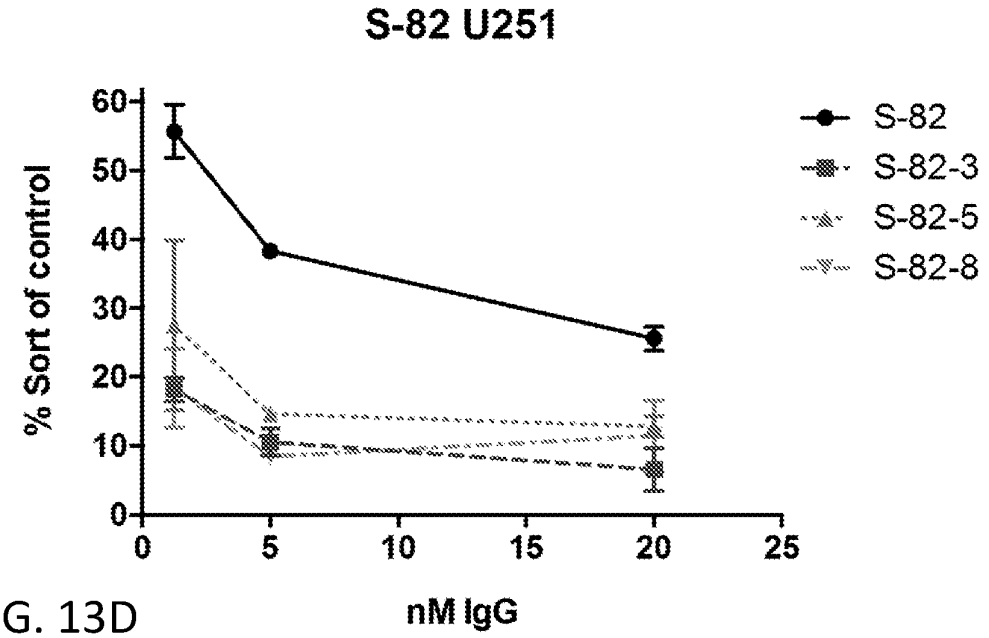


FIG. 13D

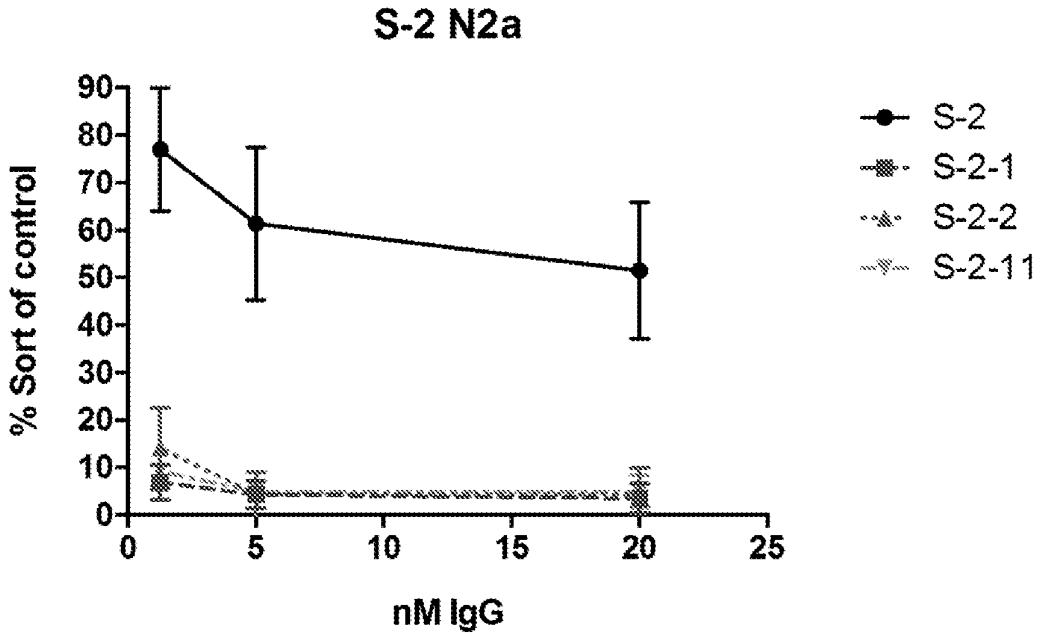


FIG. 13E

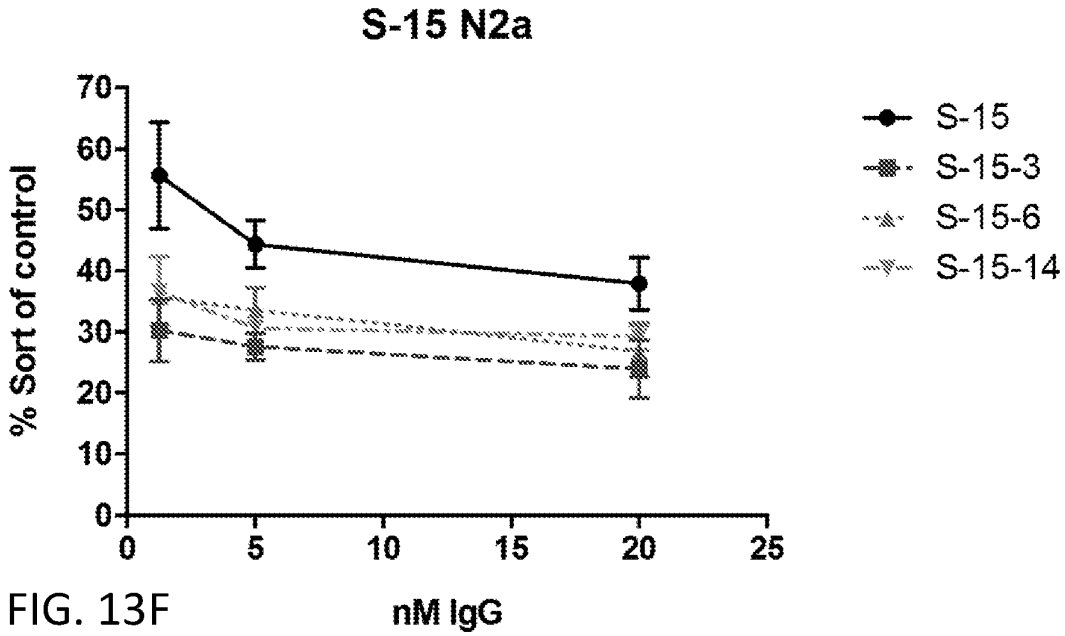


FIG. 13F

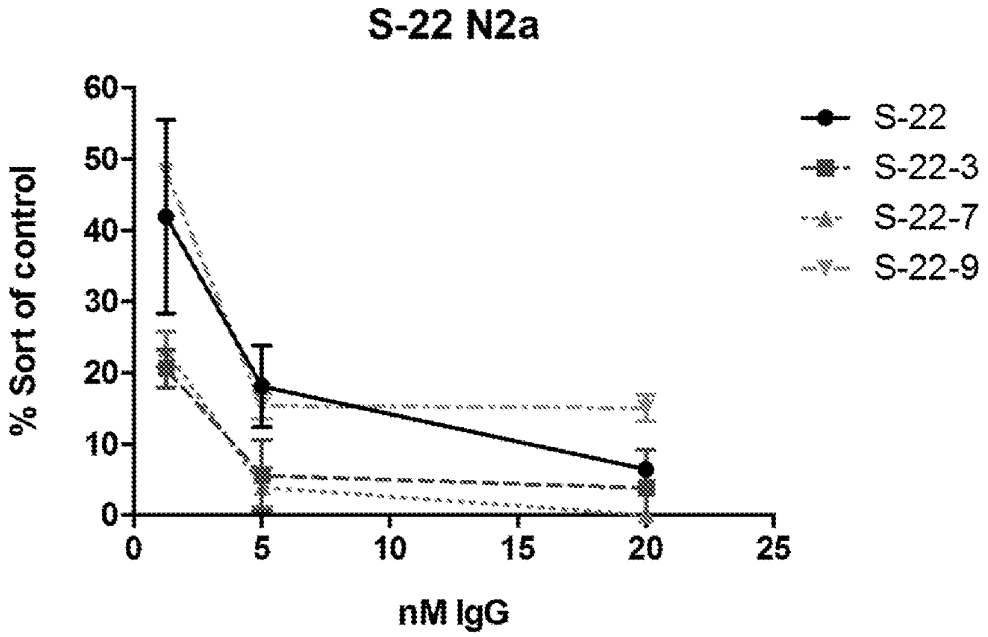

S-22 N2a
% Sort of control
60
50
40
30
20
10
0
0
5
10
15
20
25
nM IgG
S-22
S-22-3
S-22-7
S-22-9

FIG. 13G

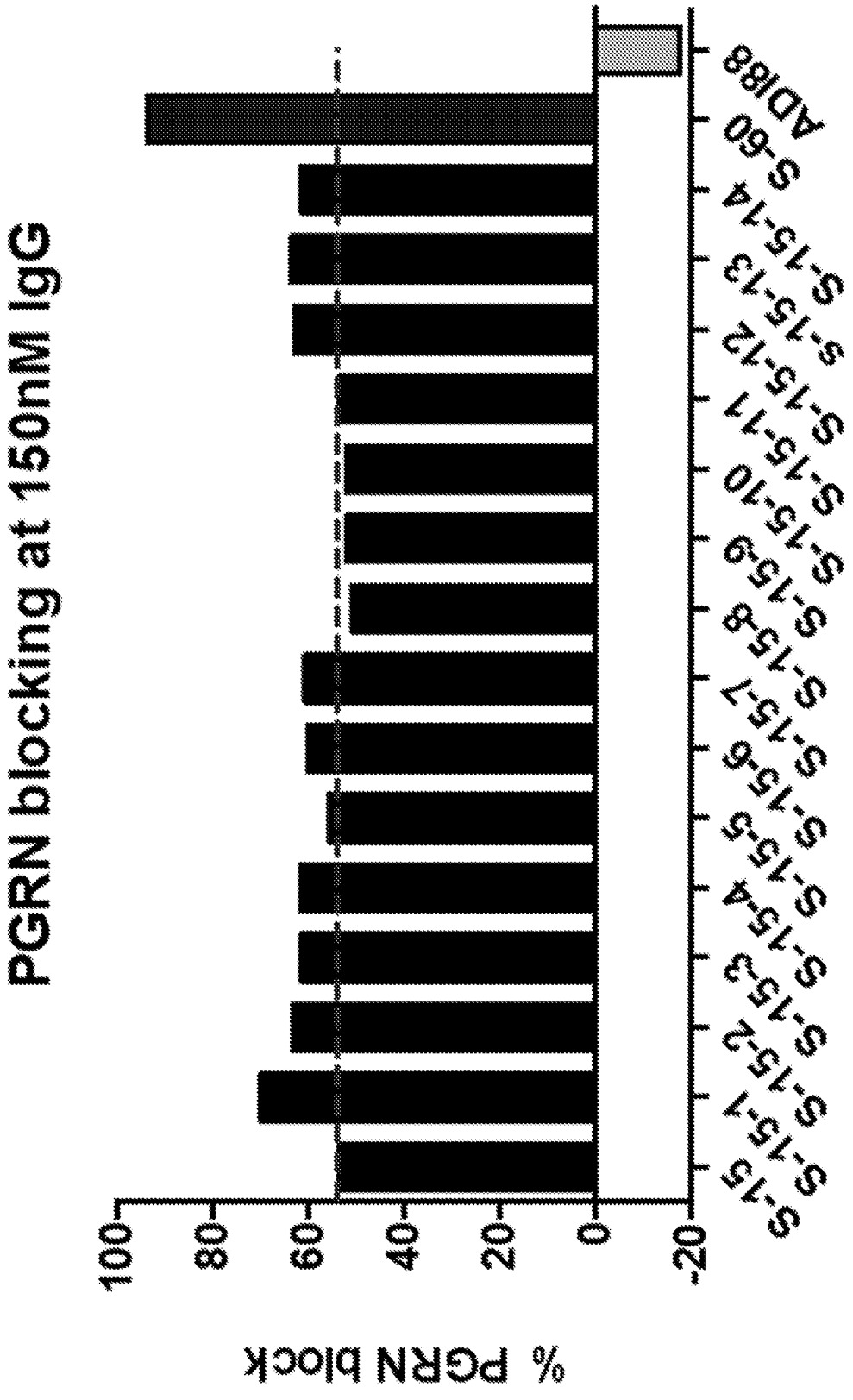

PGRN blocking at 150nM IgG
% PGRN block
100
80
60
40
20
0
-20
S-15
S-15-1
S-15-2
S-15-3
S-15-4
S-15-5
S-15-6
S-15-7
S-15-8
S-15-9
S-15-10
S-15-11
S-15-12
S-15-13
S-15-14
S-60
ADI88

