FIG. 1A
Day 1

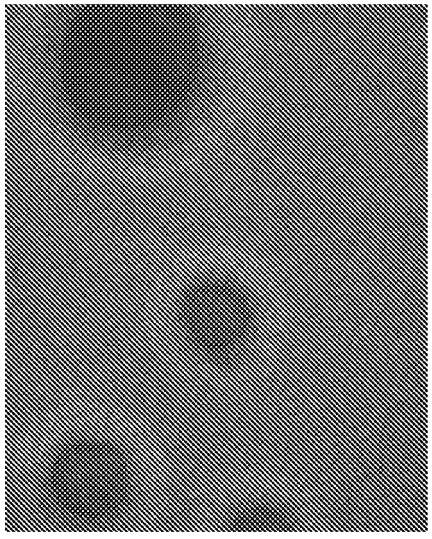


FIG. 1B
Day 5

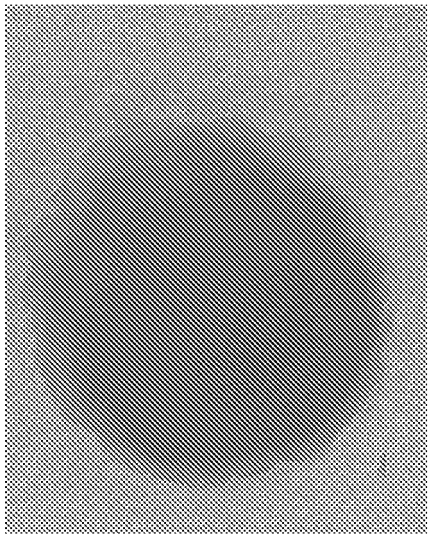


FIG. 1C
Day 6

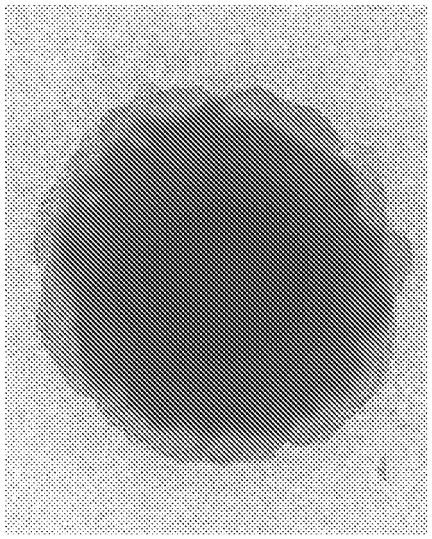


FIG. 1D
Day 7

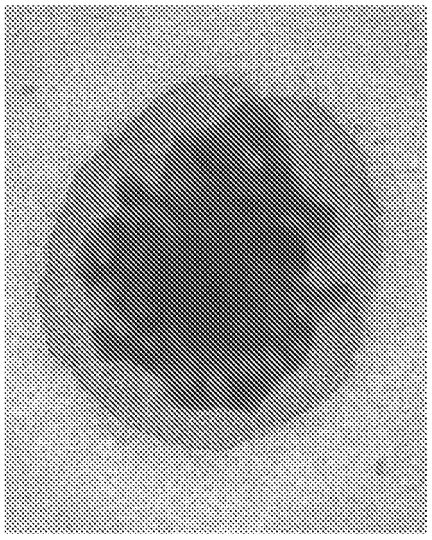


FIG. 1E
Day 9

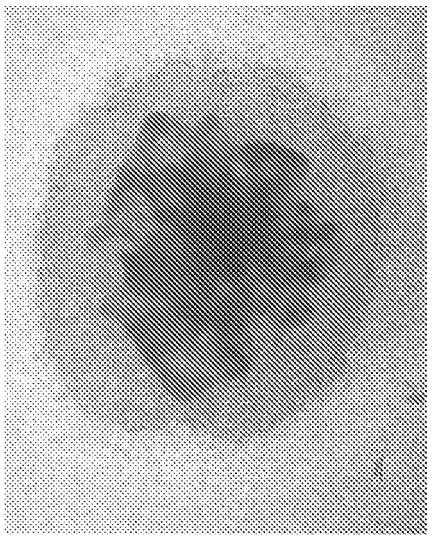


FIG. 1F
Day 13

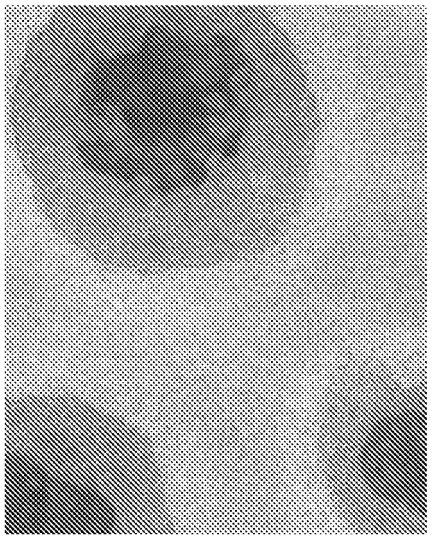


FIG. 1G

Day 16

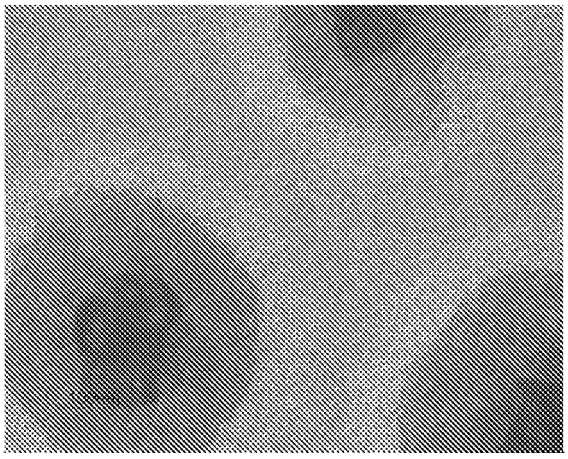


FIG. 1H

Day 21

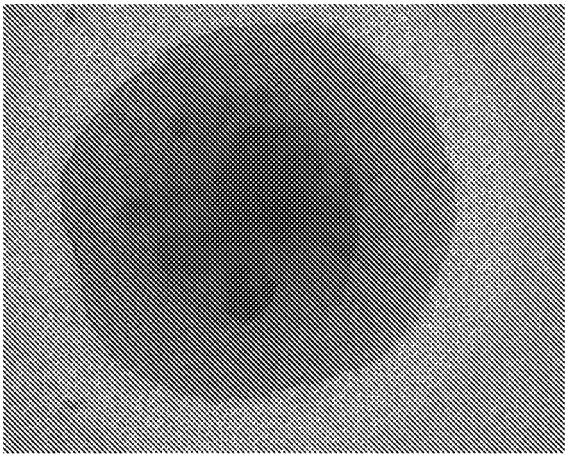


FIG. 2A

DAPI

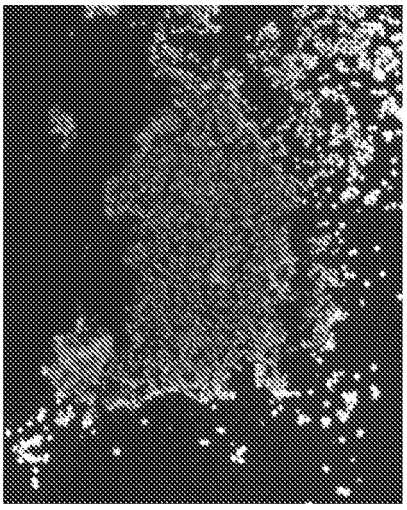


FIG. 2B

Insulin

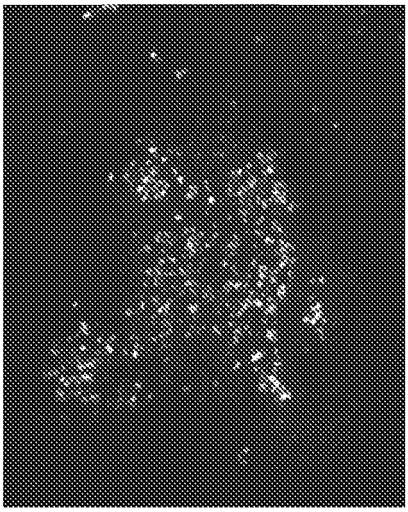


FIG. 2C

Hb9

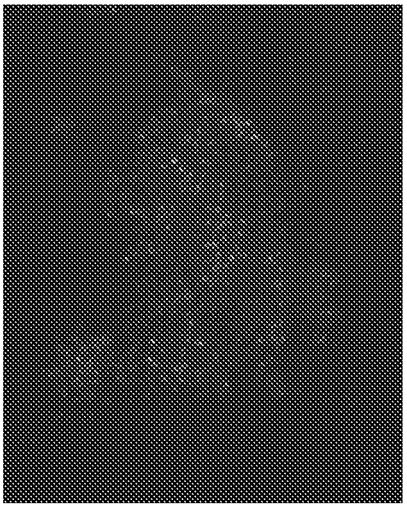


FIG. 2D

DAPI

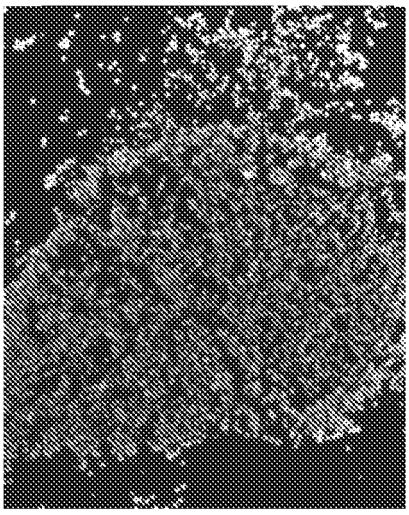


FIG. 2E

Glucagon

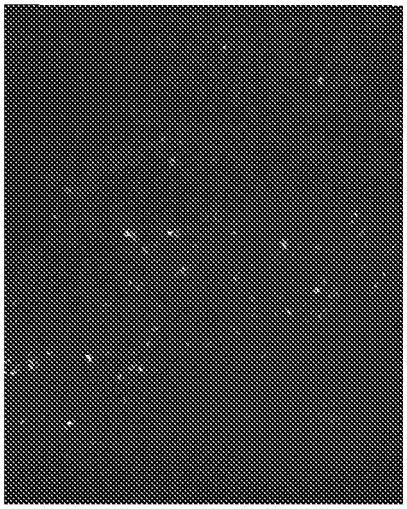


FIG. 2F

Insulin

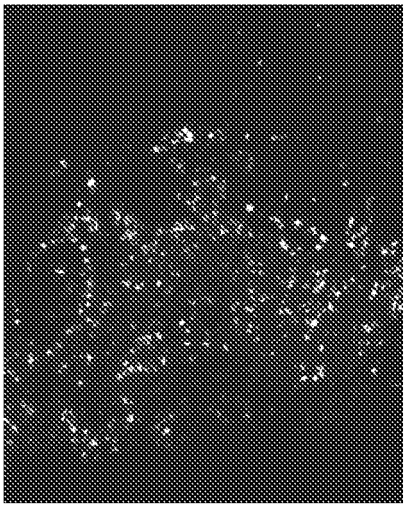


FIG. 2I

Somatostatin

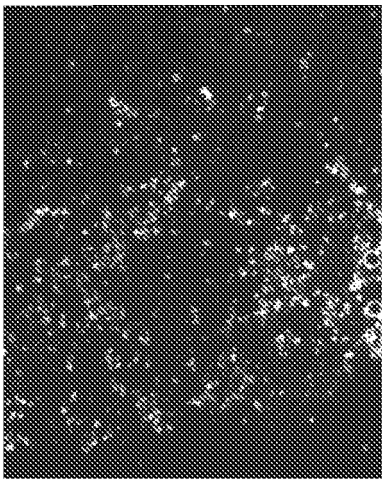


FIG. 2H

Insulin

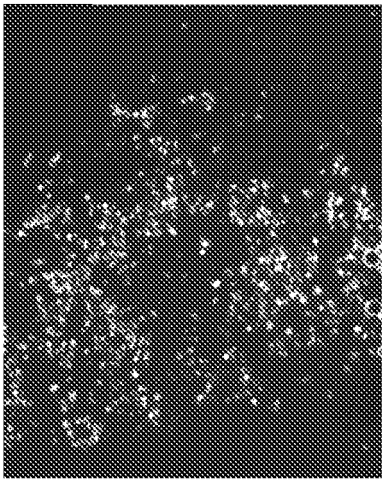


FIG. 2K

Insulin



FIG. 2G

DAPI

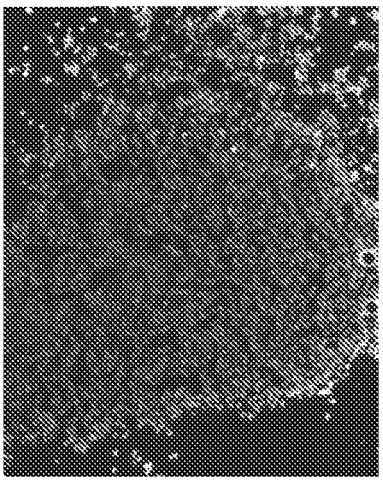


FIG. 2J

NKX6.1