FIG. 14

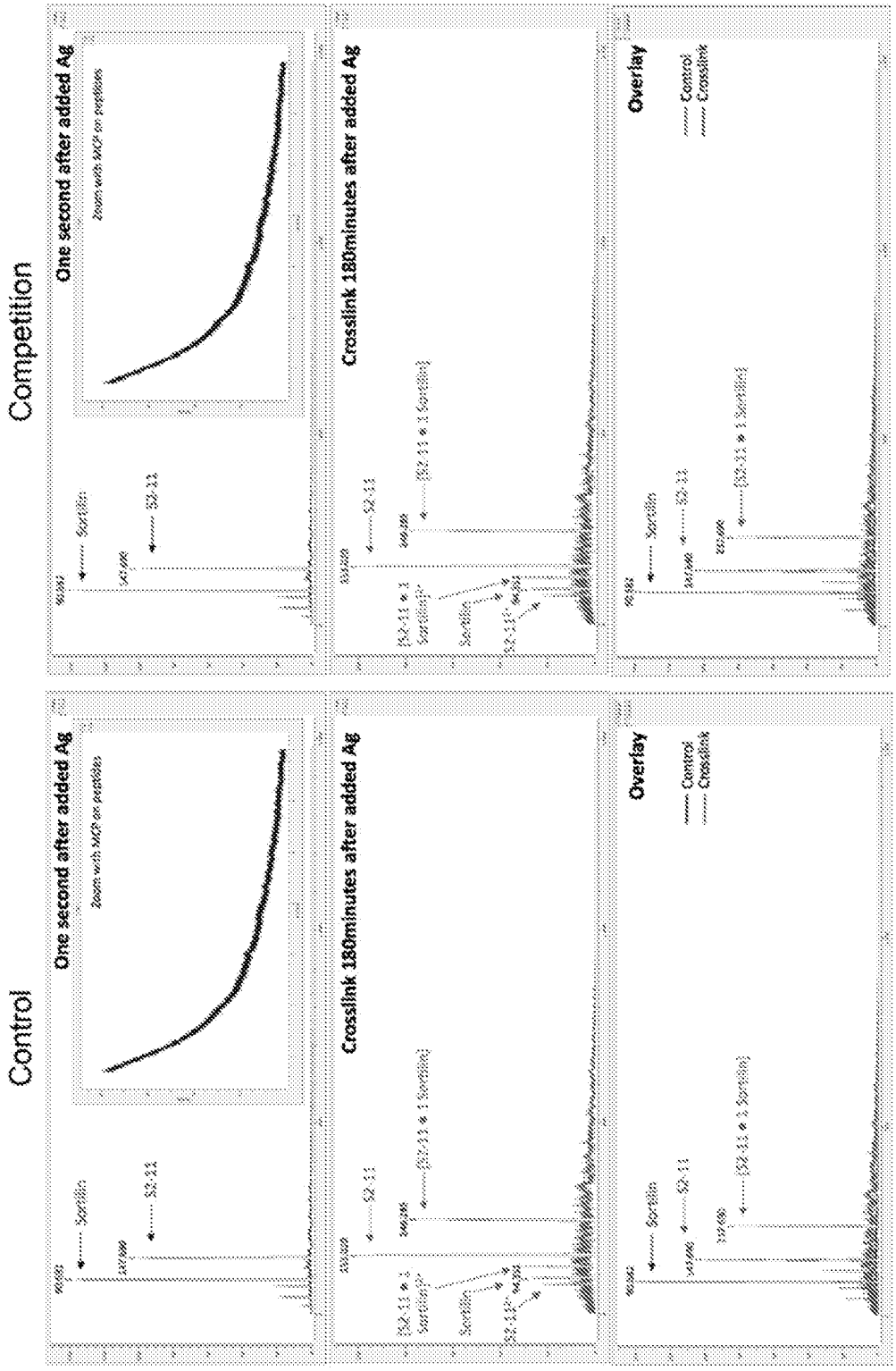


FIG. 15B

FIG. 15A

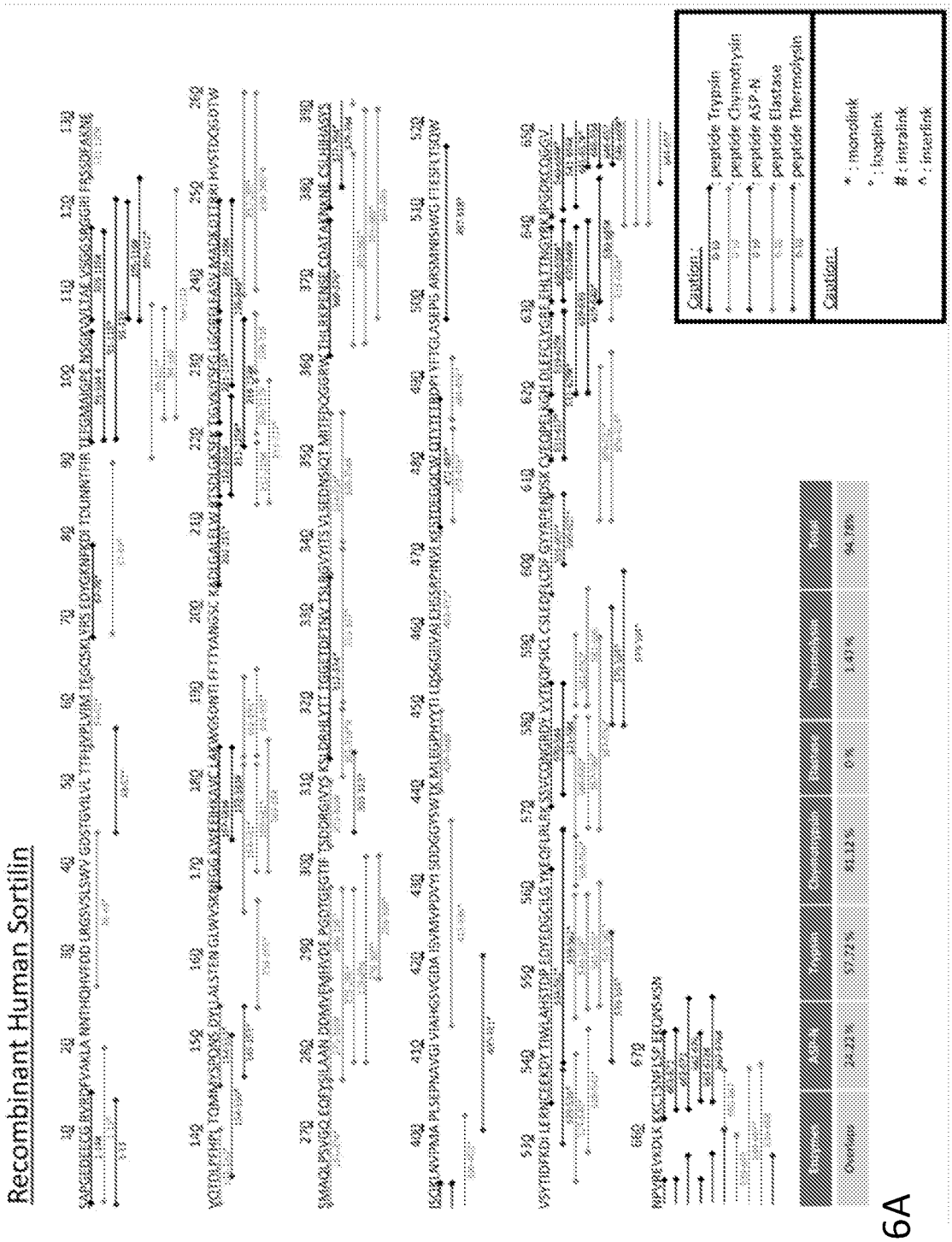

Recombinant Human Sortilin
Caption:
peptide Trypsin
peptide Chymotrypsin
peptide ASP-N
peptide Elastase
peptide Thermolysin
Caption:
*: monolink
°: loop link
#: interlink
^: intralink

FIG. 16A

FIG. 16B

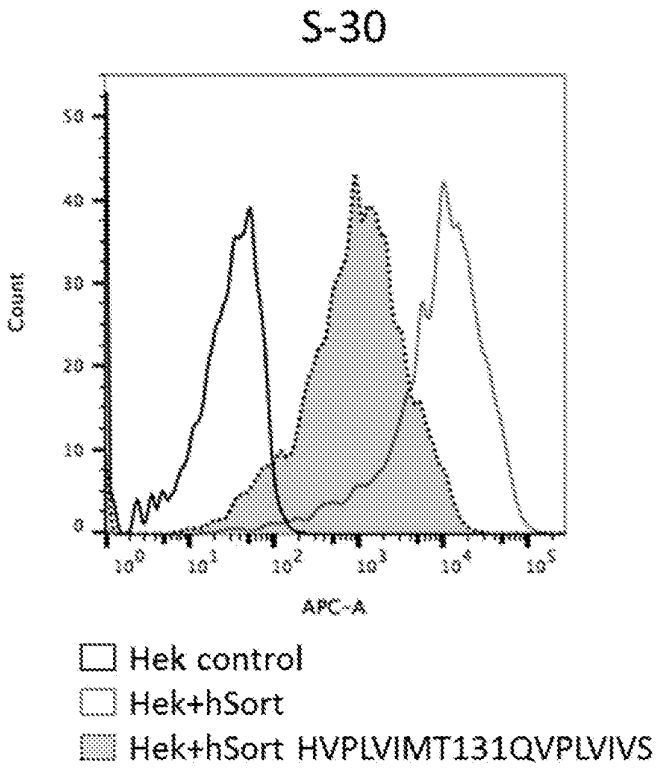
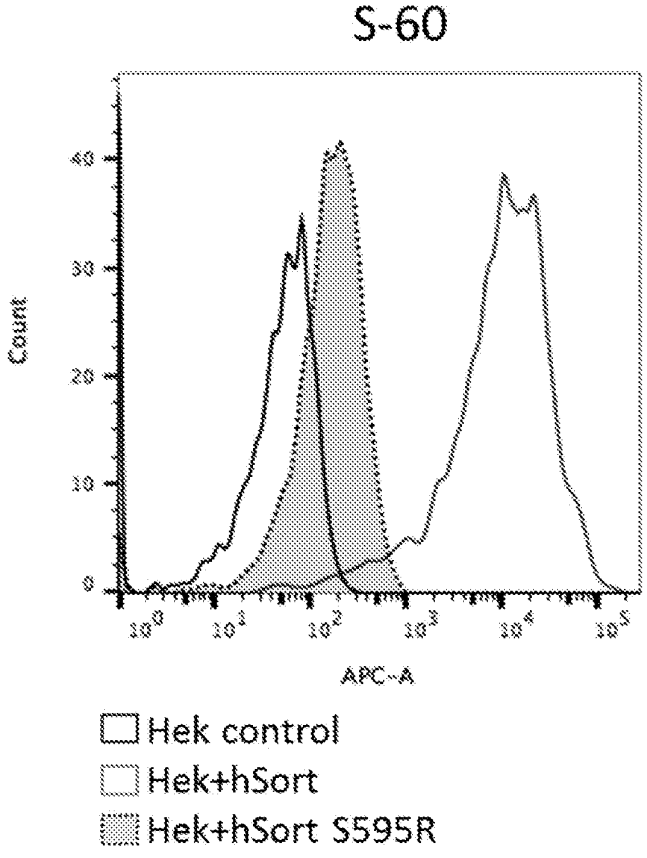


FIG. 16C



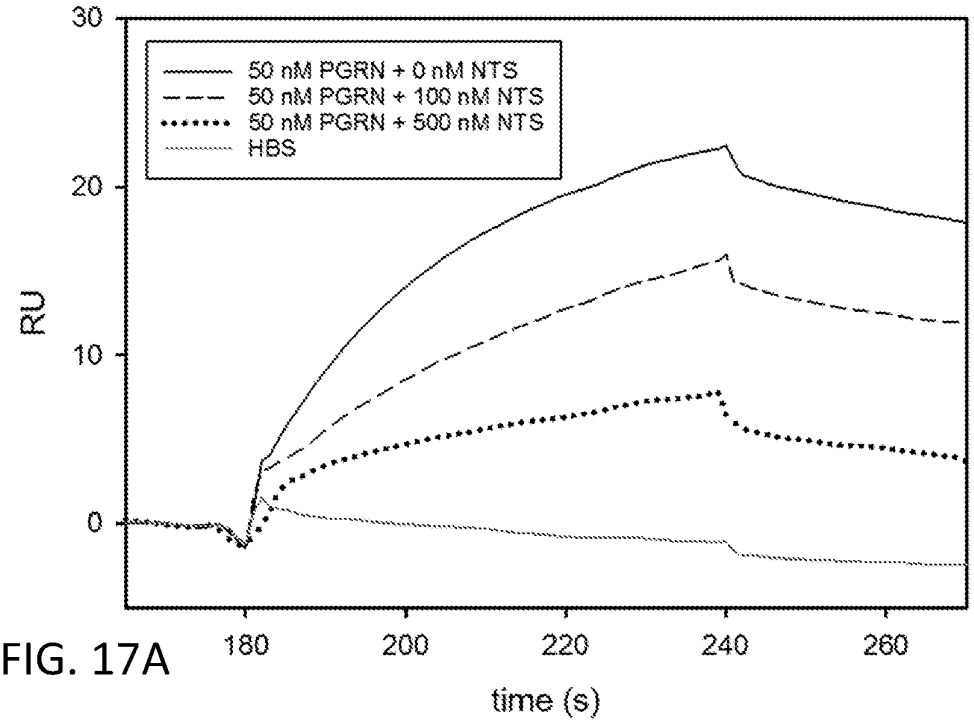


FIG. 17A

S-15

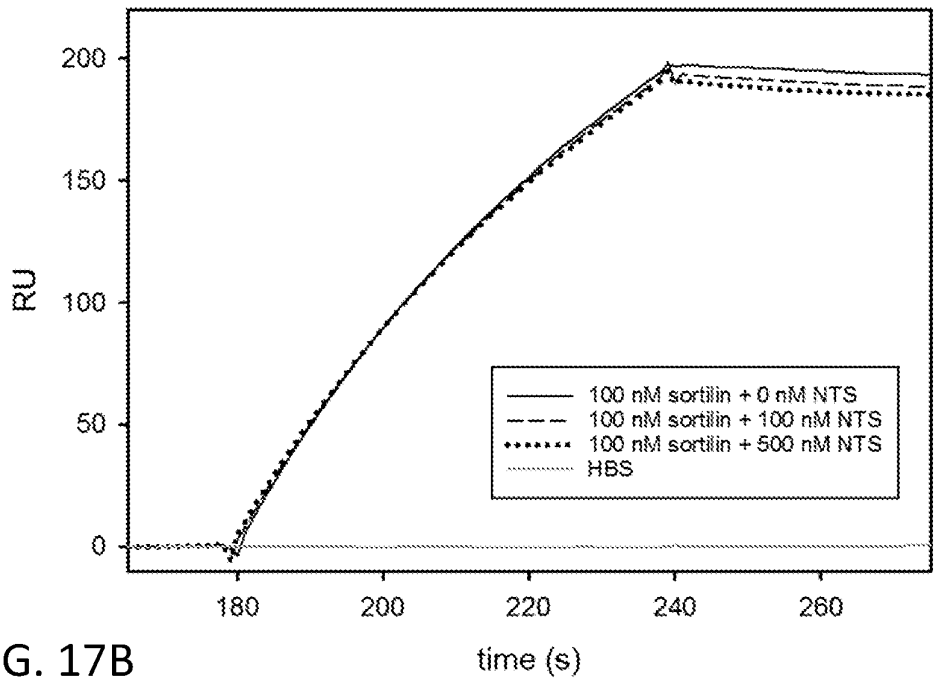


FIG. 17B

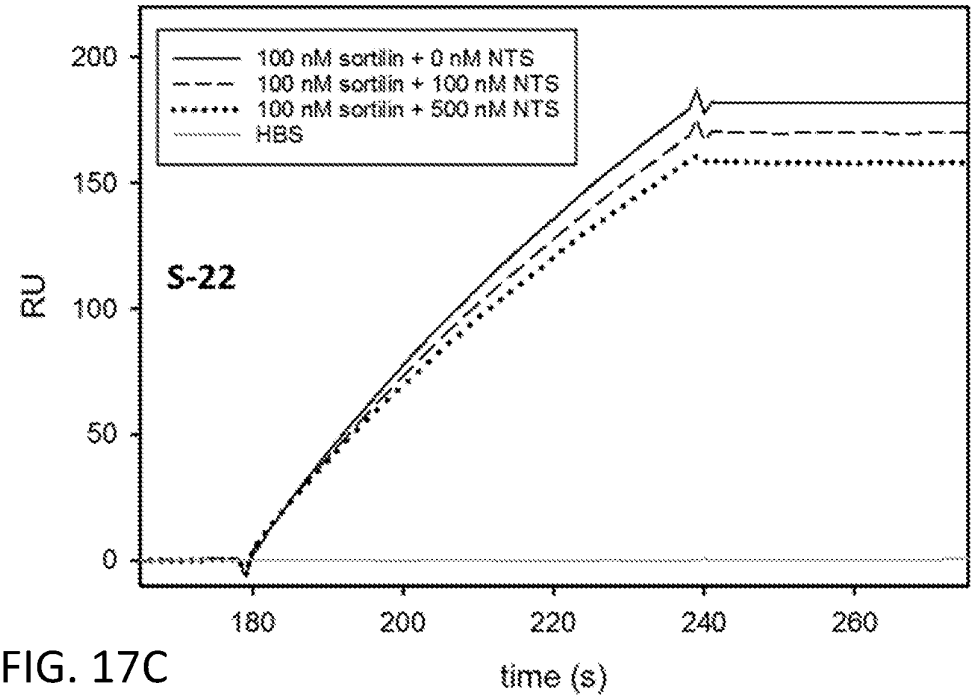


FIG. 17C

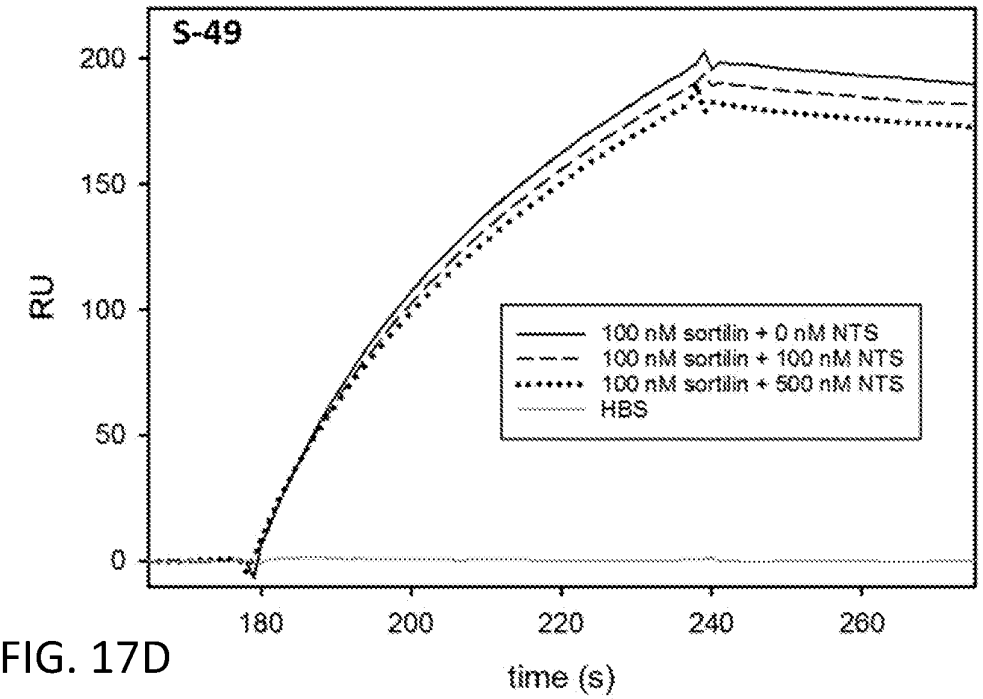


FIG. 17D

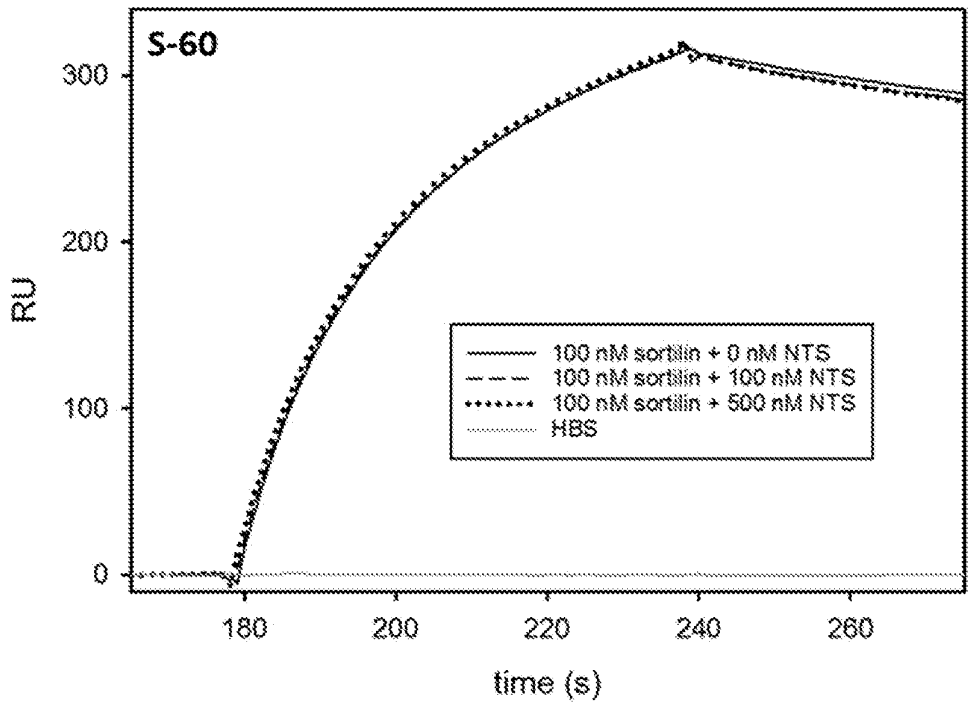

S-60
300
200
100
0
RU
180
200
220
240
260
time (s)
100 nM sortilin + 0 nM NTS
100 nM sortilin + 100 nM NTS
100 nM sortilin + 500 nM NTS
HBS