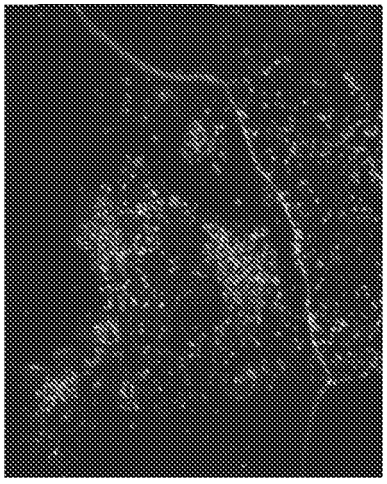


FIG. 3A

Insulin

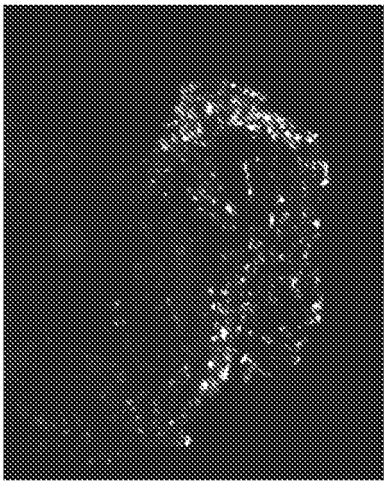


FIG. 3B

Glucagon

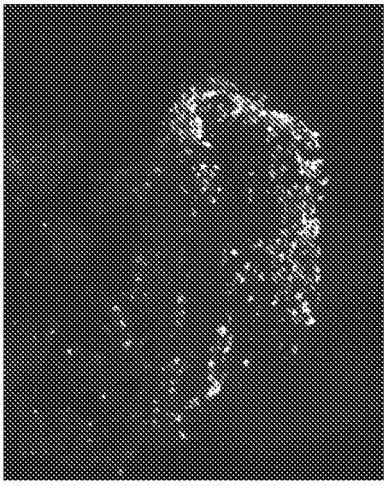


FIG. 3C

Insulin

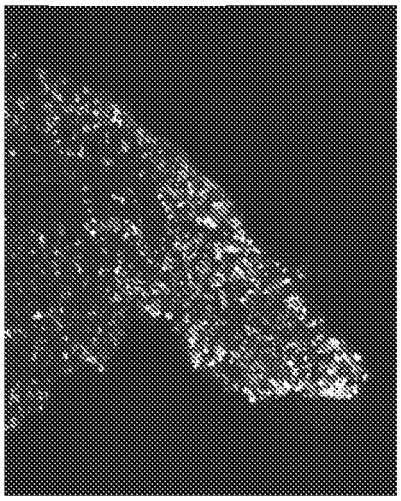


FIG. 3D

Somatostatin

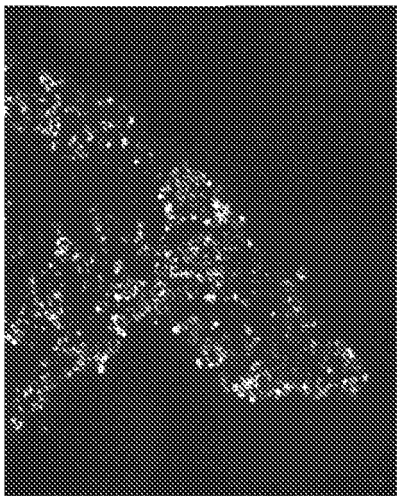


FIG. 3F

NKX6.1

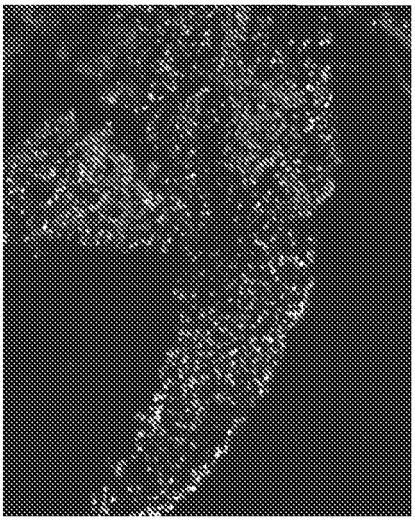


FIG. 3H

NKX6.1

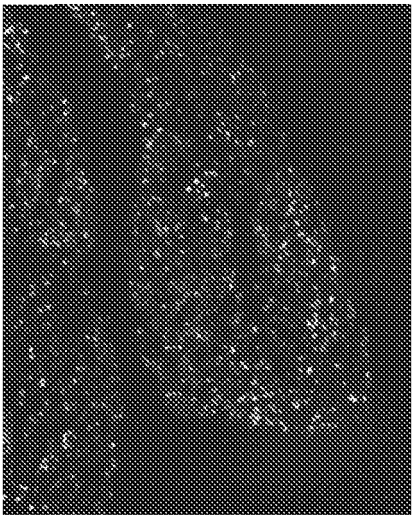


FIG. 3E

Insulin

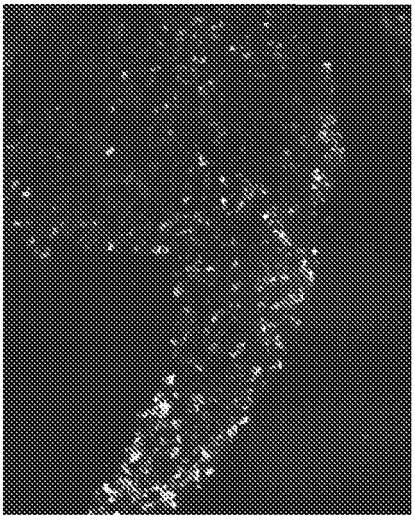


FIG. 3G

Hb9

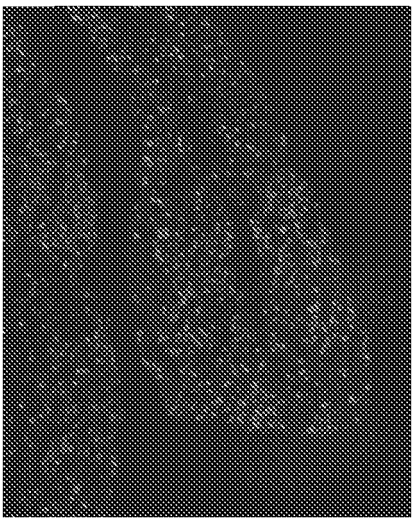


FIG. 4A
Insulin

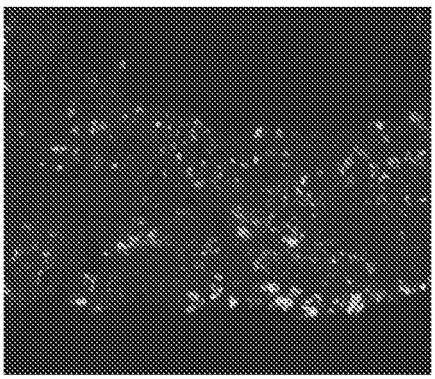


FIG. 4B
Glucagon

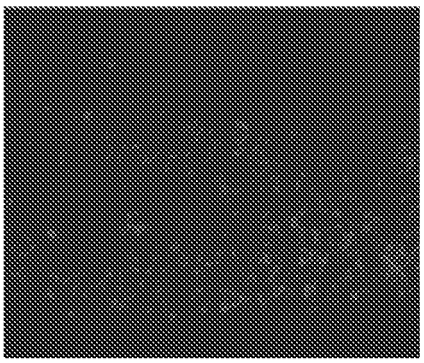


FIG. 4C
Insulin

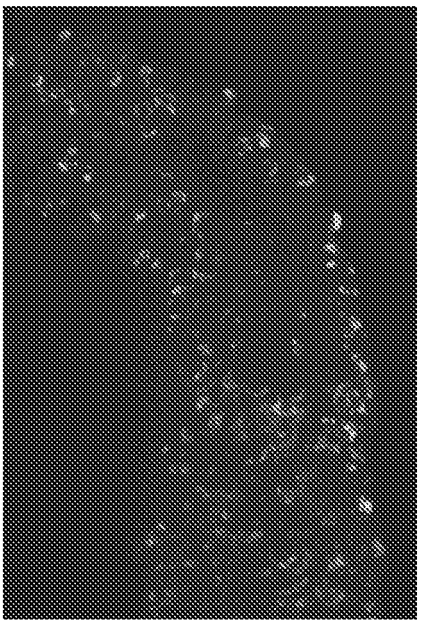


FIG. 4D
Somatostatin

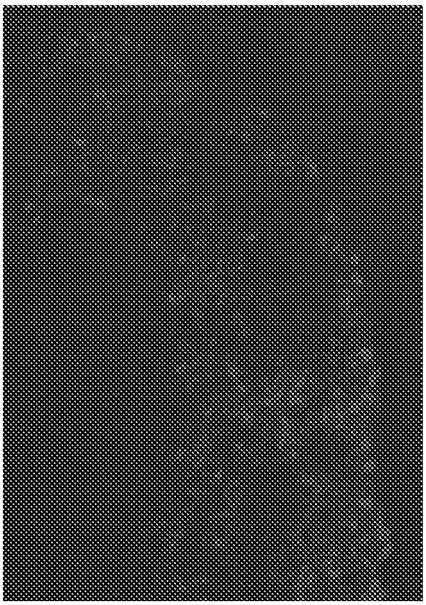


FIG. 5A

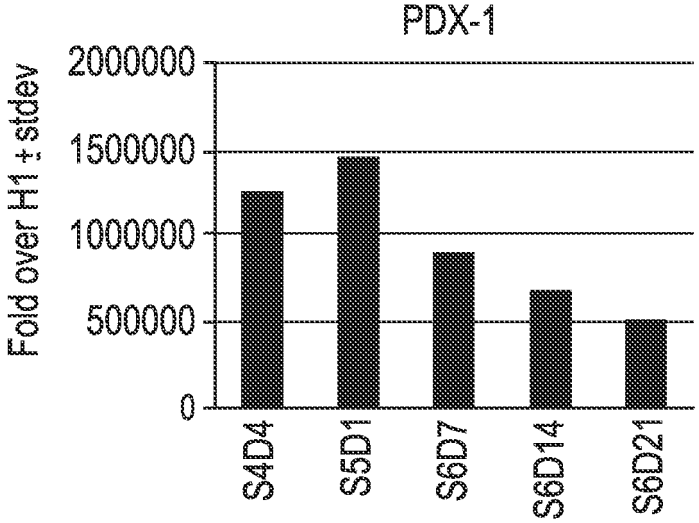


FIG. 5B

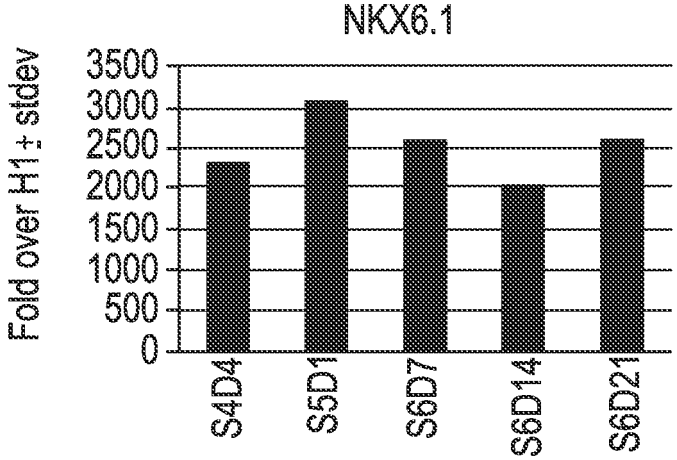


FIG. 5C

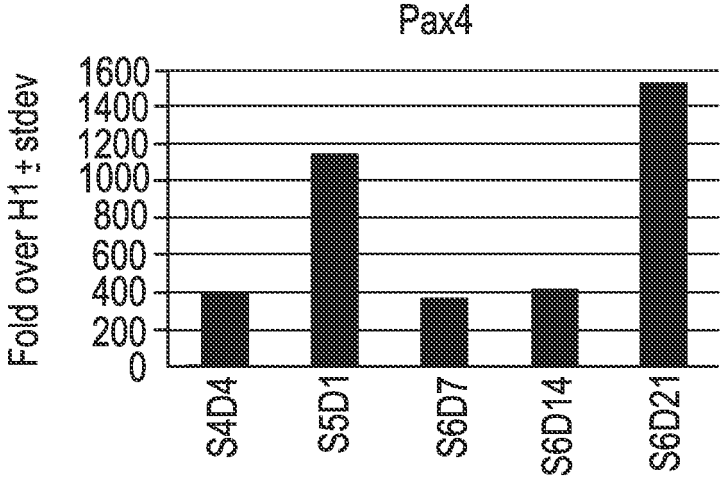


FIG. 5D

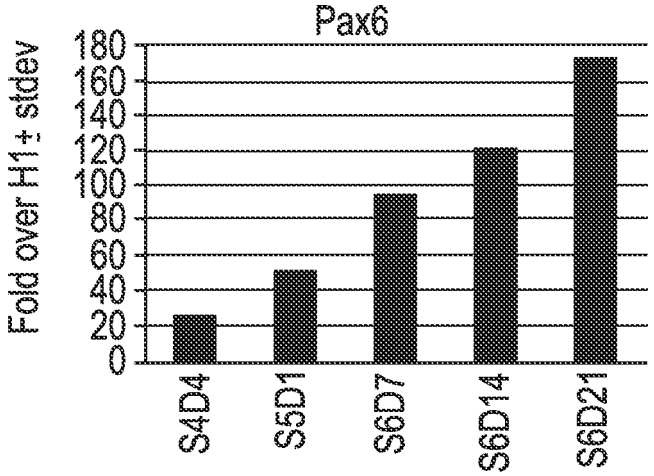


FIG. 5E

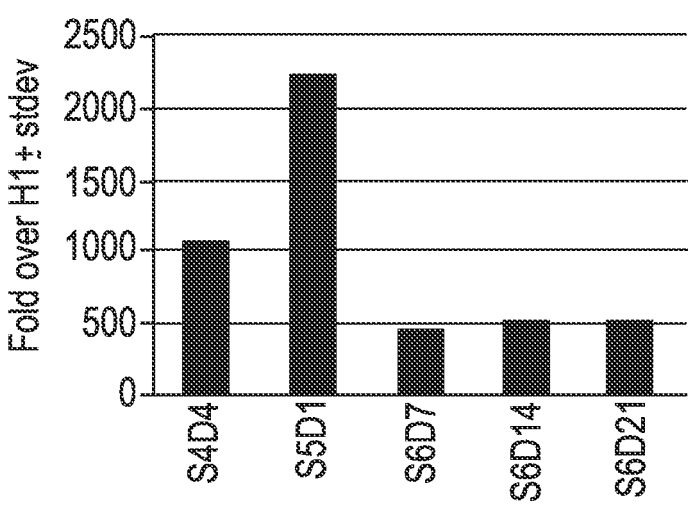


FIG. 5F