FIG. 17E

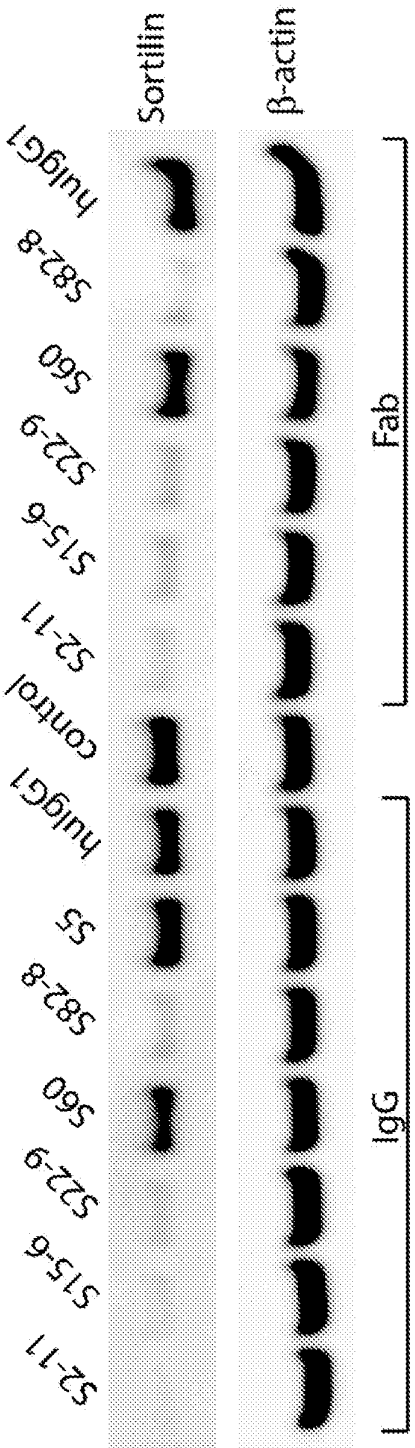


FIG. 18A

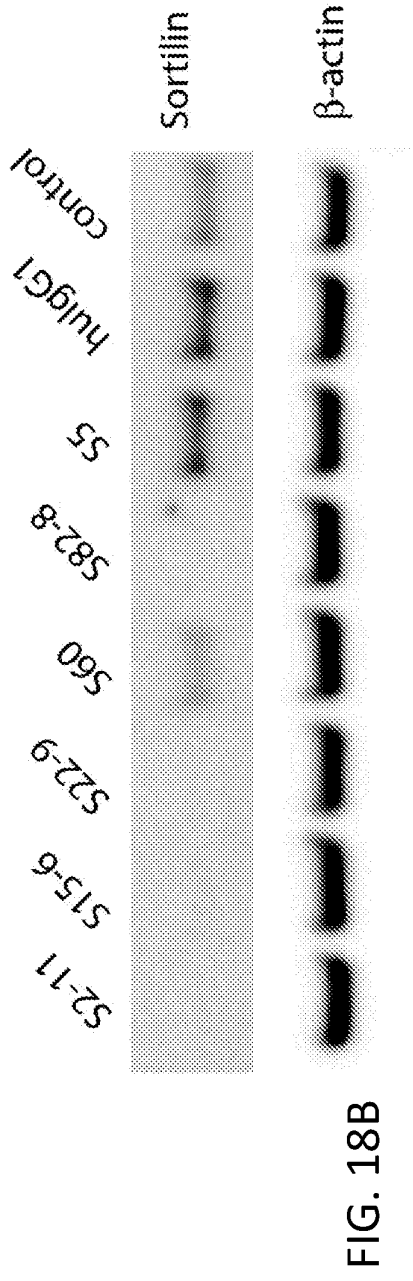


FIG. 18B

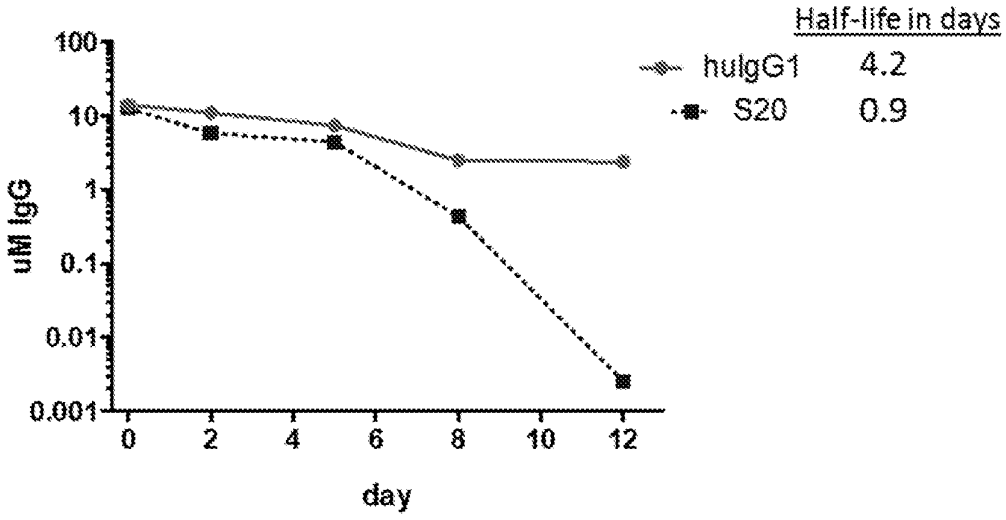


FIG. 19A

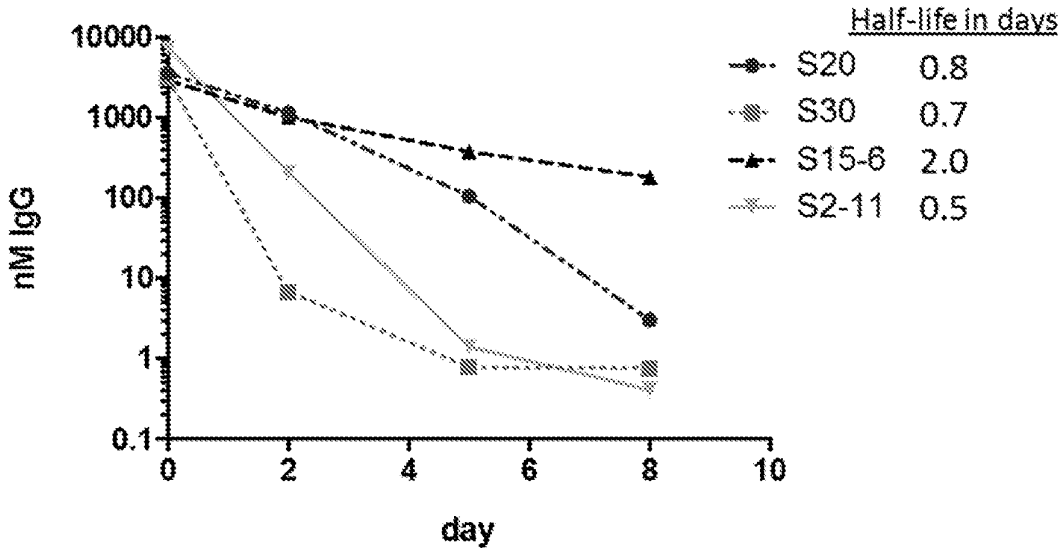


FIG. 19B

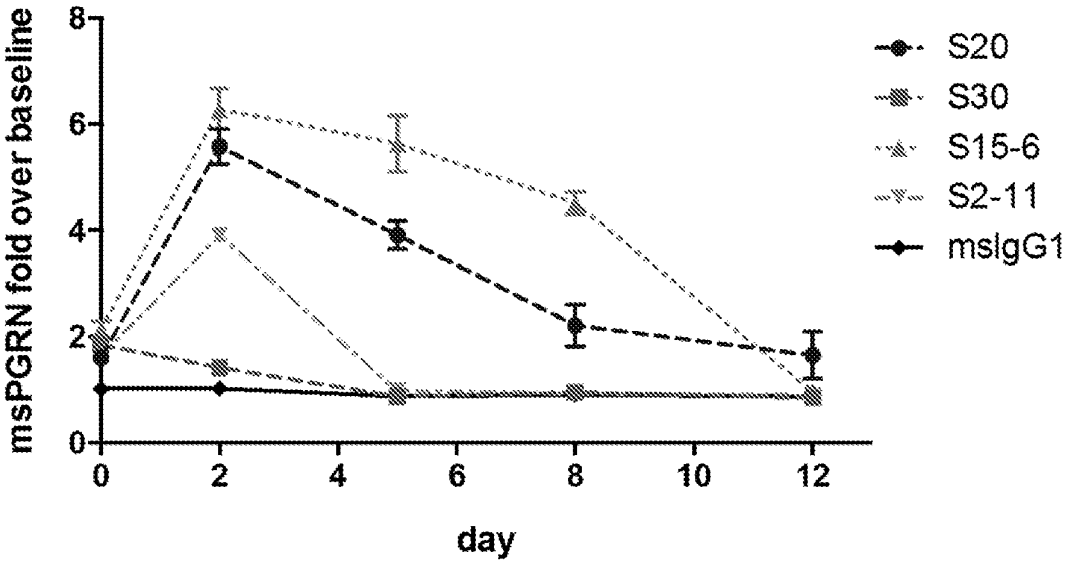


FIG. 20A

day	0 (4h)	2	5	8	12
S20	**	****	****	***	n.s.
S30	***	n.s.	n.s.	n.s.	n.s.
S15-6	****	****	****	****	n.s.
S2-11	**	****	n.s.	n.s.	n.s.

FIG. 20B

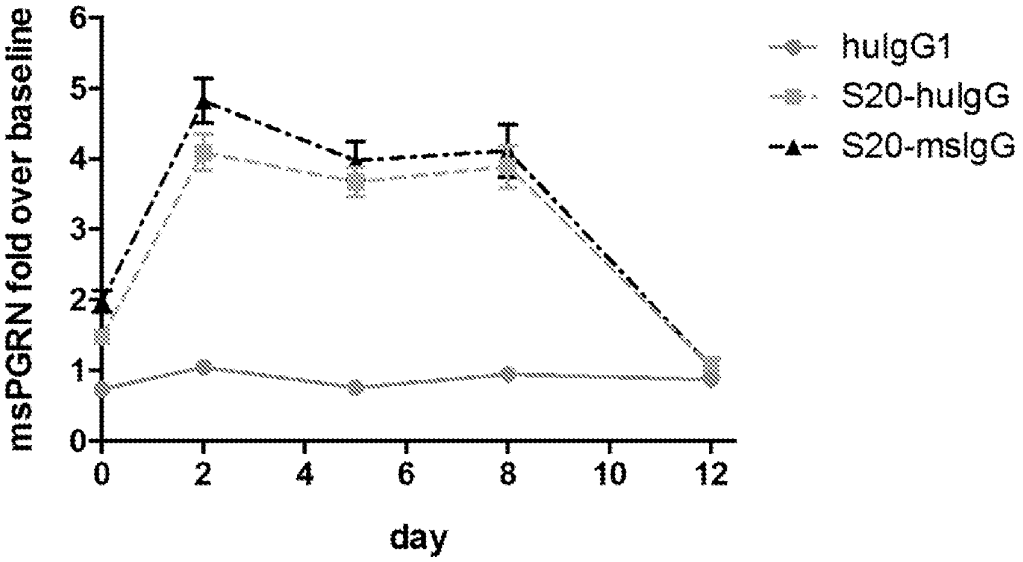


FIG. 20C

day	0 (4h)	2	5	8	12
S20 huIgG	***	****	****	****	*
S20 msIgG	****	****	****	****	n.s.

FIG. 20D

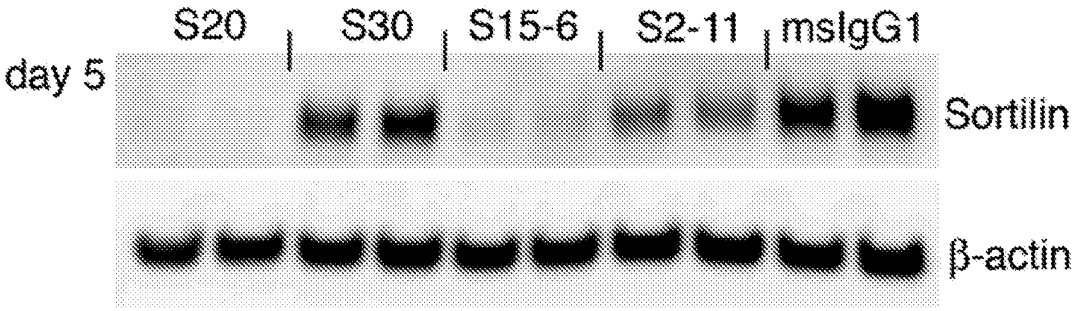


FIG. 21A

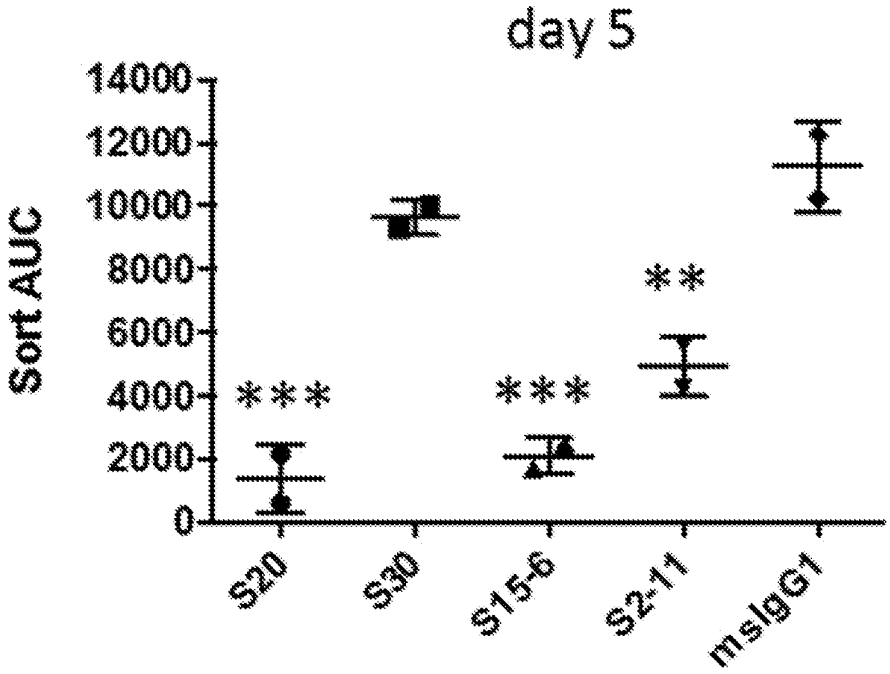


FIG. 21B

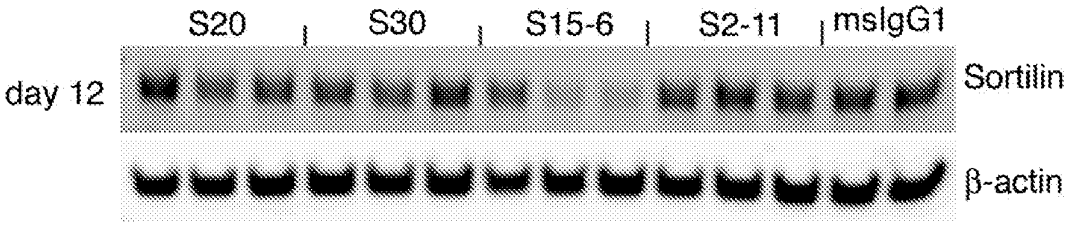


FIG. 21C

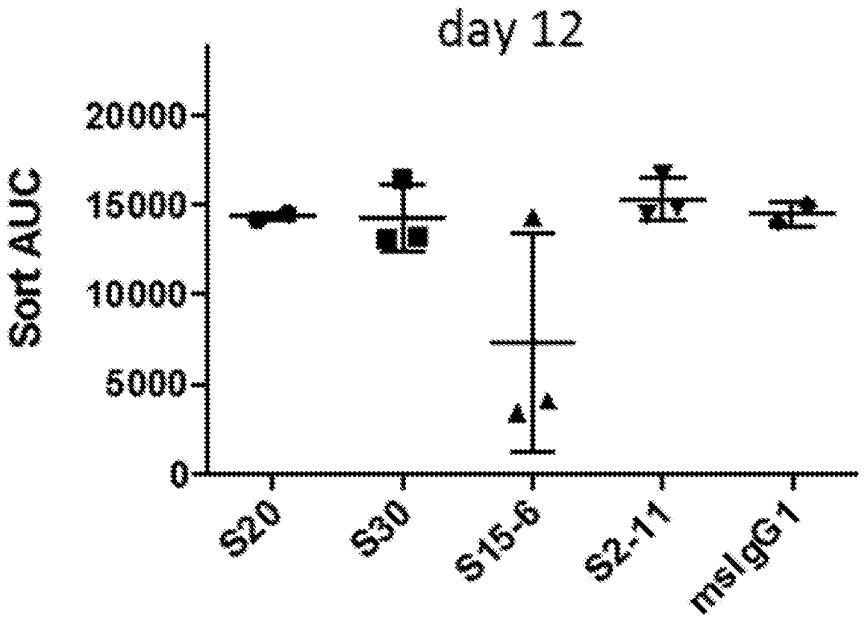


FIG. 21D

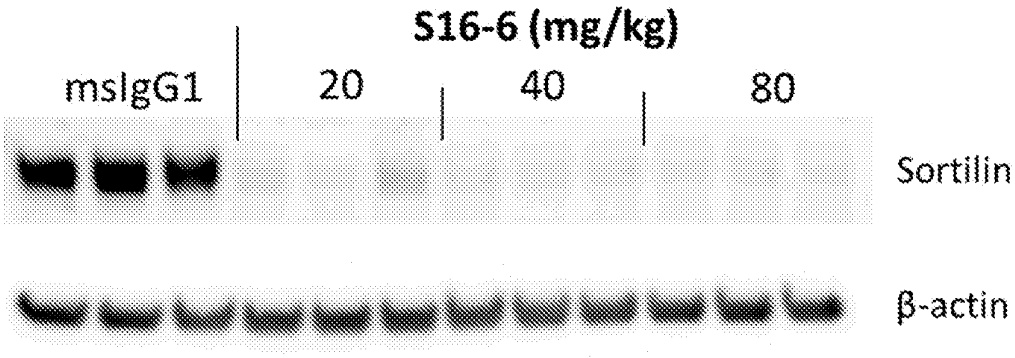


FIG. 21E

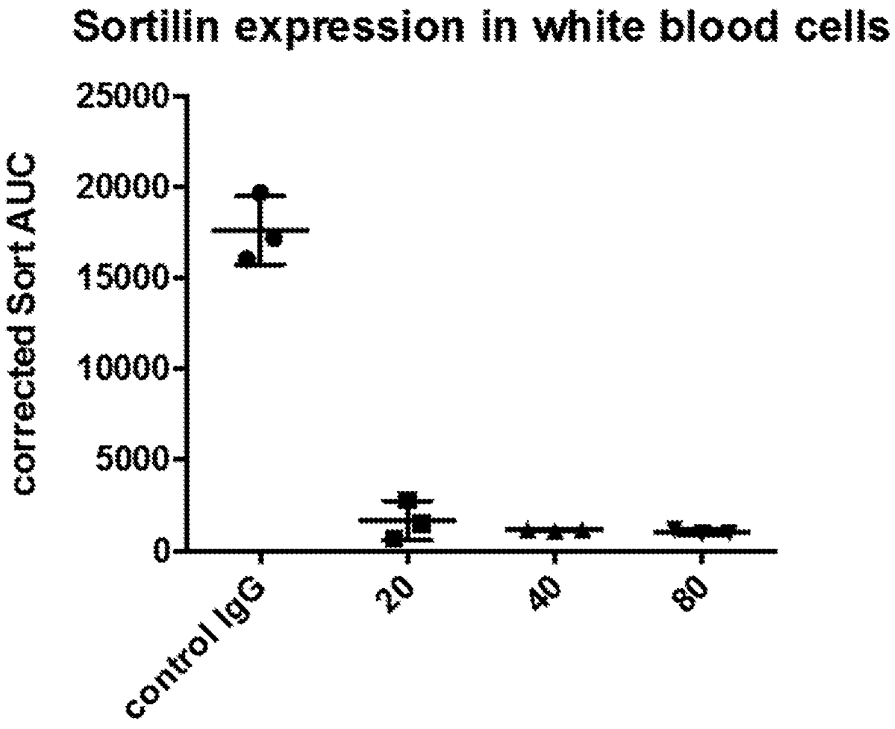


FIG. 21F

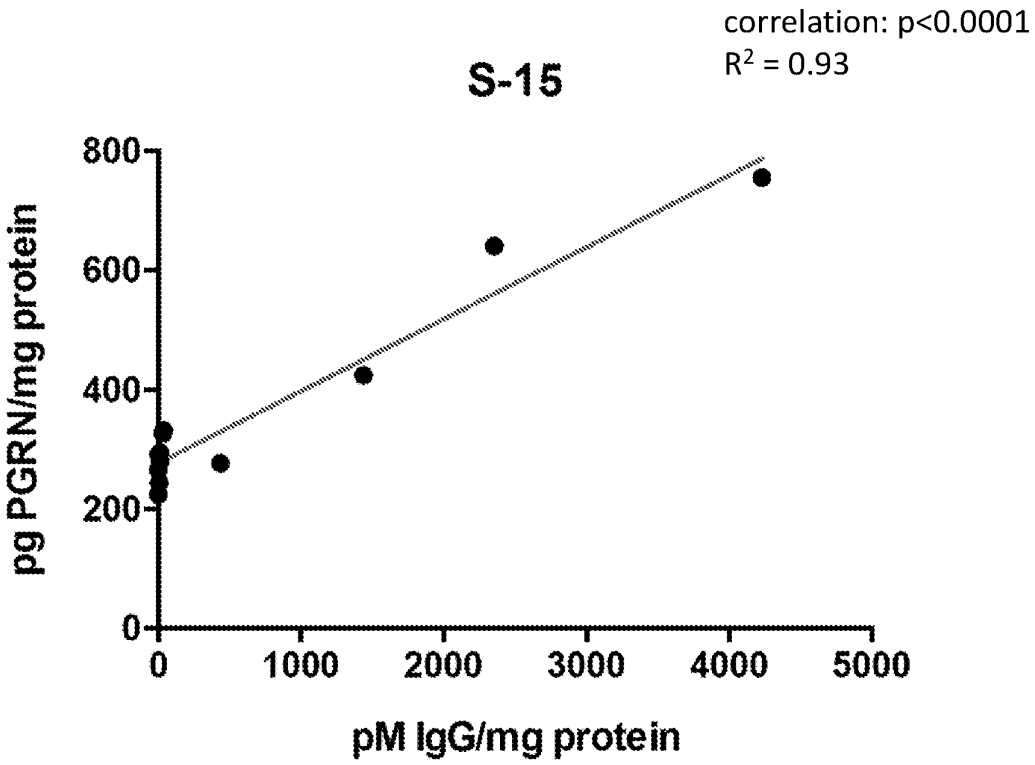


FIG. 22A

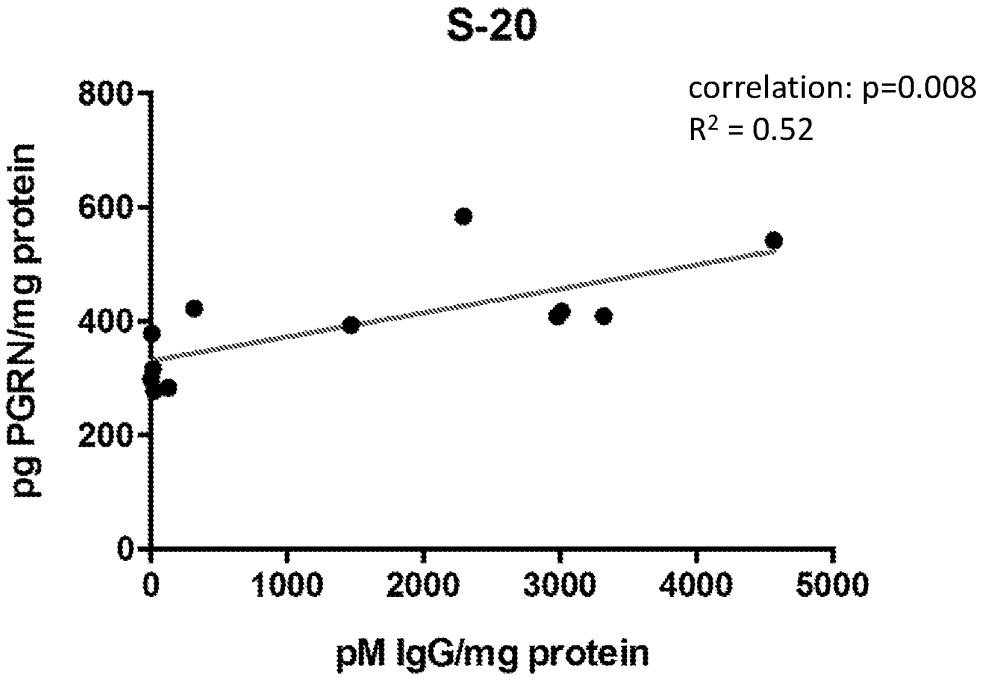


FIG. 22B

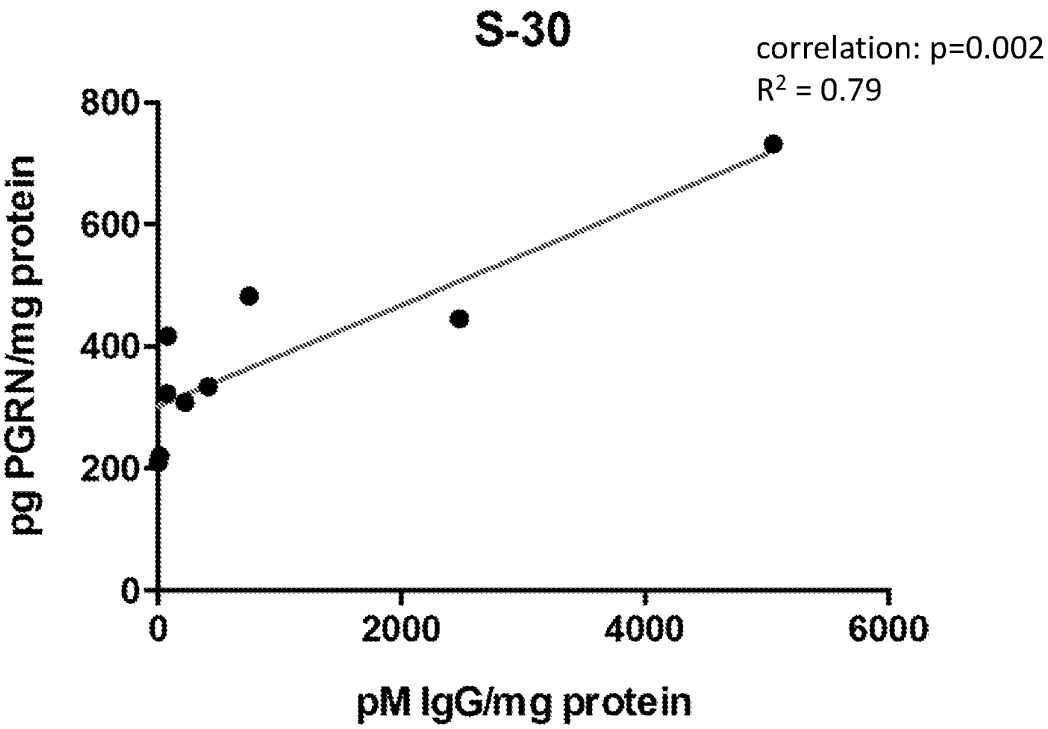


FIG. 22C

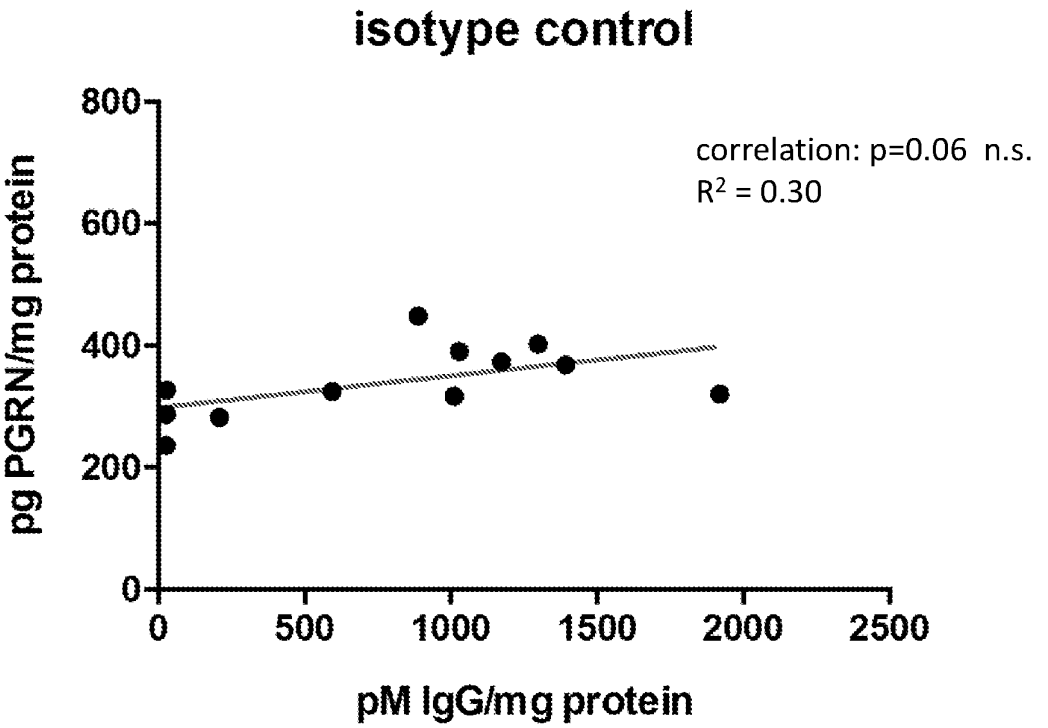