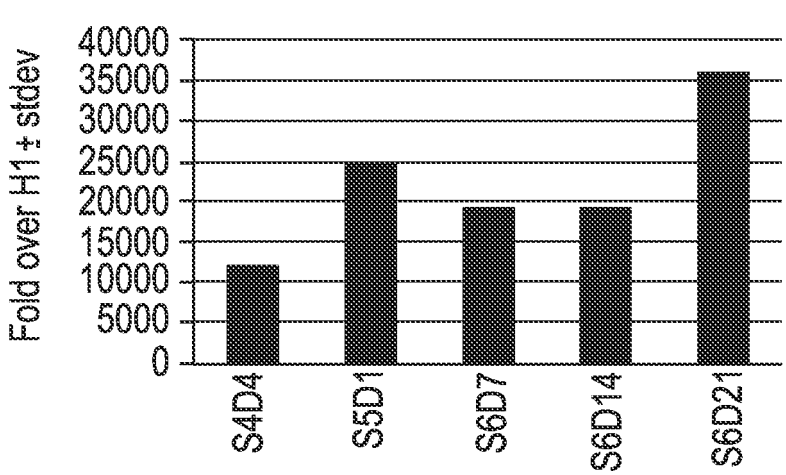


FIG. 5G

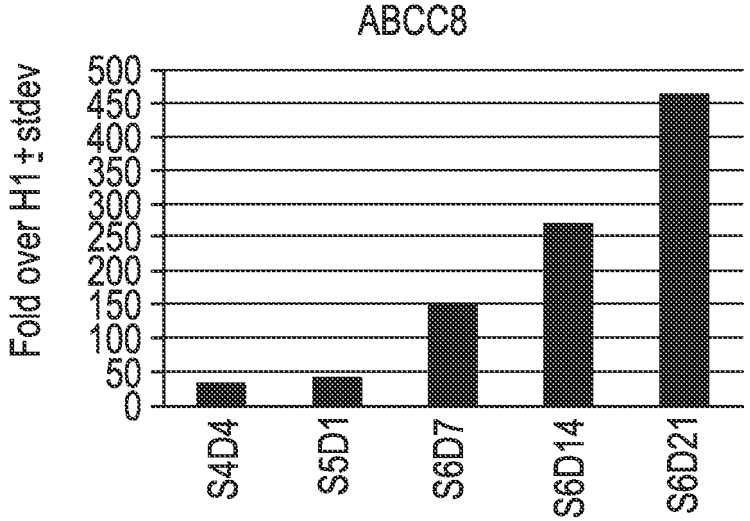


FIG. 5H

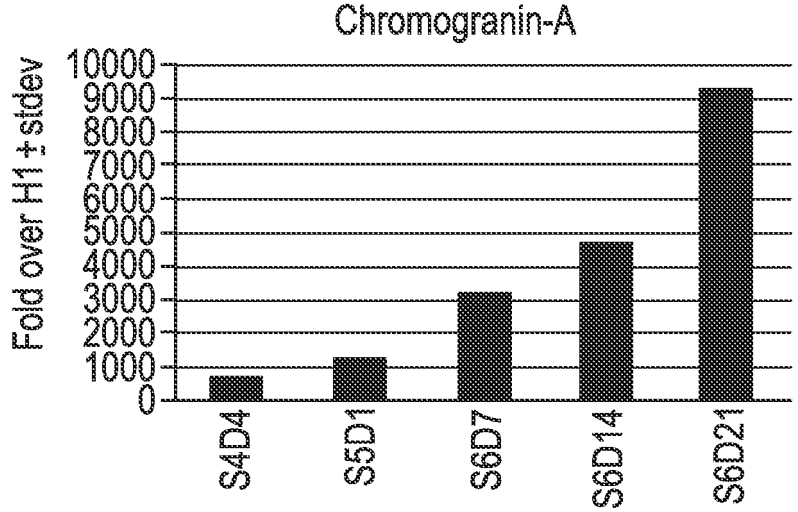


FIG. 5I

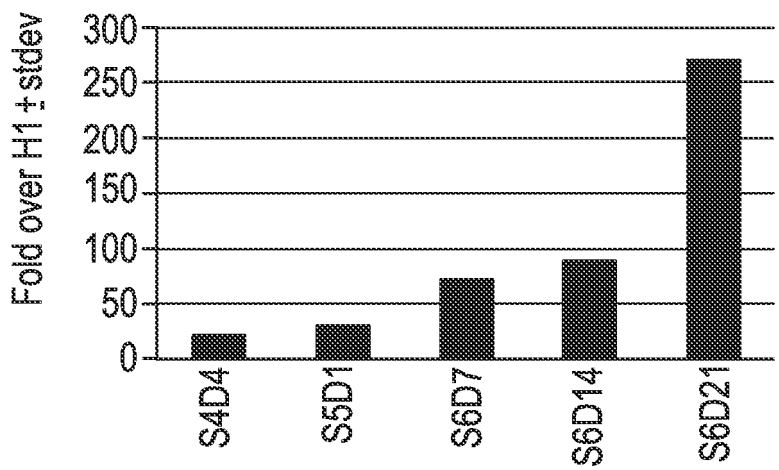


FIG. 5J

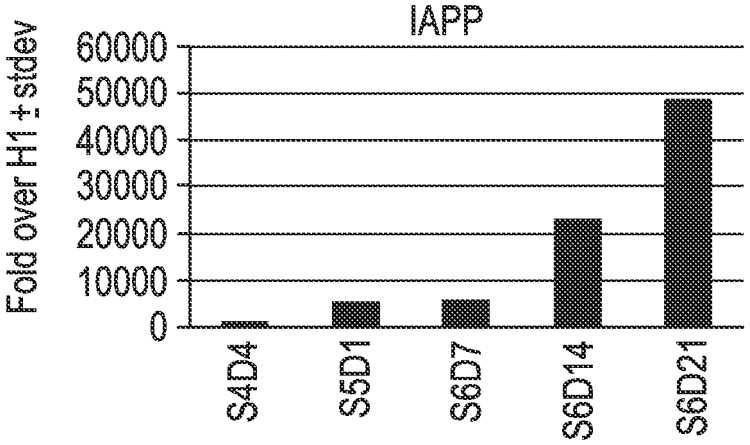


FIG. 5K

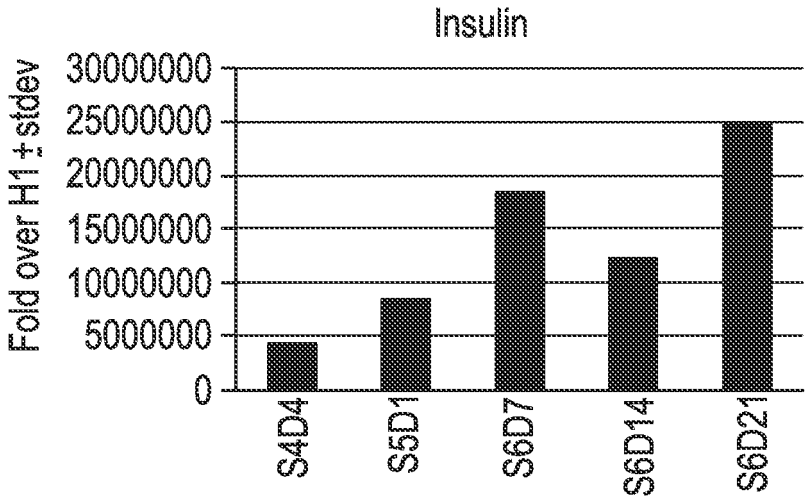


FIG. 5L

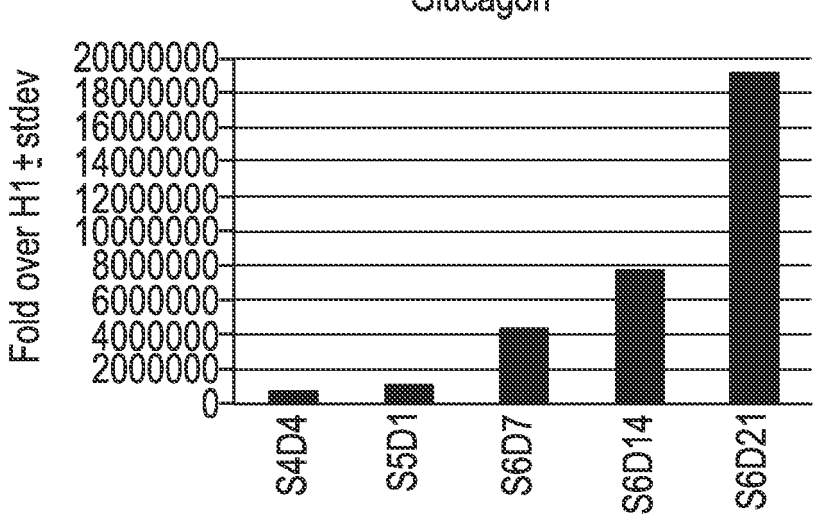


FIG. 5M

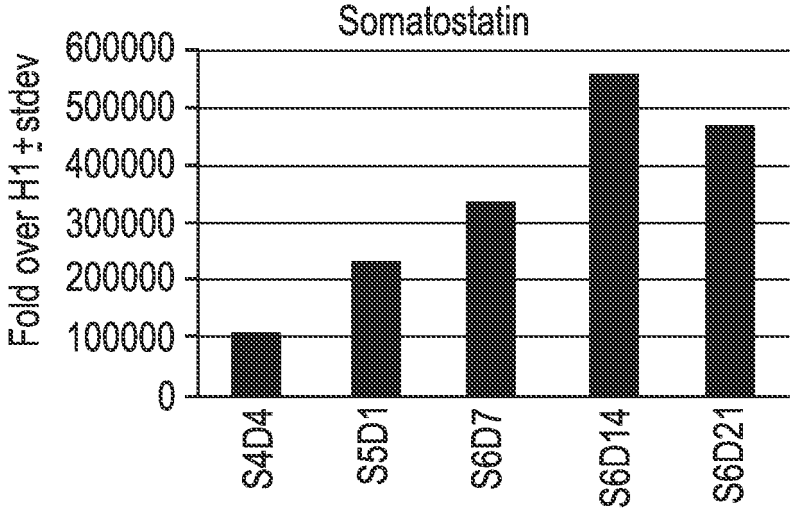


FIG. 5N

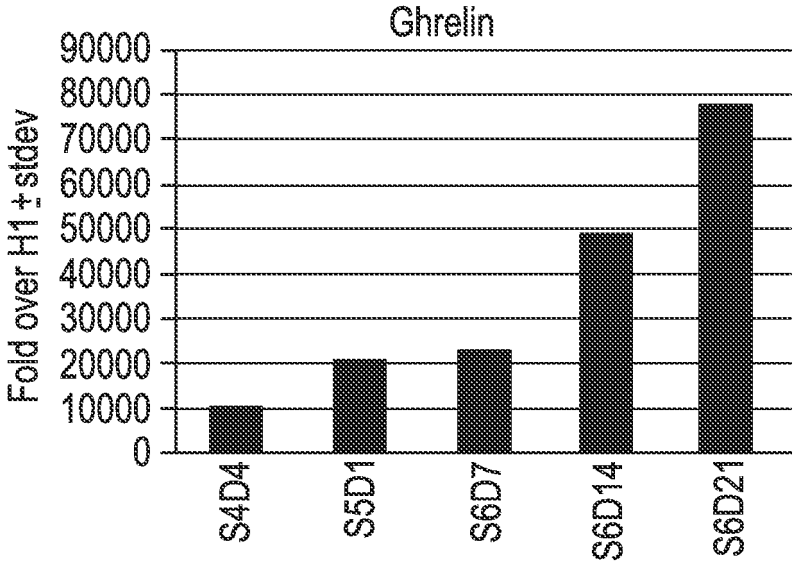


FIG. 5O

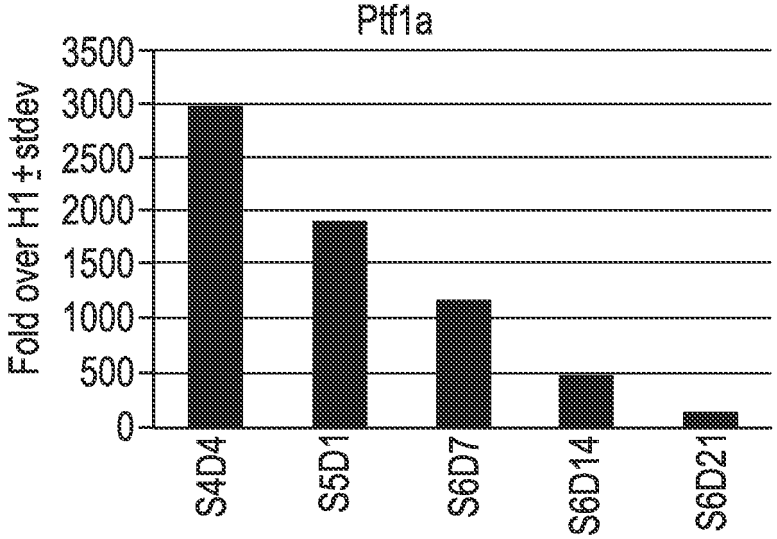


FIG. 5P

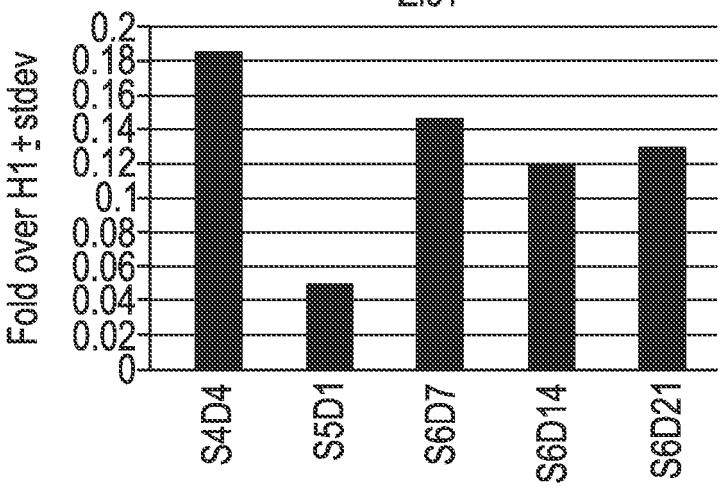


FIG. 5Q

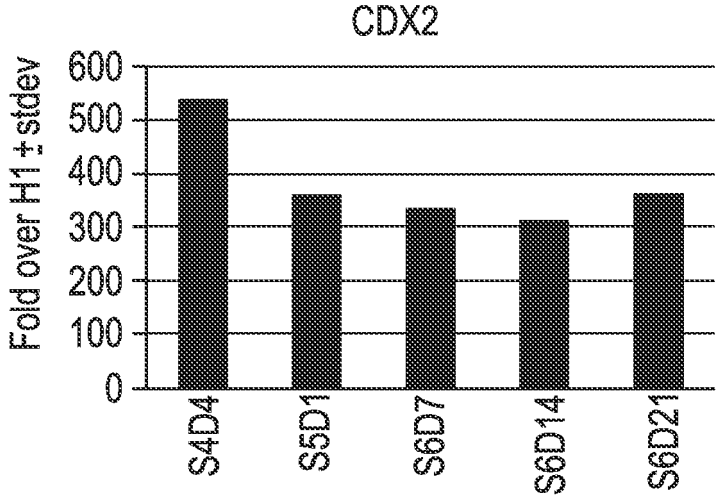


FIG. 5R

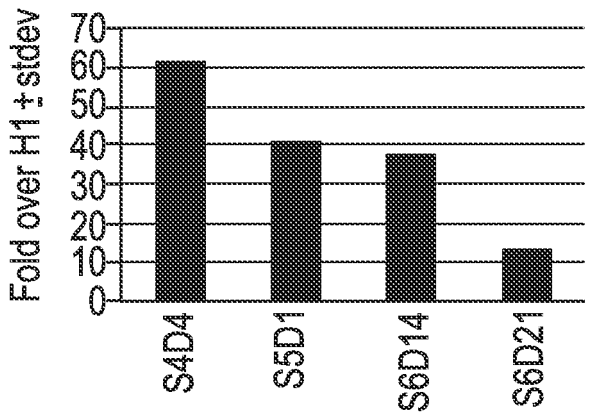


FIG. 6A

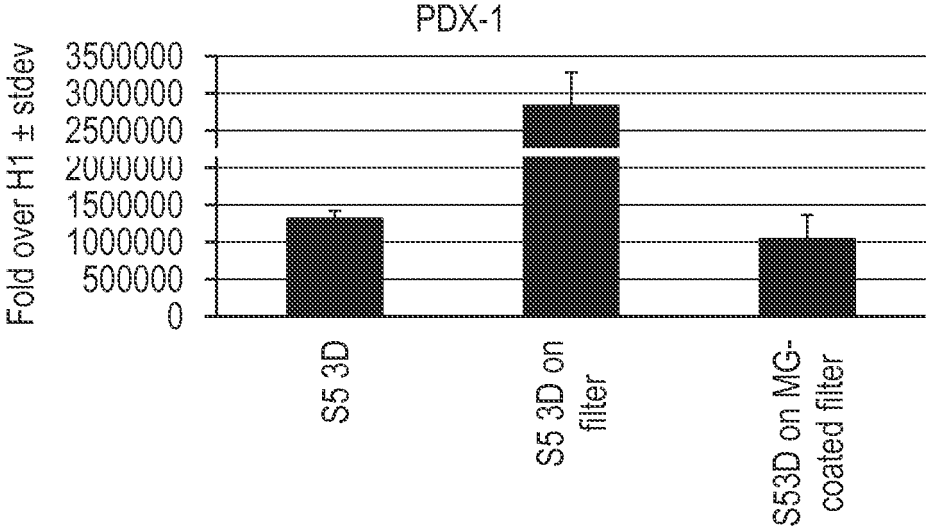


FIG. 6B

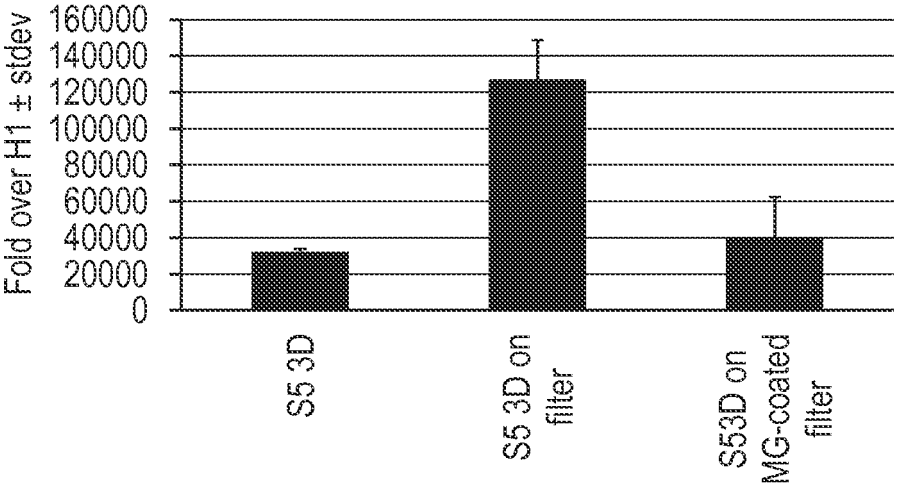


FIG. 6C

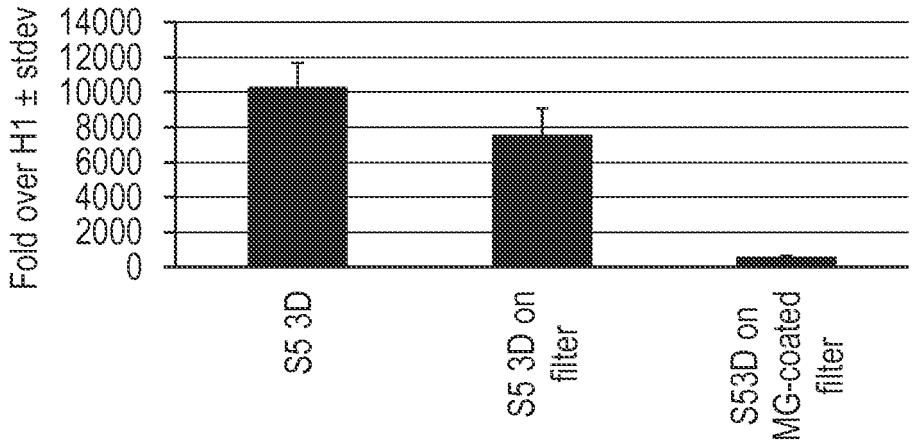


FIG. 6D

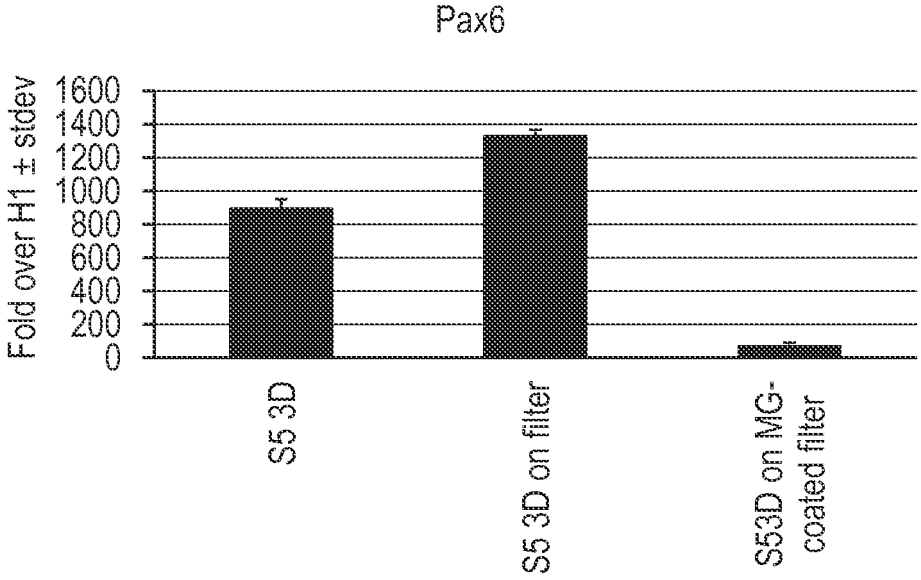


FIG. 6E

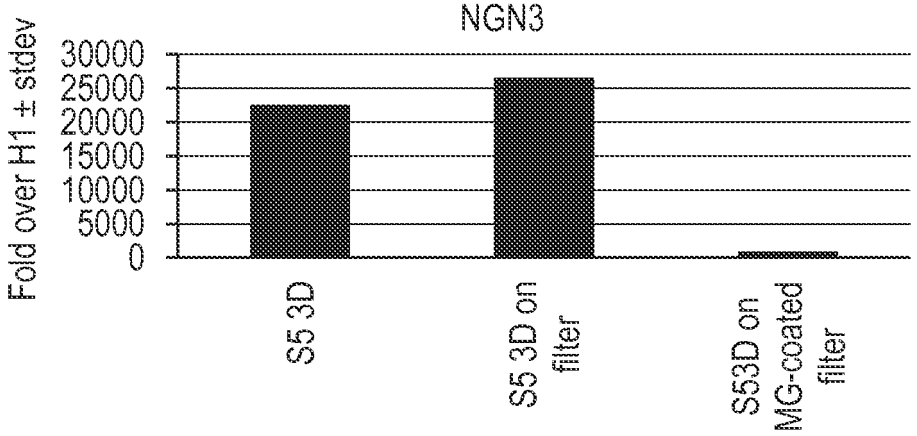


FIG. 6F

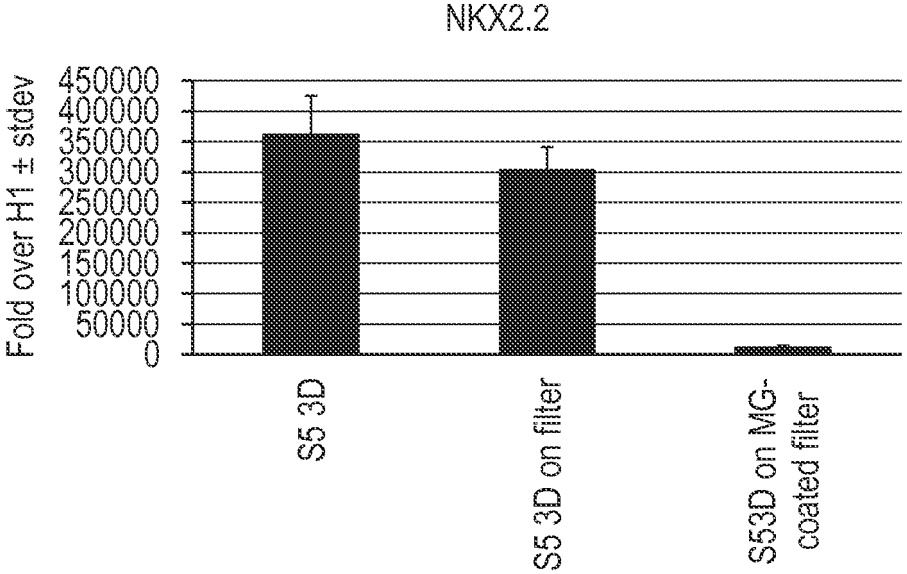


FIG. 6G

ABCC8

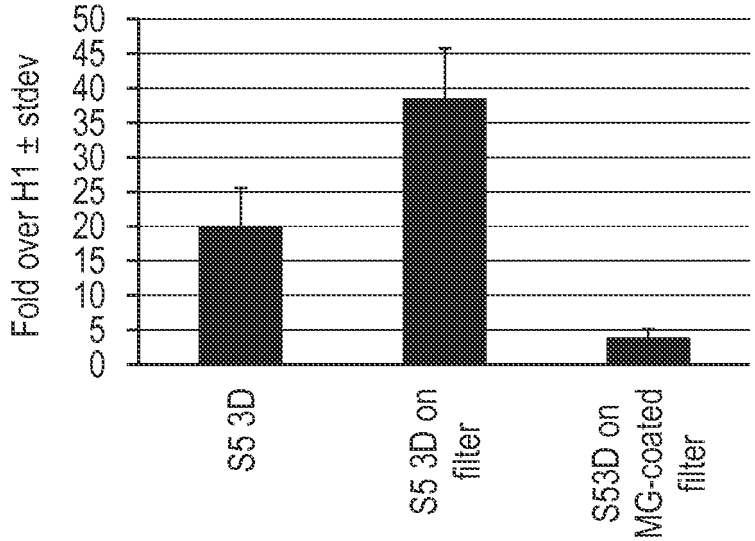


FIG. 6H

Chromogranin-A