FIG. 22D

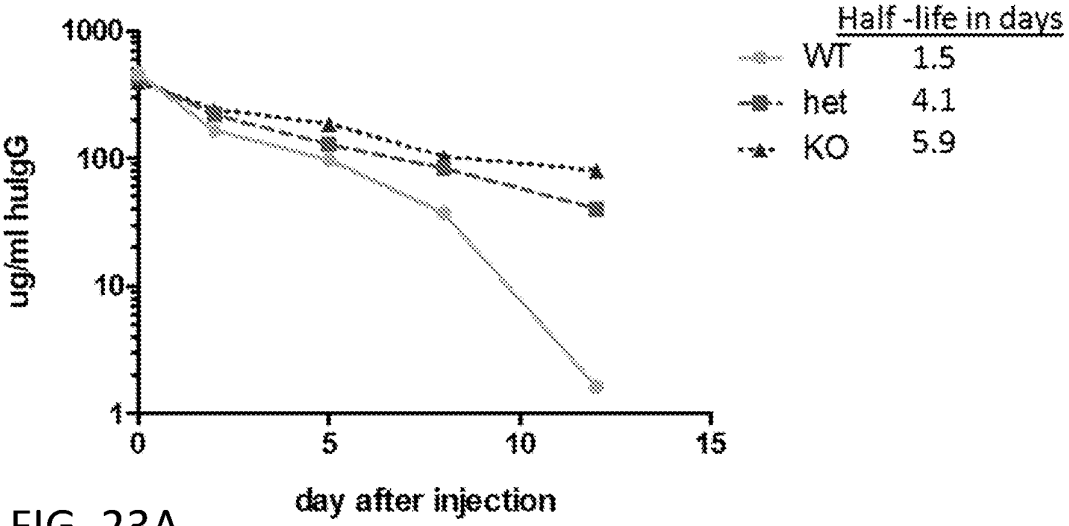


FIG. 23A

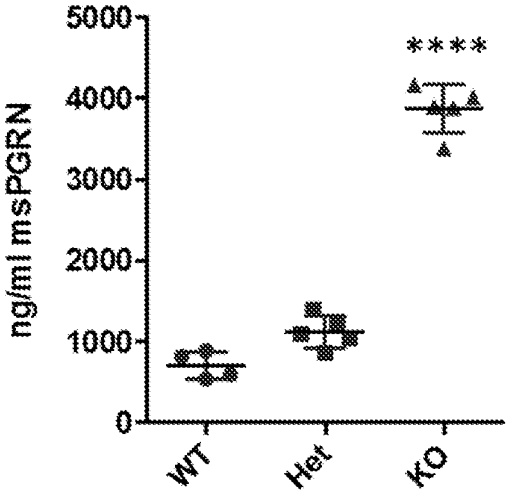


FIG. 23B

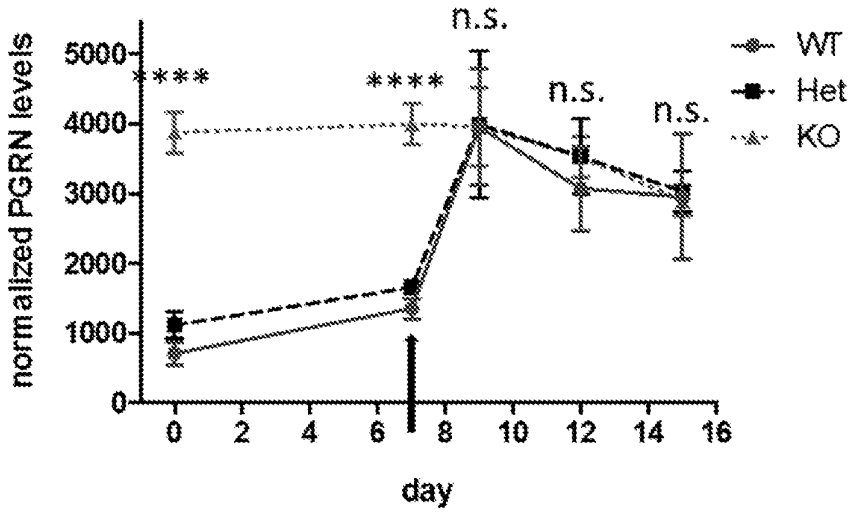


FIG. 23C

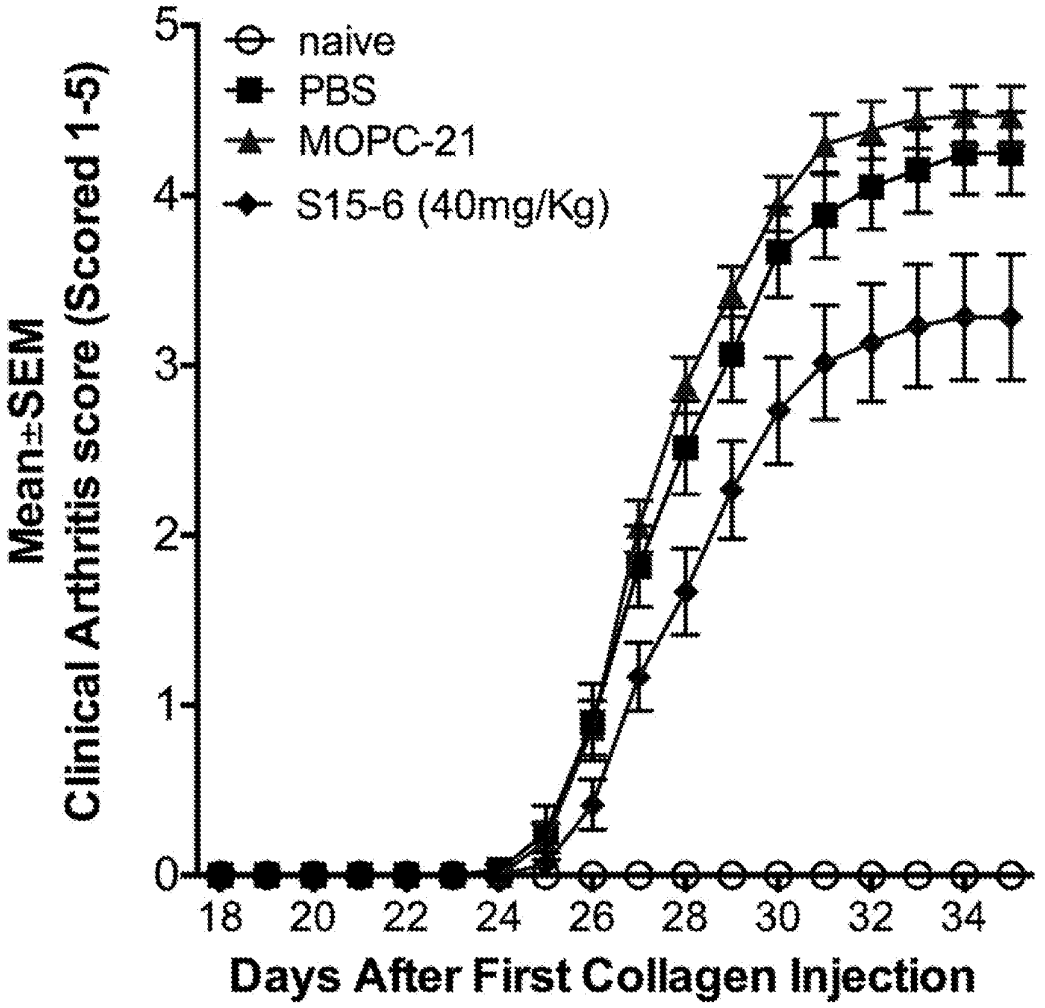

naive
PBS
MOPC-21
S15-6 (40mg/Kg)
Mean±SEM
Clinical Arthritis score (Scored 1-5)
0
1
2
3
4
5
18
20
22
24
26
28
30
32
34
Days After First Collagen Injection

FIG. 24

FIG. 25A

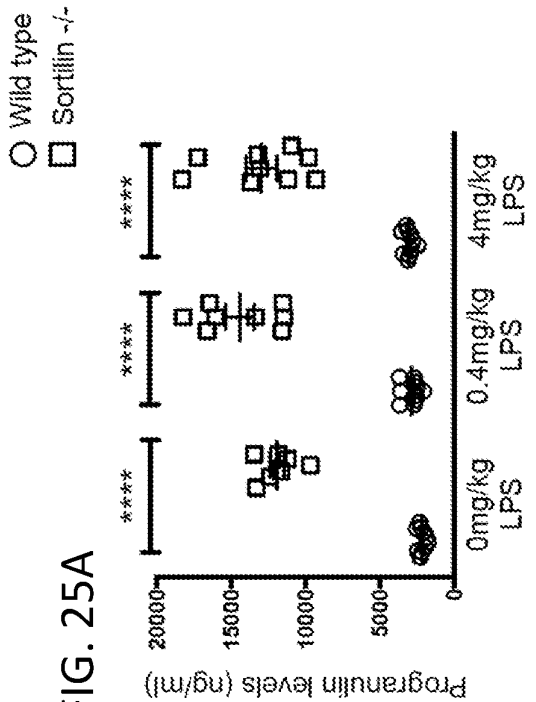


FIG. 25B

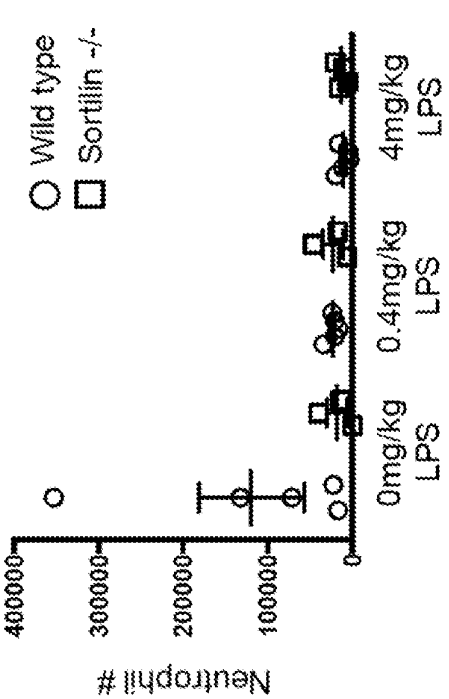
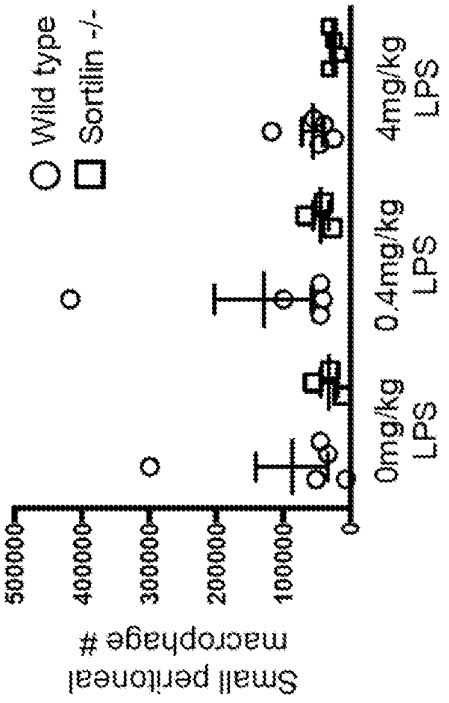