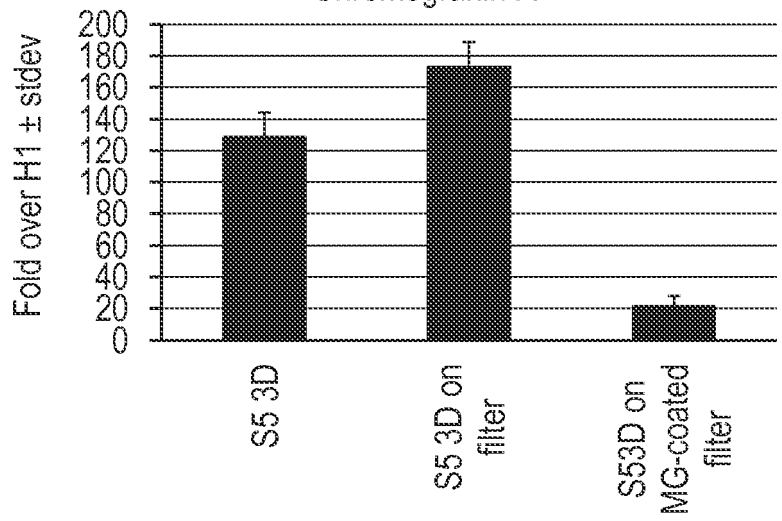


FIG. 6I

PCSK1

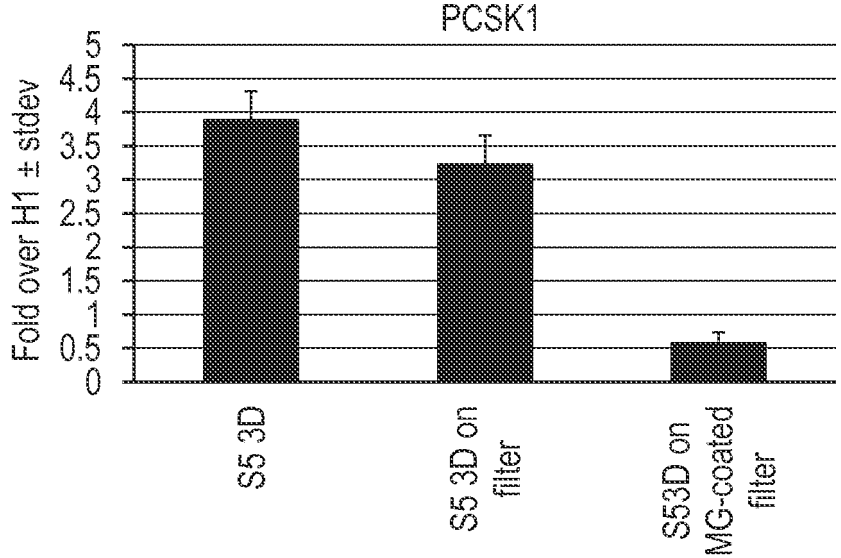


FIG. 6J

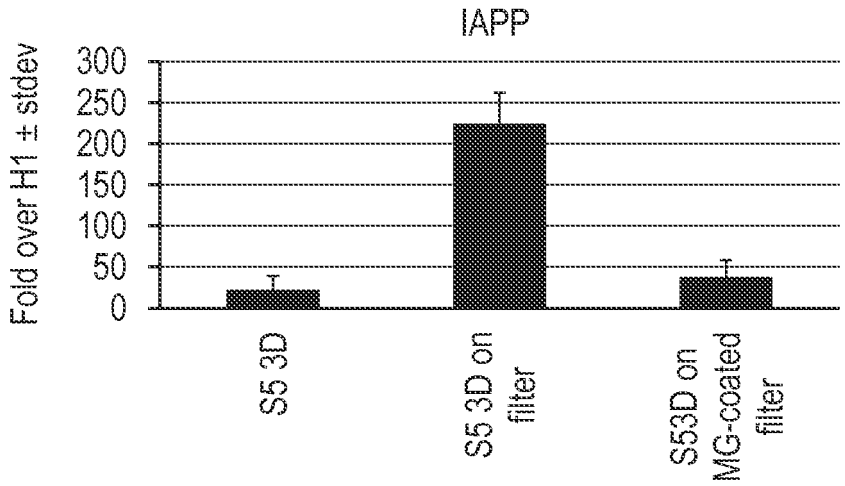


FIG. 6K

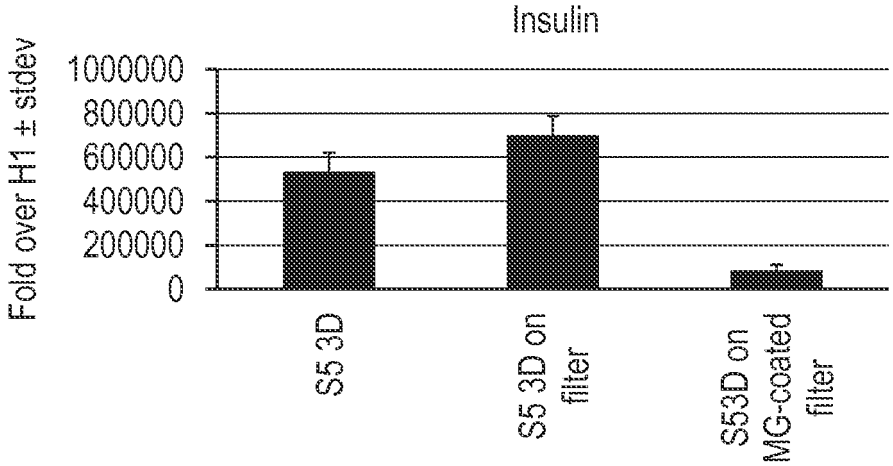


FIG. 6L

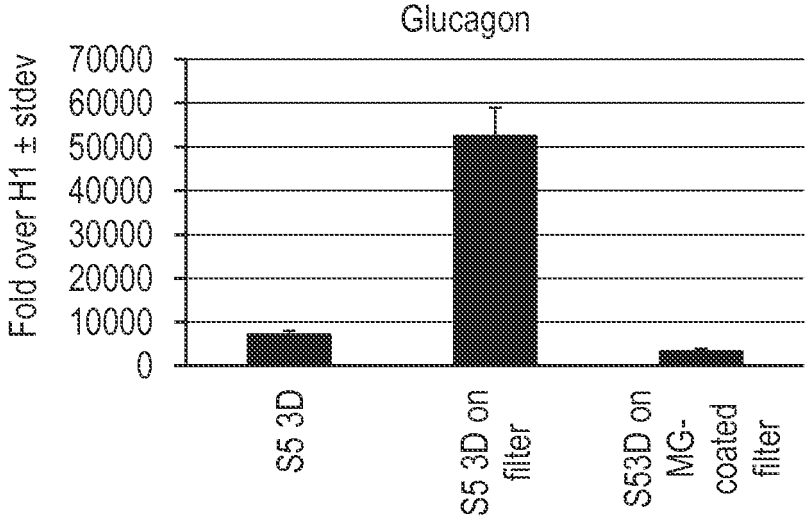


FIG. 7A

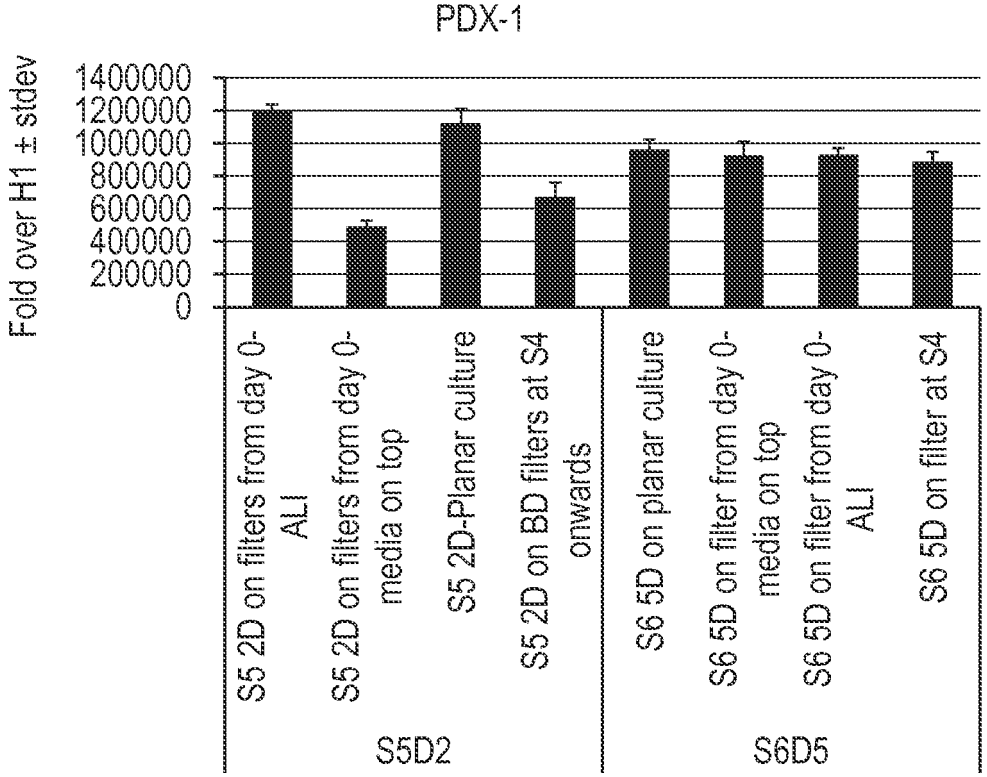

PDX-1
Fold over H1 ± stdev
1400000
1200000
1000000
800000
600000
400000
200000
0
S5 2D on filters from day 0-ALI
S5 2D on filters from day 0-media on top
S5 2D-Planar culture
S5 2D on BD filters at S4 onwards
S6 5D on planar culture
S6 5D on filter from day 0-media on top
S6 5D on filter from day 0-ALI
S6 5D on filter at S4
S5D2
S6D5

FIG. 7B

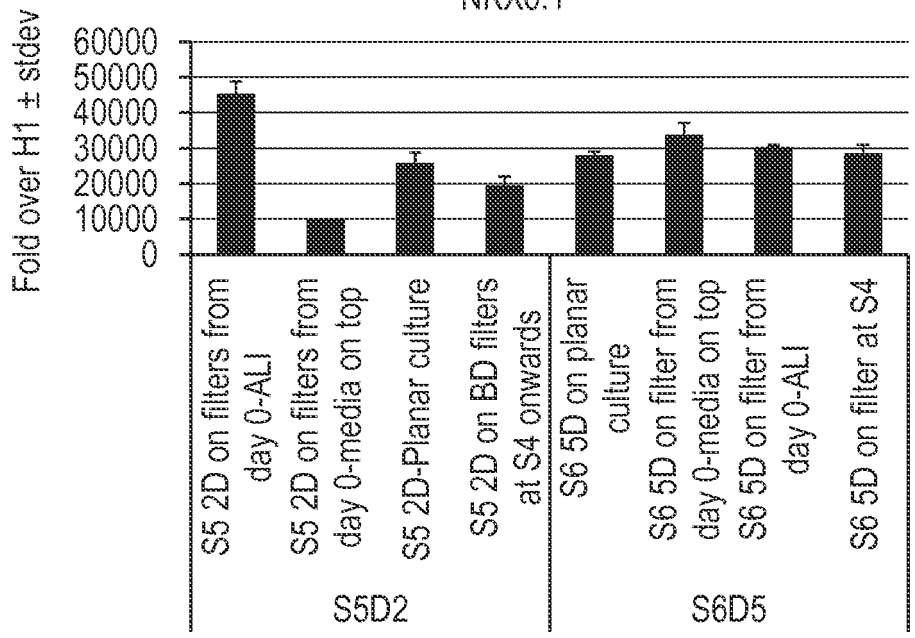

NKX6.1
Fold over H1 ± stdev
60000
50000
40000
30000
20000
10000
0
S5 2D on filters from day 0-ALI
S5 2D on filters from day 0-media on top
S5 2D-Planar culture
S5 2D on BD filters at S4 onwards
S6 5D on planar culture
S6 5D on filter from day 0-media on top
S6 5D on filter from day 0-ALI
S6 5D on filter at S4
S5D2
S6D5

FIG. 7C

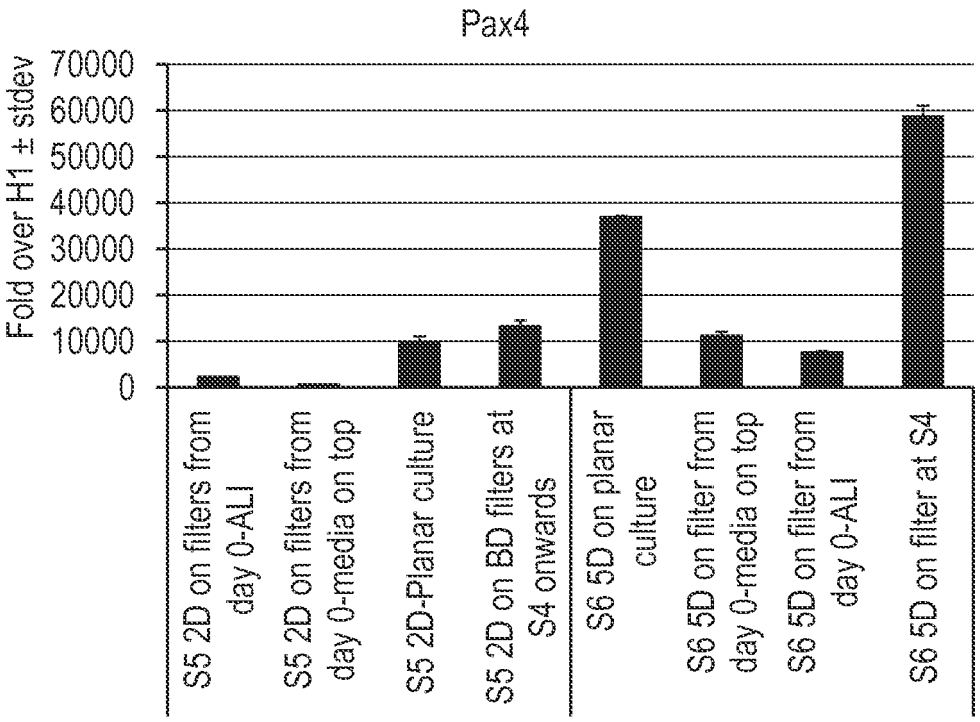

Pax4
Fold over H1 ± stdev
70000
60000
50000
40000
30000
20000
10000
0
S5 2D on filters from day 0-ALI
S5 2D on filters from day 0-media on top
S5 2D-Planar culture
S5 2D on BD filters at S4 onwards
S6 5D on planar culture
S6 5D on filter from day 0-media on top
S6 5D on filter from day 0-ALI
S6 5D on filter at S4

FIG. 7D

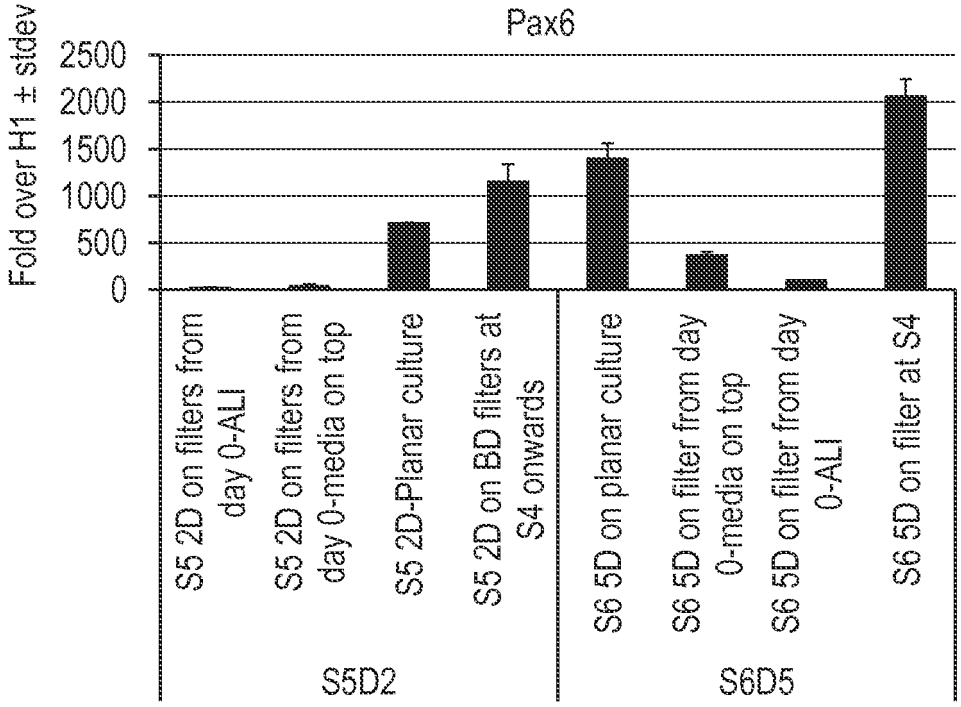

Pax6
Fold over H1 ± stdev
2500
2000
1500
1000
500
0
S5 2D on filters from day 0-ALI
S5 2D on filters from day 0-media on top
S5 2D-Planar culture
S5 2D on BD filters at S4 onwards
S6 5D on planar culture
S6 5D on filter from day 0-media on top
S6 5D on filter from day 0-ALI
S6 5D on filter at S4
S5D2
S6D5

FIG. 7E

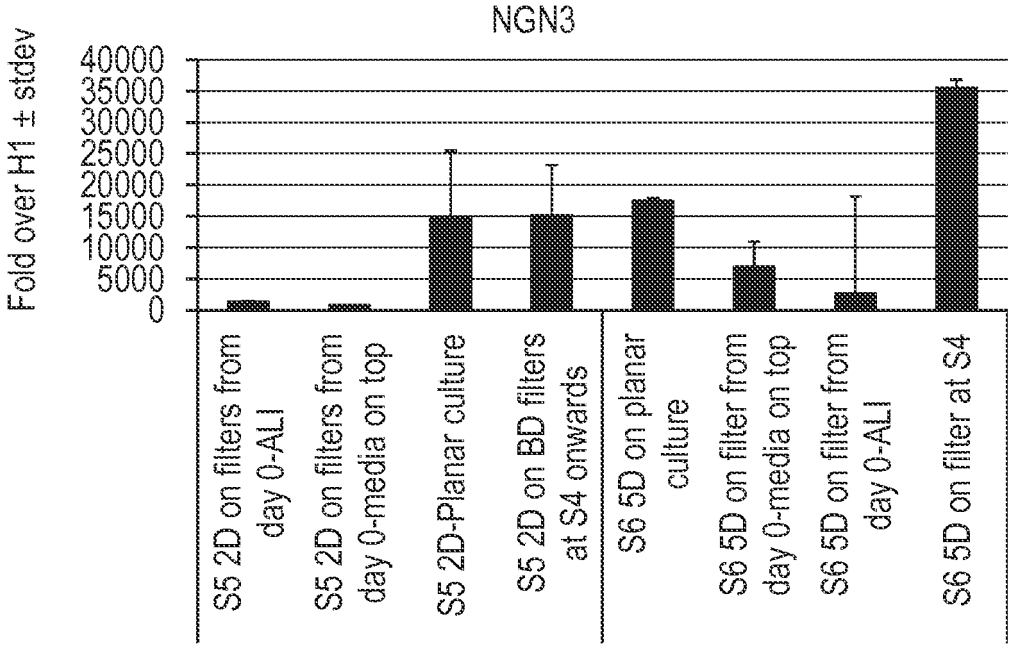

NGN3
Fold over H1 ± stdev
40000
35000
30000
25000
20000
15000
10000
5000
0
S5 2D on filters from day 0-ALI
S5 2D on filters from day 0-media on top
S5 2D-Planar culture
S5 2D on BD filters at S4 onwards
S6 5D on planar culture
S6 5D on filter from day 0-media on top
S6 5D on filter from day 0-ALI
S6 5D on filter at S4