FIG. 25C

FIG. 25D



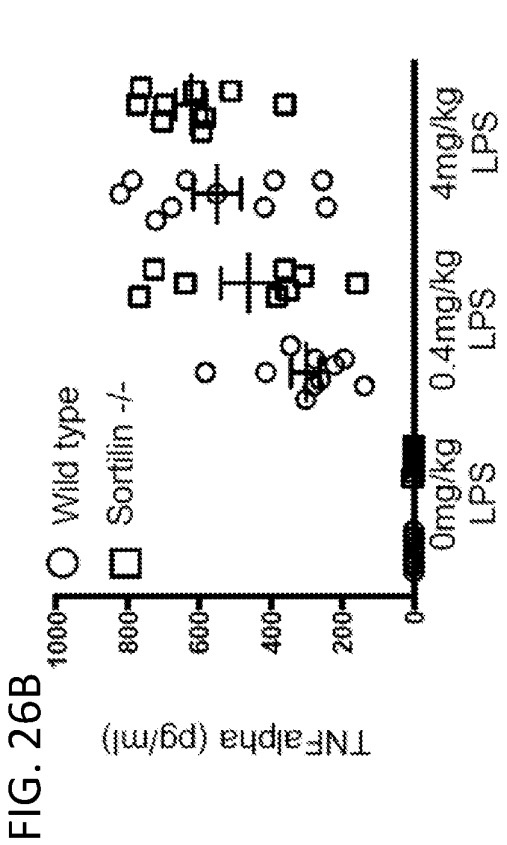


FIG. 26B

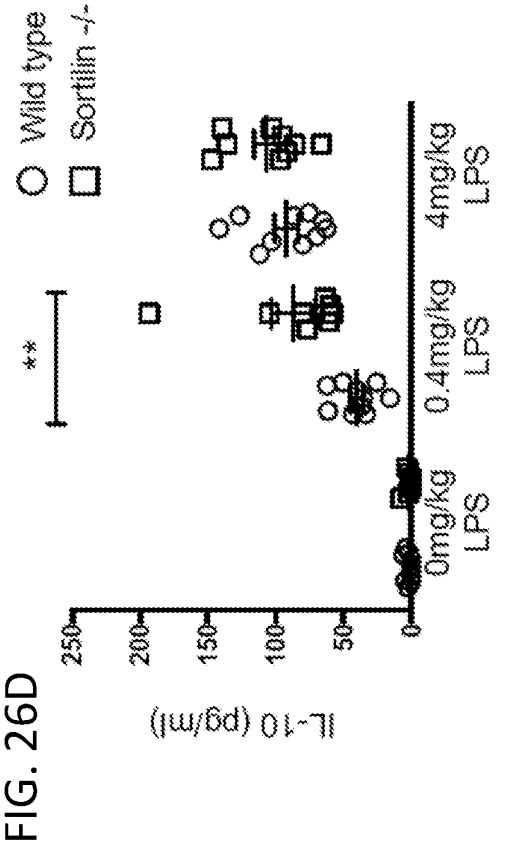


FIG. 26D

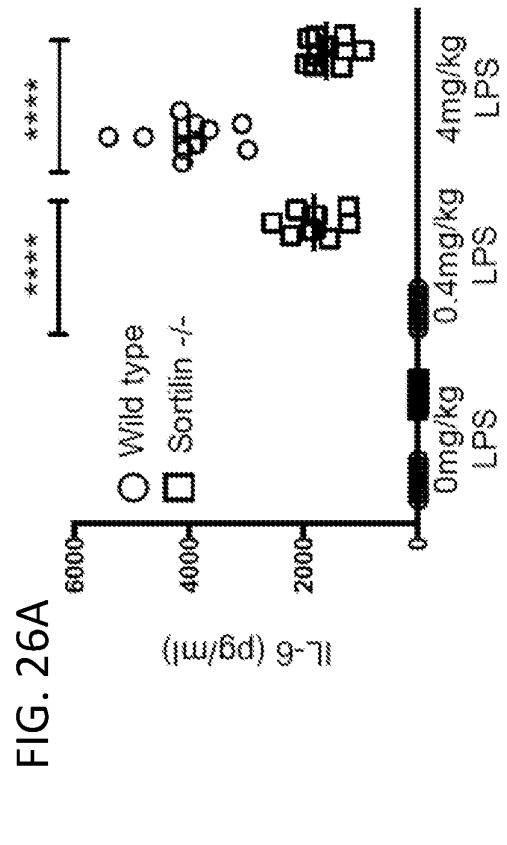


FIG. 26A

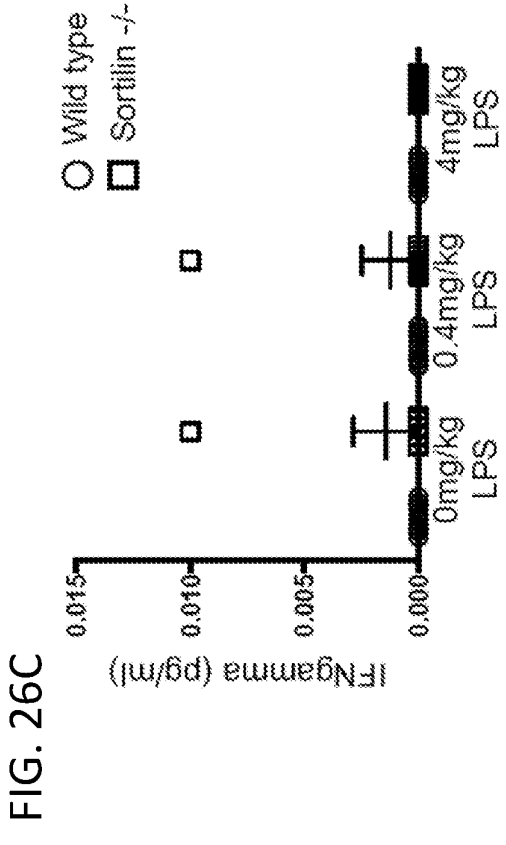


FIG. 26C

FIG. 26F

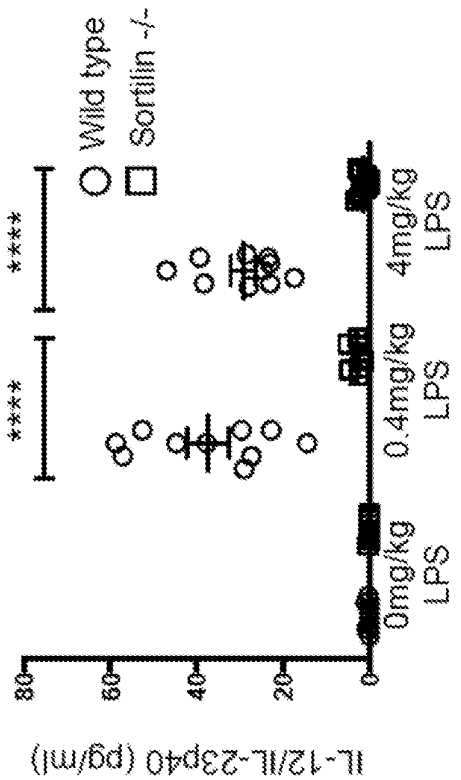


FIG. 26H

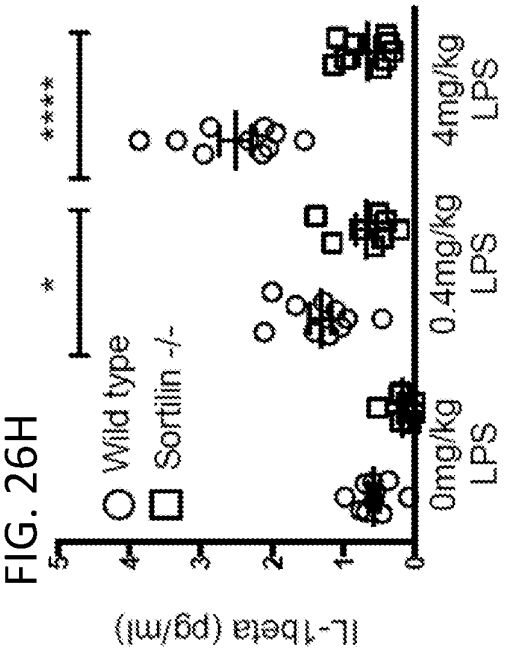


FIG. 26E

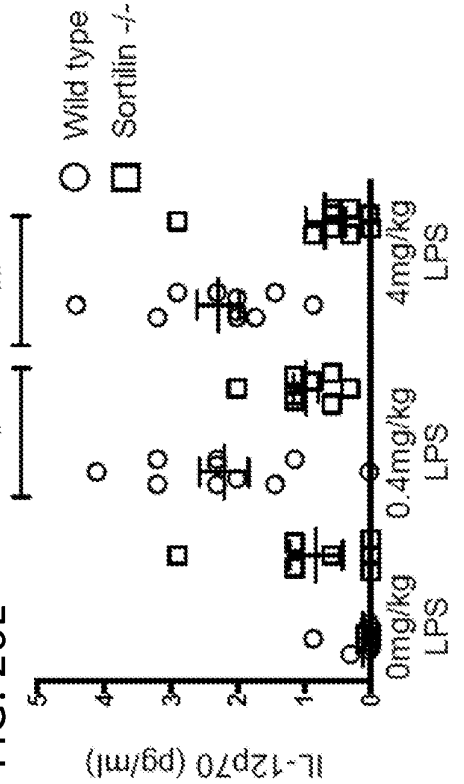
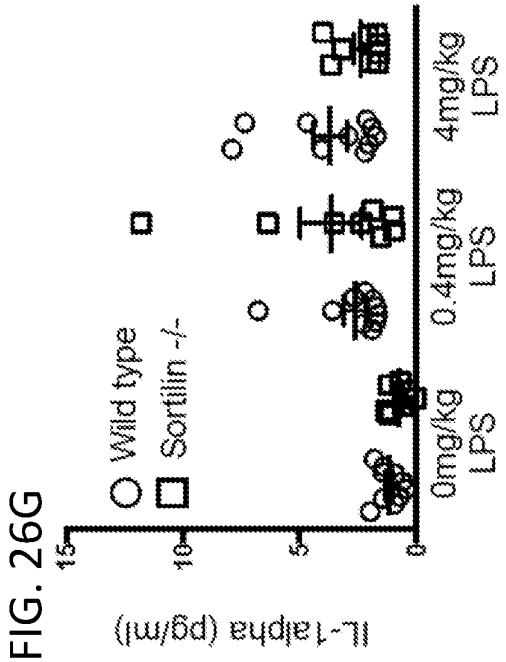