FIG. 7F

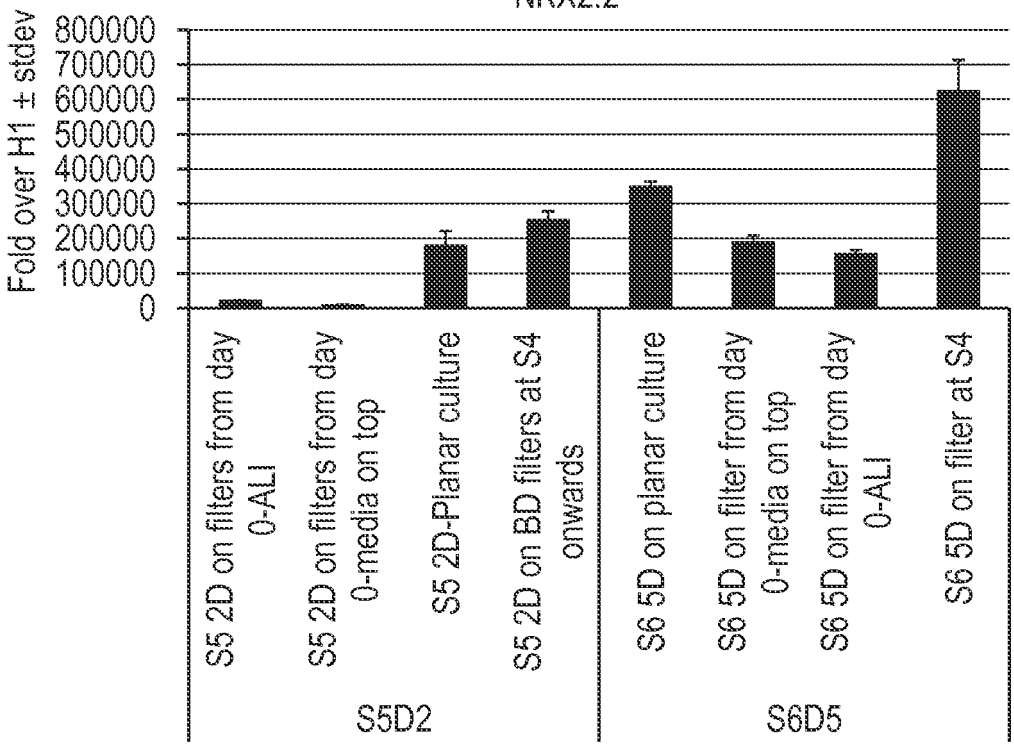

NKX2.2
Fold over H1 ± stdev
800000
700000
600000
500000
400000
300000
200000
100000
0
S5 2D on filters from day 0-ALI
S5 2D on filters from day 0-media on top
S5 2D-Planar culture
S5 2D on BD filters at S4 onwards
S6 5D on planar culture
S6 5D on filter from day 0-media on top
S6 5D on filter from day 0-ALI
S6 5D on filter at S4
S5D2
S6D5

FIG. 7G

ABCC8

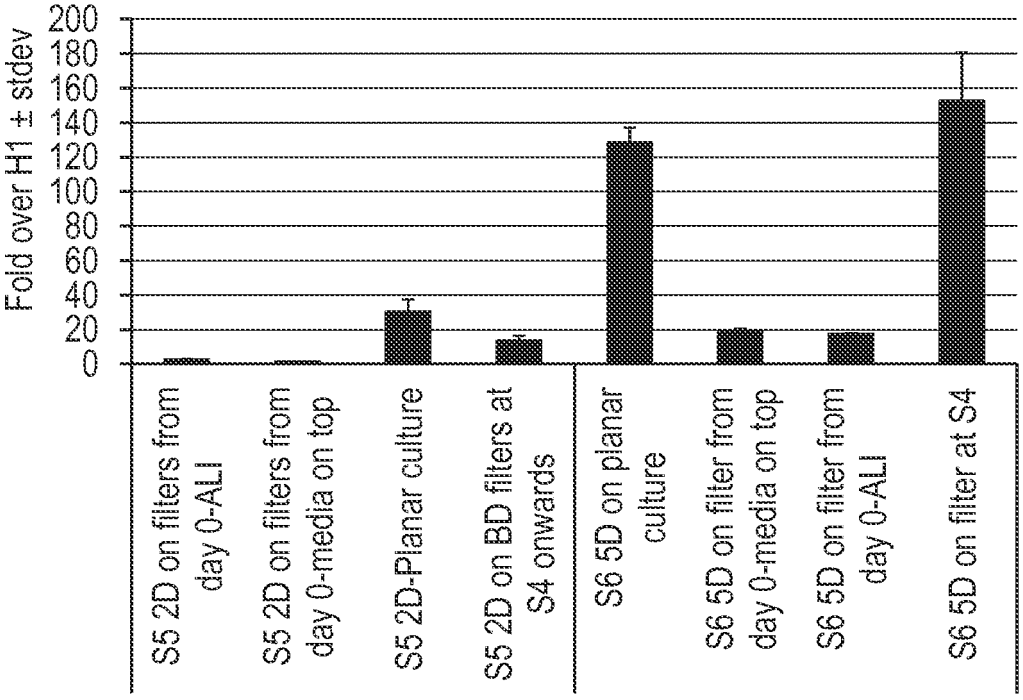


FIG. 7H

Chromogranin-A

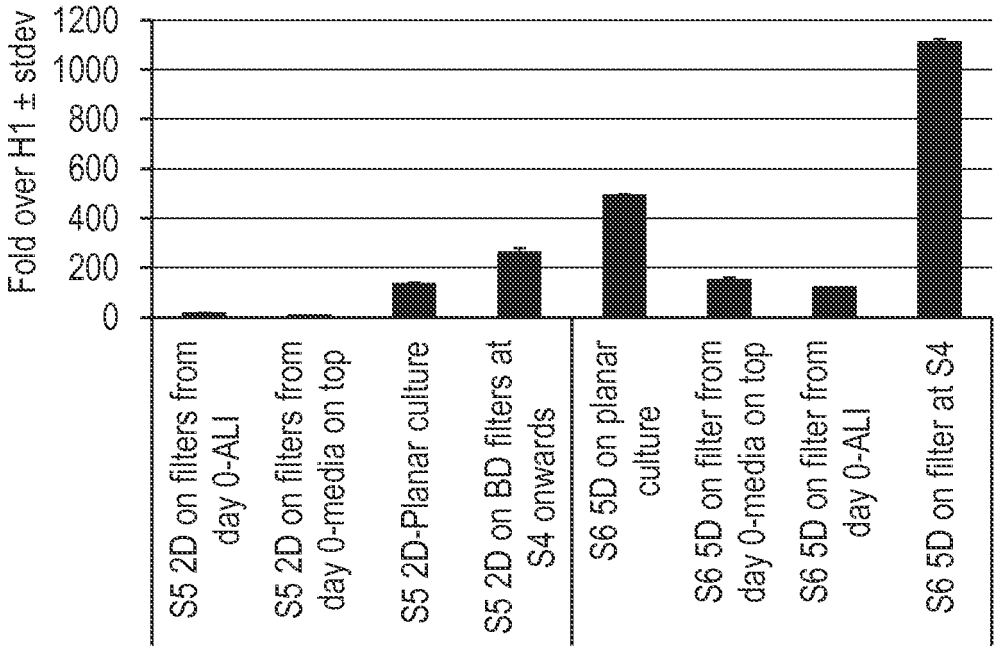


FIG. 7I

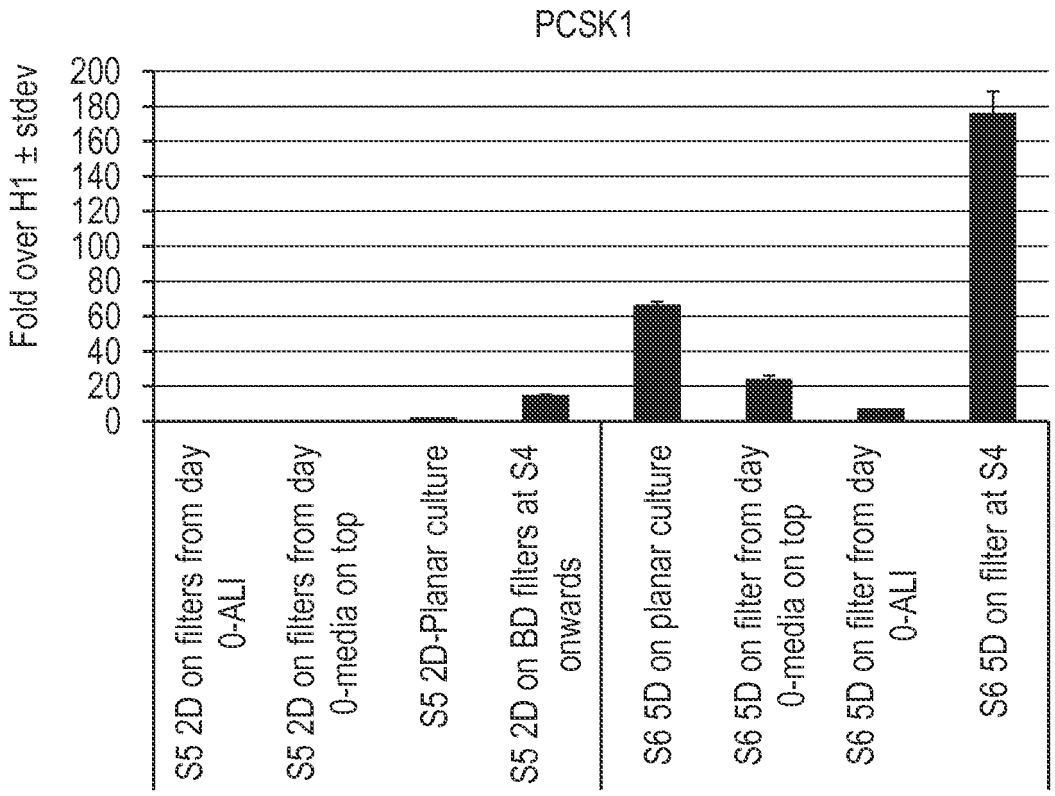

PCSK1
Fold over H1 ± stdev
200
180
160
140
120
100
80
60
40
20
0
S5 2D on filters from day 0-ALI
S5 2D on filters from day 0-media on top
S5 2D-Planar culture
S5 2D on BD filters at S4 onwards
S6 5D on planar culture
S6 5D on filter from day 0-media on top
S6 5D on filter from day 0-ALI
S6 5D on filter at S4

FIG. 7J

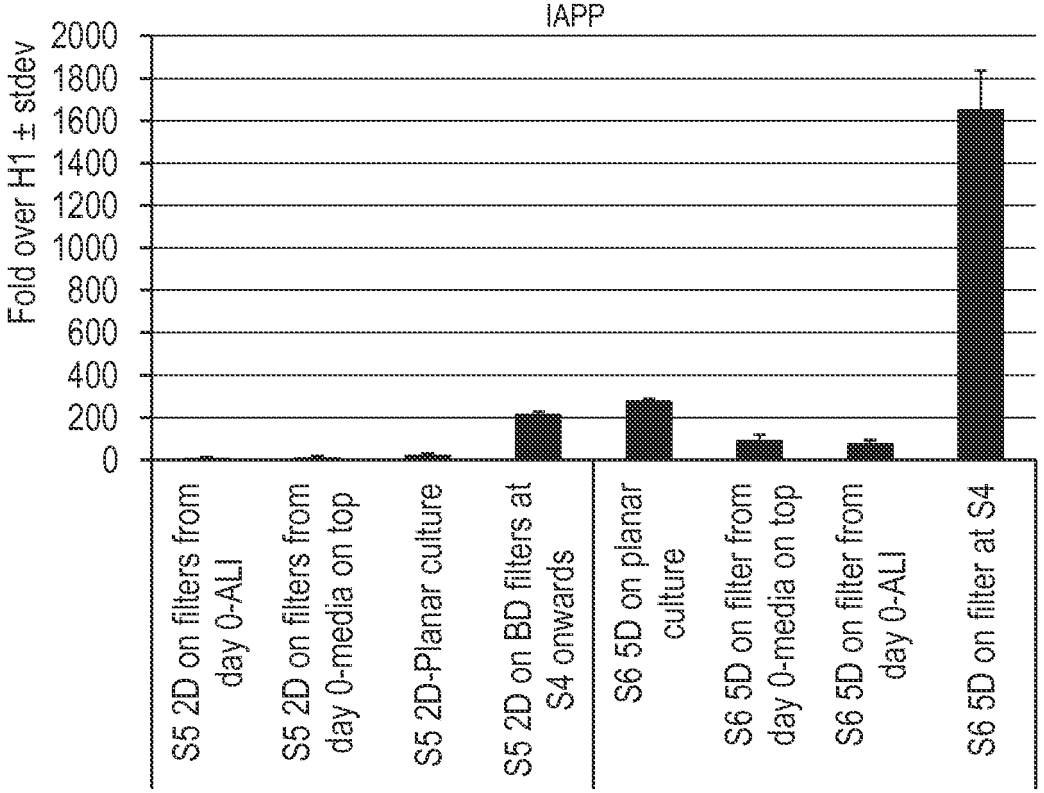

IAPP
Fold over H1 ± stdev
2000
1800
1600
1400
1200
1000
800
600
400
200
0
S5 2D on filters from day 0-ALI
S5 2D on filters from day 0-media on top
S5 2D-Planar culture
S5 2D on BD filters at S4 onwards
S6 5D on planar culture
S6 5D on filter from day 0-media on top
S6 5D on filter from day 0-ALI
S6 5D on filter at S4

FIG. 7K

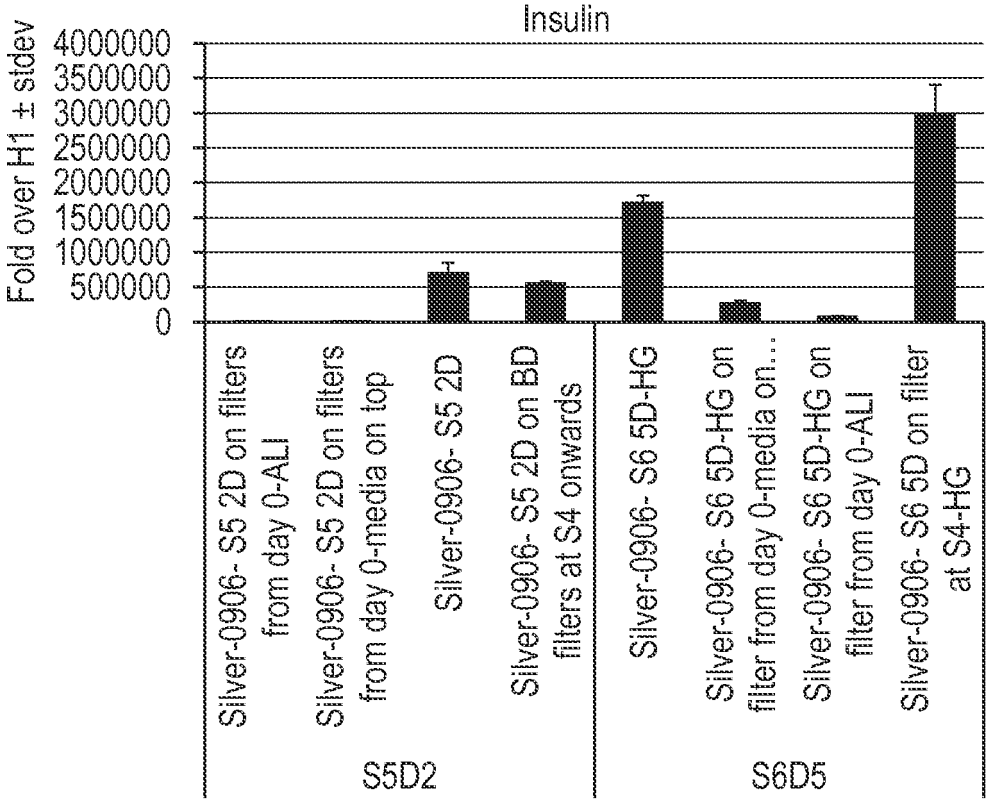
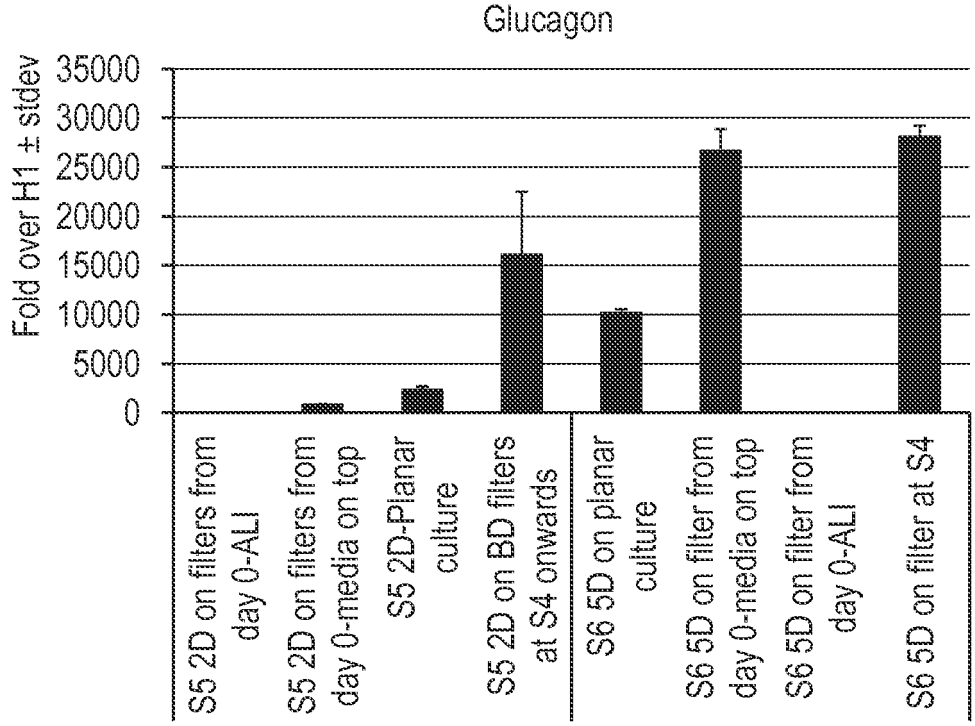

Insulin
Fold over H1 ± stdev
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
Silver-0906- S5 2D on filters from day 0-ALI
Silver-0906- S5 2D on filters from day 0-media on top
Silver-0906- S5 2D
Silver-0906- S5 2D on BD filters at S4 onwards
Silver-0906- S6 5D-HG
Silver-0906- S6 5D-HG on filter from day 0-media on...
Silver-0906- S6 5D-HG on filter from day 0-ALI
Silver-0906- S6 5D on filter at S4-HG
S5D2
S6D5

FIG. 7L


Glucagon
Fold over H1 ± stdev
35000
30000
25000
20000
15000
10000
5000
0
S5 2D on filters from day 0-ALI
S5 2D on filters from day 0-media on top
S5 2D-Planar culture
S5 2D on BD filters at S4 onwards
S6 5D on planar culture
S6 5D on filter from day 0-media on top
S6 5D on filter from day 0-ALI
S6 5D on filter at S4