FIG. 26G



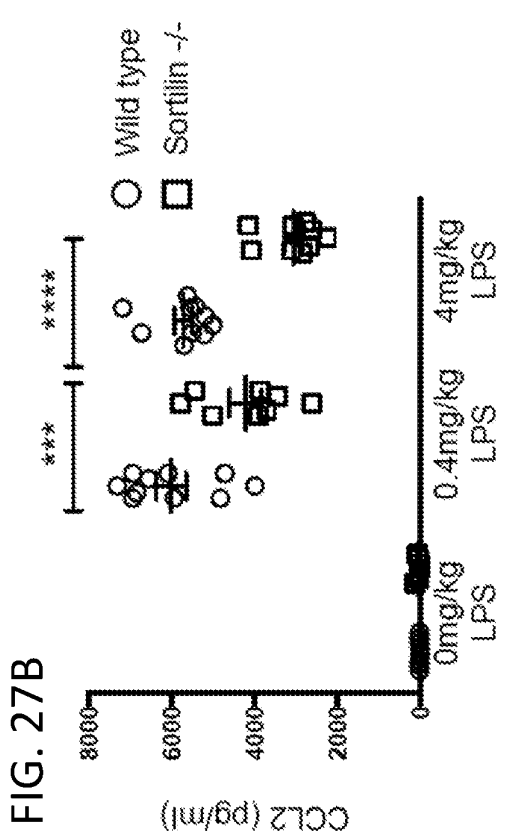


FIG. 27A

FIG. 27B

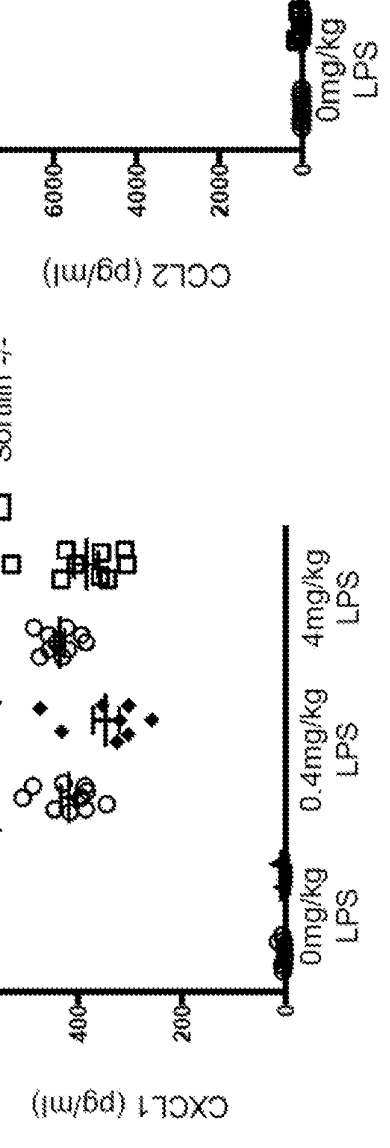


FIG. 27C

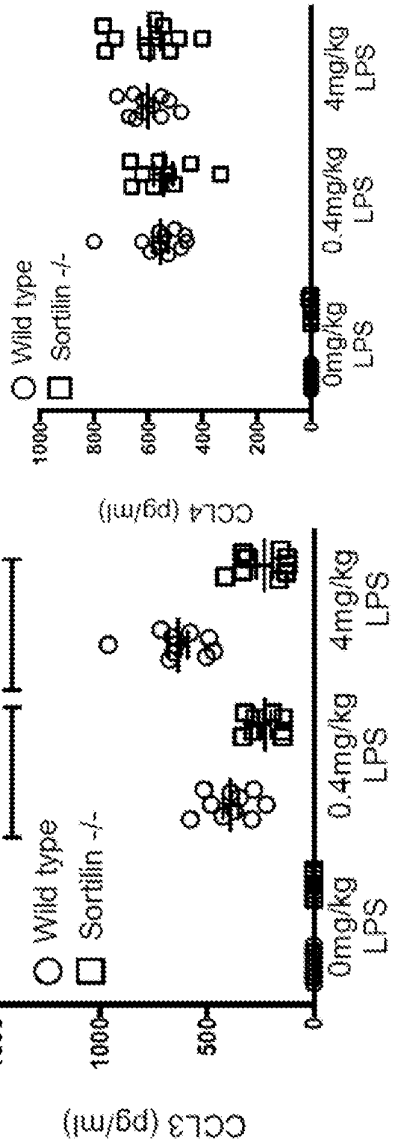


FIG. 27D

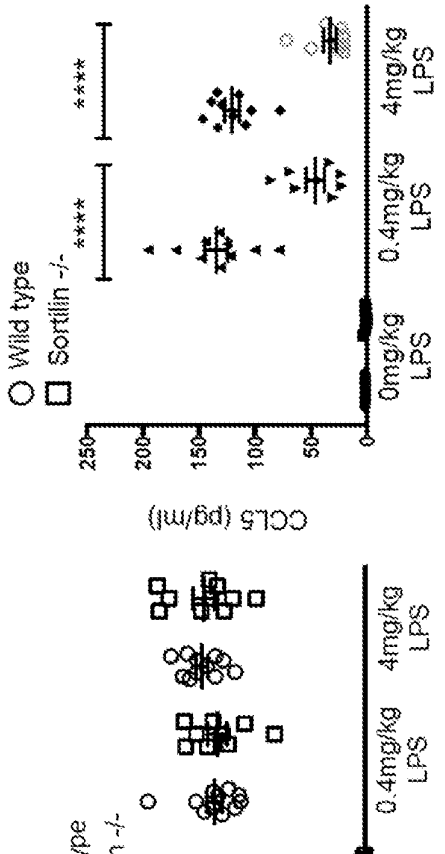


FIG. 27E

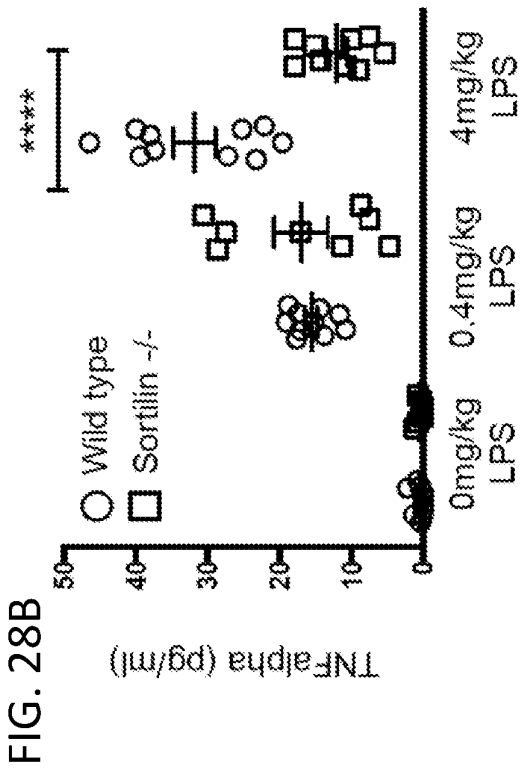


FIG. 28B

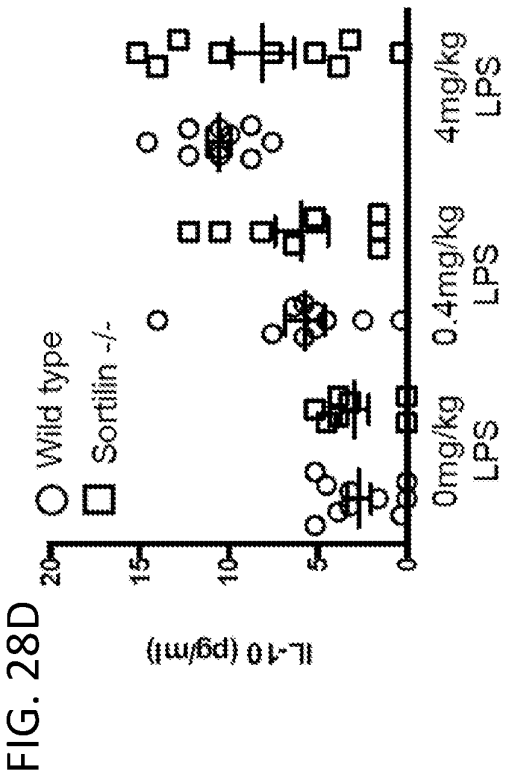


FIG. 28D

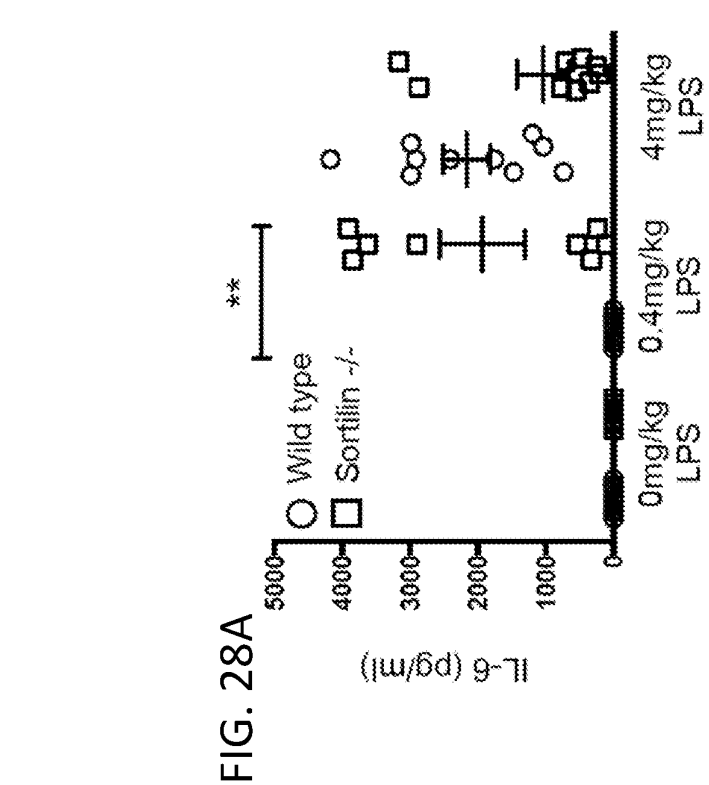


FIG. 28A

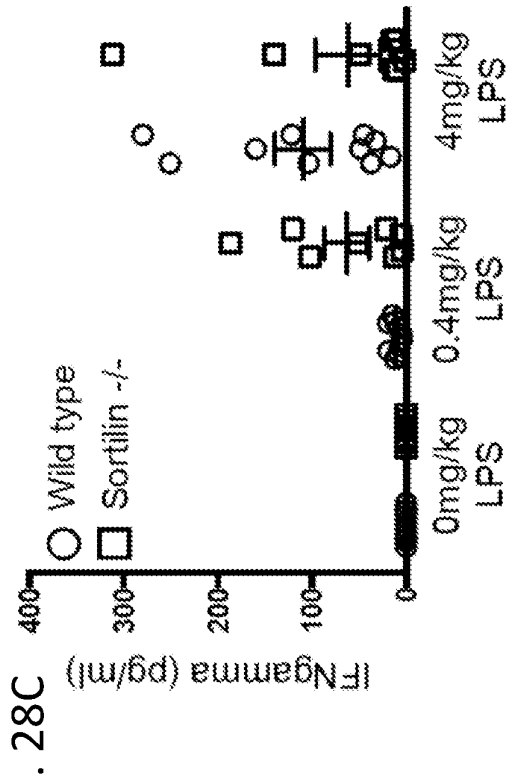


FIG. 28C

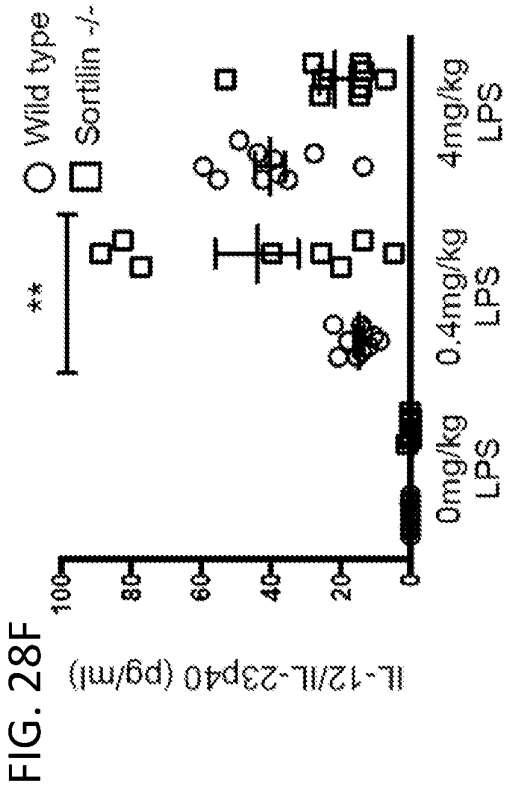


FIG. 28F

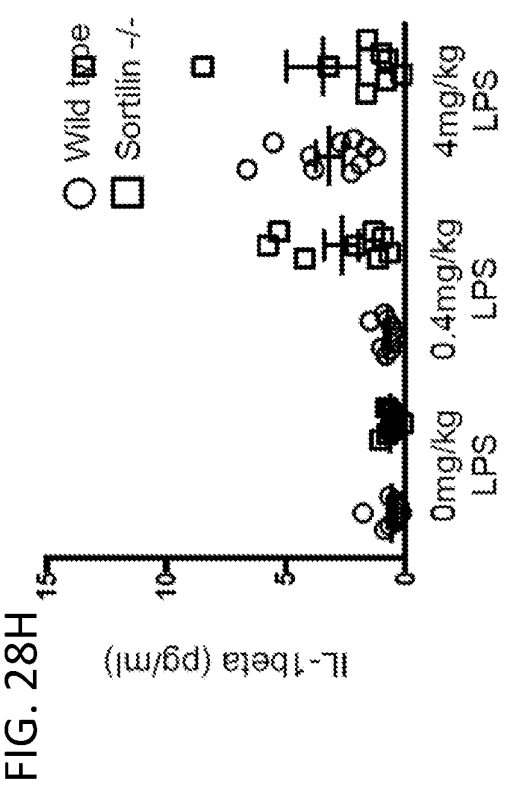


FIG. 28H

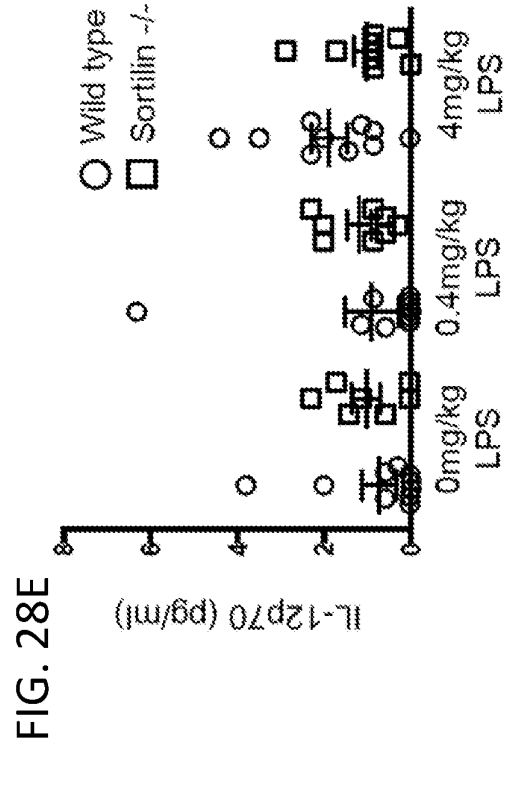


FIG. 28E



FIG. 28G

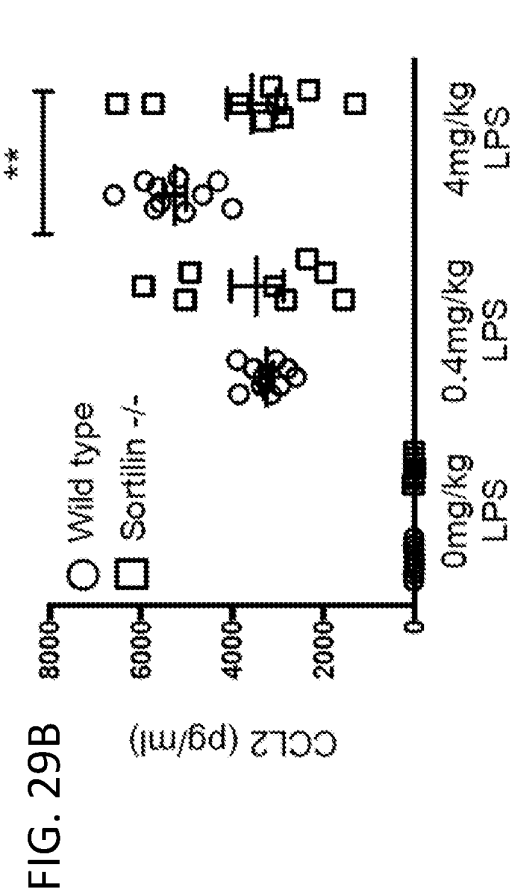


FIG. 29A

FIG. 29B

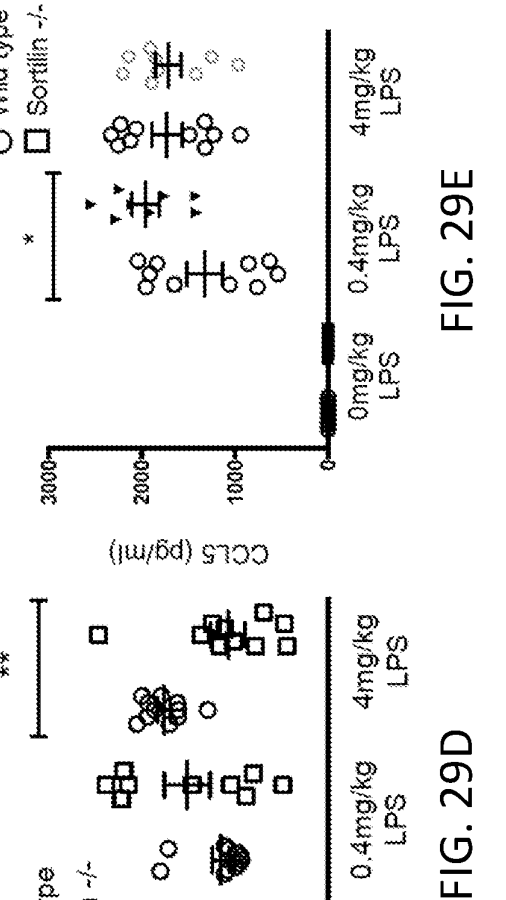


FIG. 29E

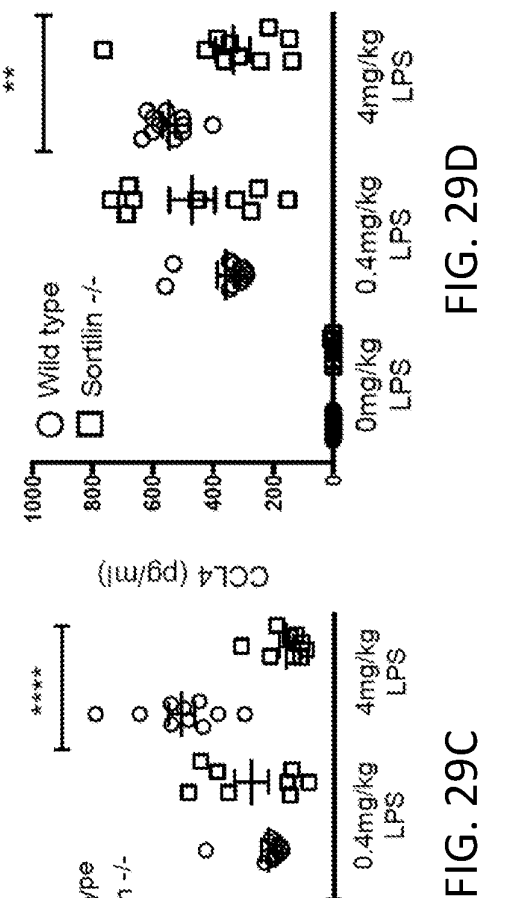


FIG. 29D

FIG. 29C