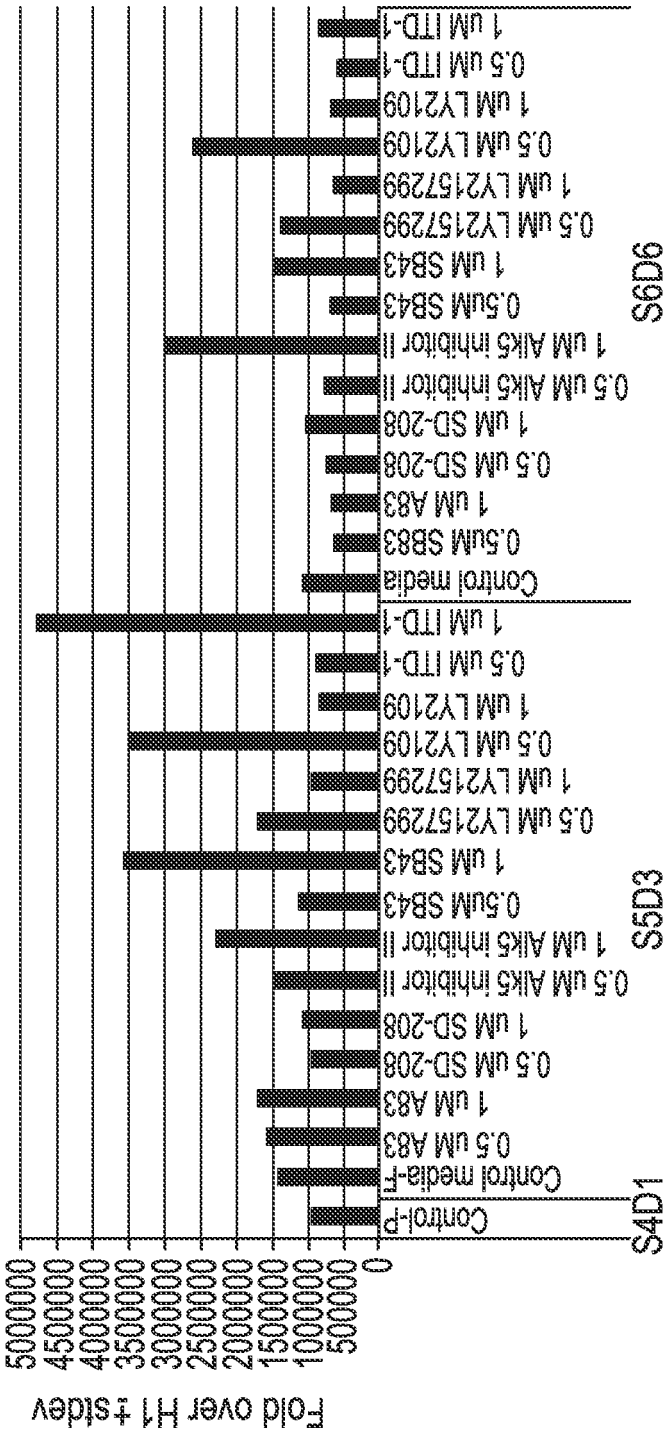


FIG. 8A
PDX1

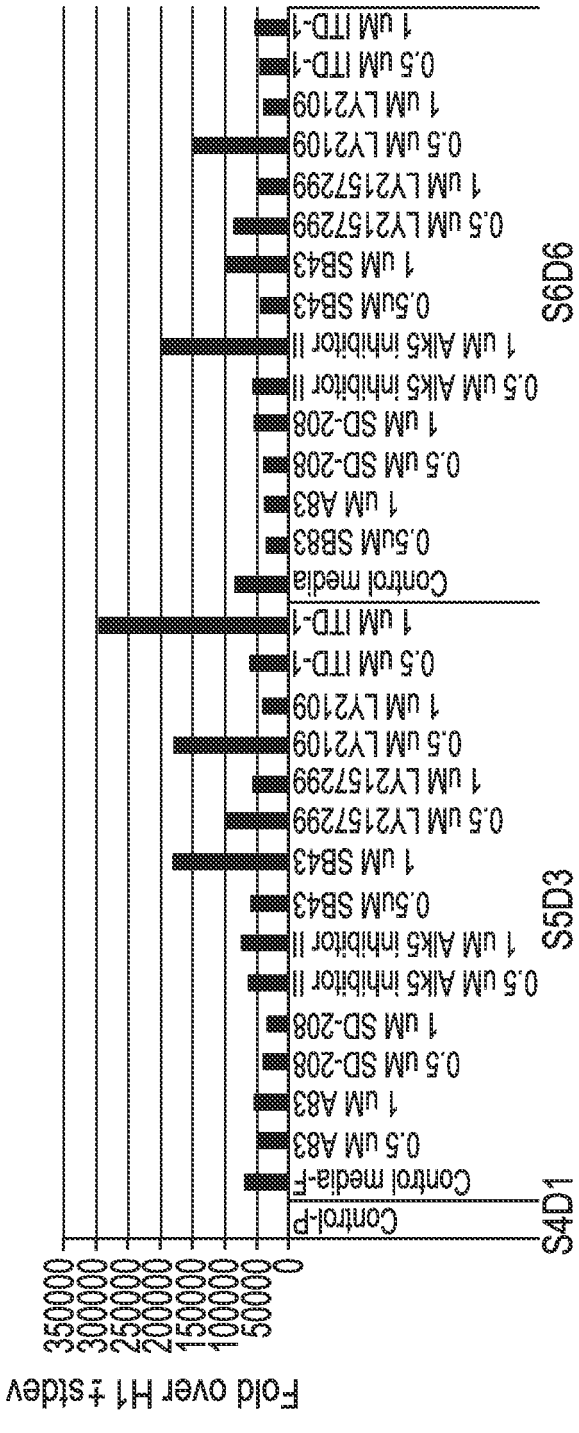


FIG. 8B
NKX6.1

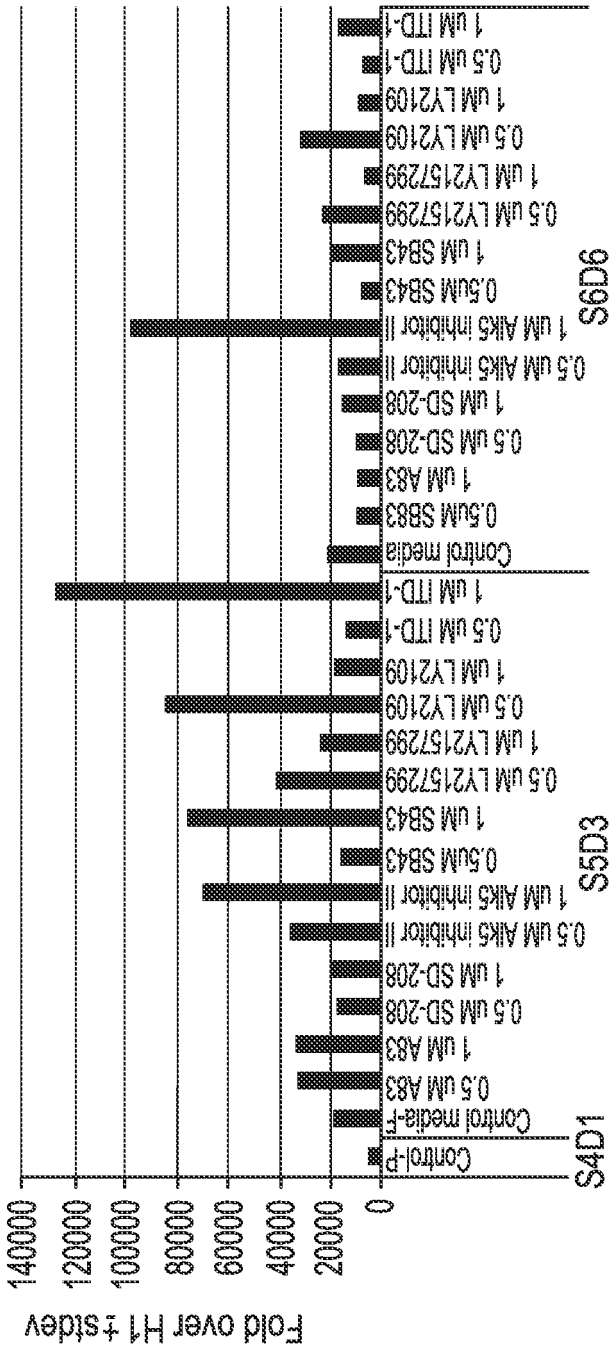


FIG. 8C
NGN3

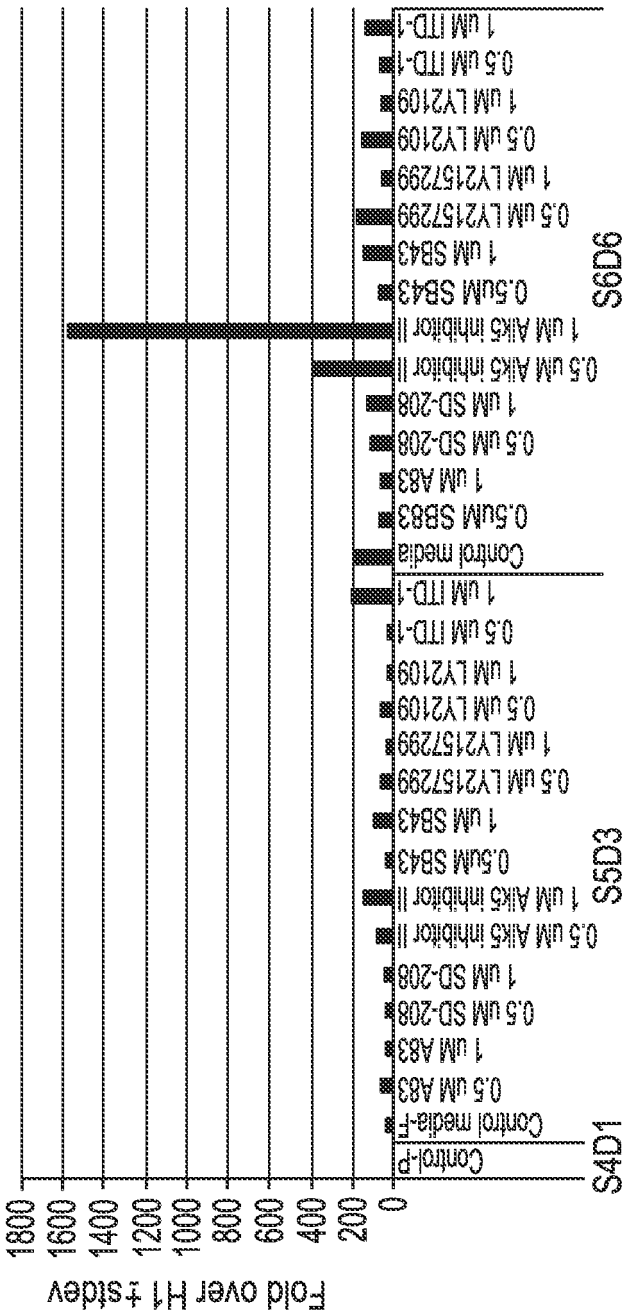


FIG. 8D
ABCC8

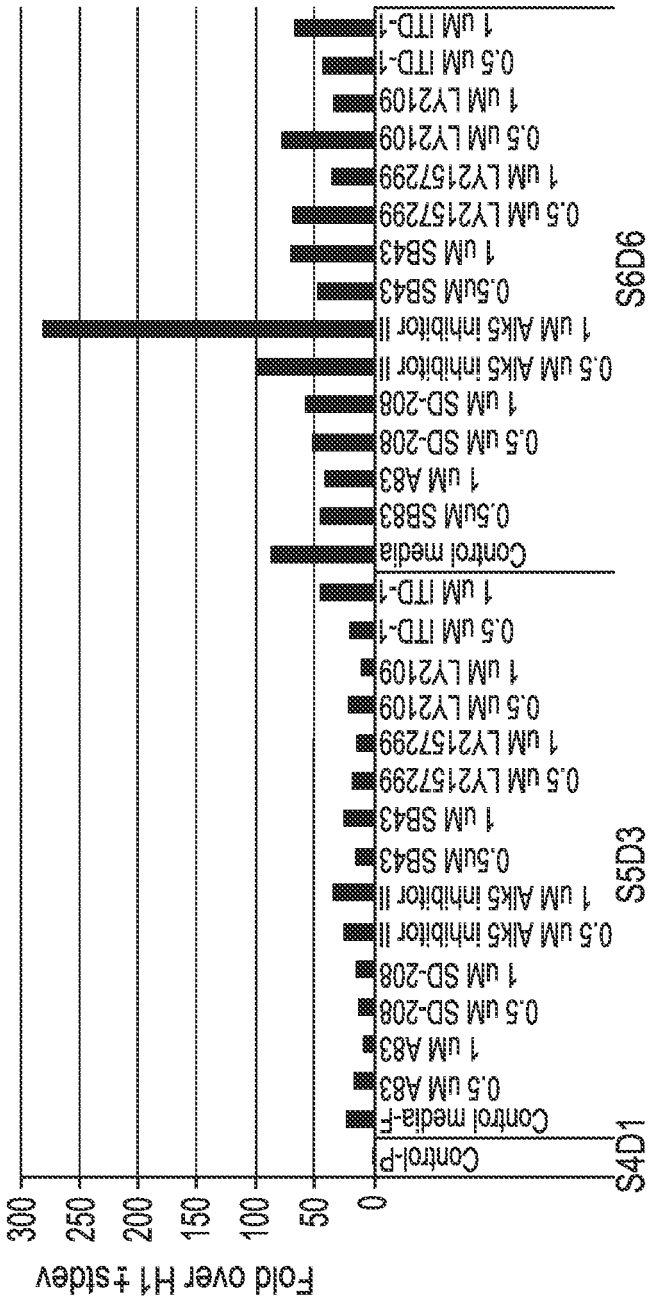


FIG. 8E
PCSK1

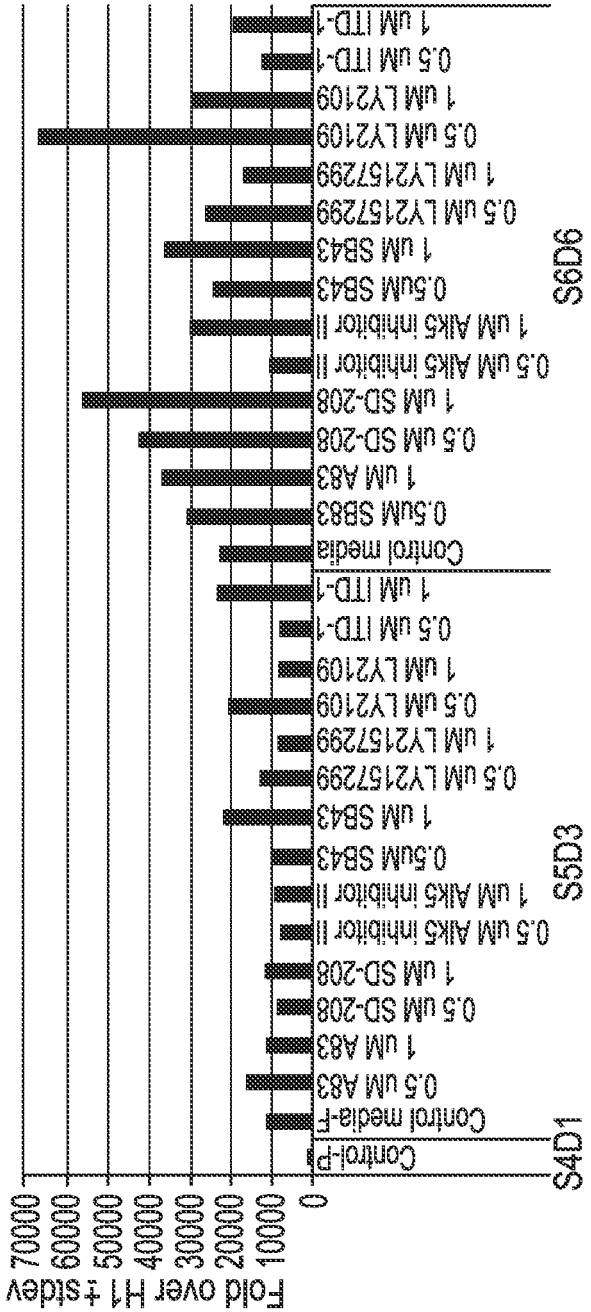


FIG. 8F
GHRL

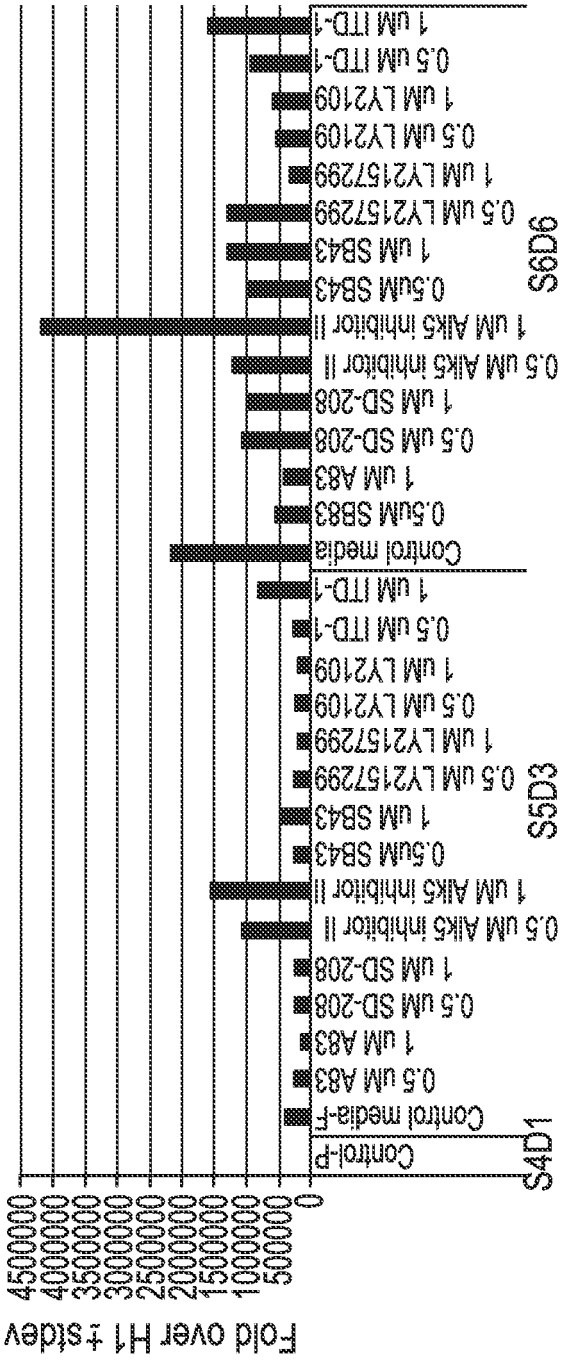


FIG. 8G
GCG

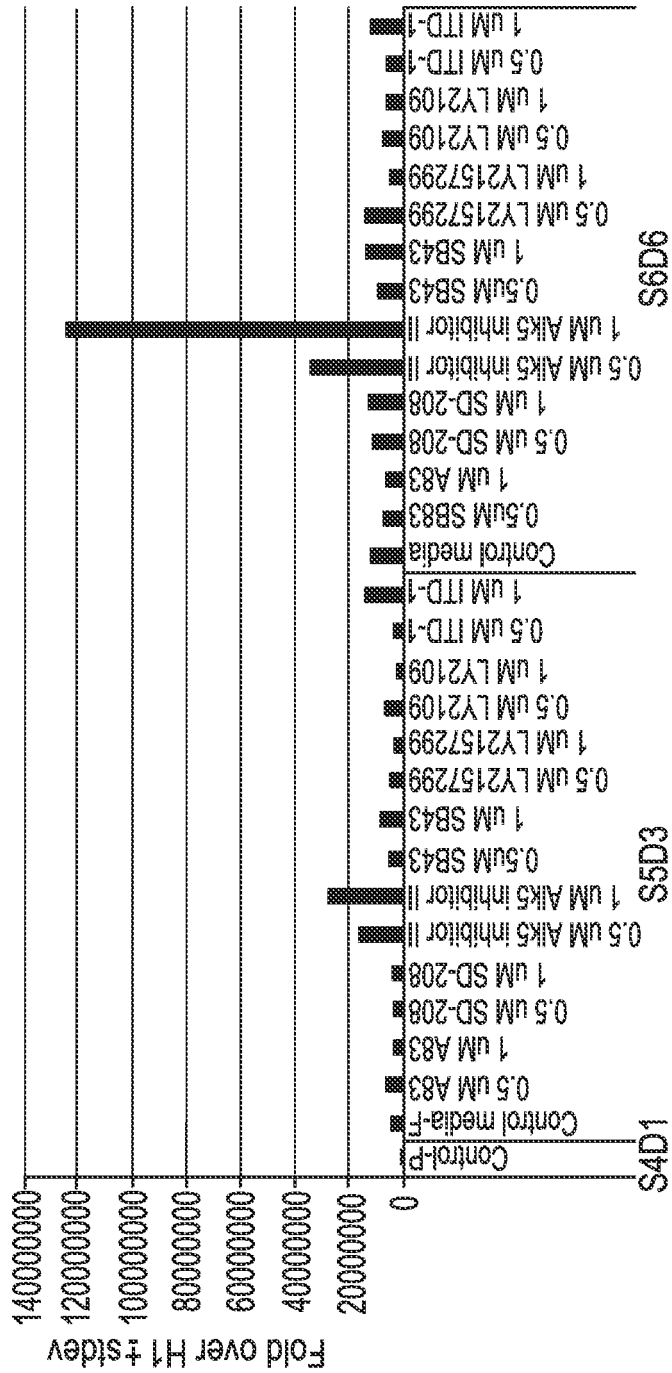


FIG. 8H
INS

FIG. 9A

PDX1

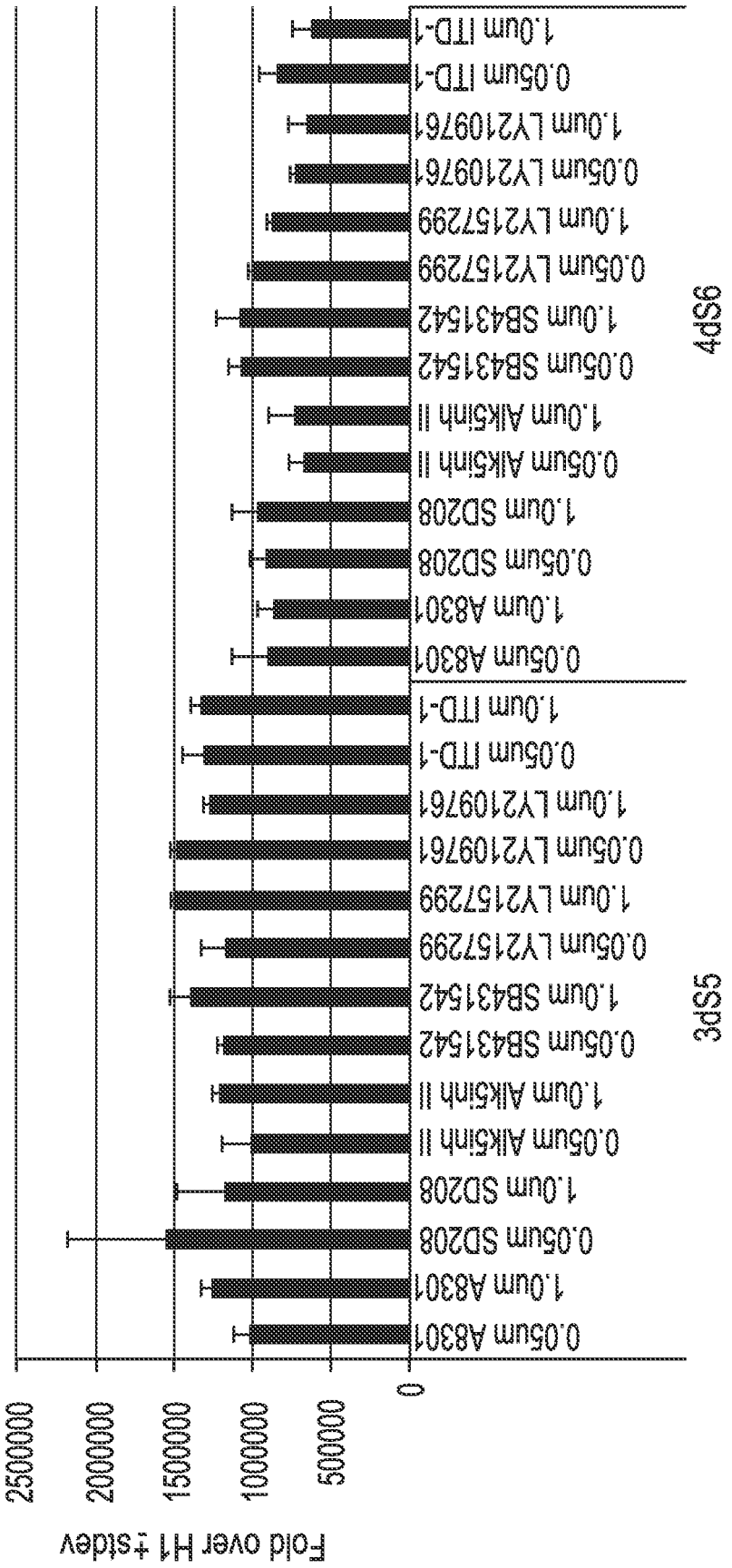

Fold over H1 ±stdev
2500000
2000000
1500000
1000000
500000
0
0.05um A8301
1.0um A8301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
3dS5
0.05um A8301
1.0um A8301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
4dS6

FIG. 9B

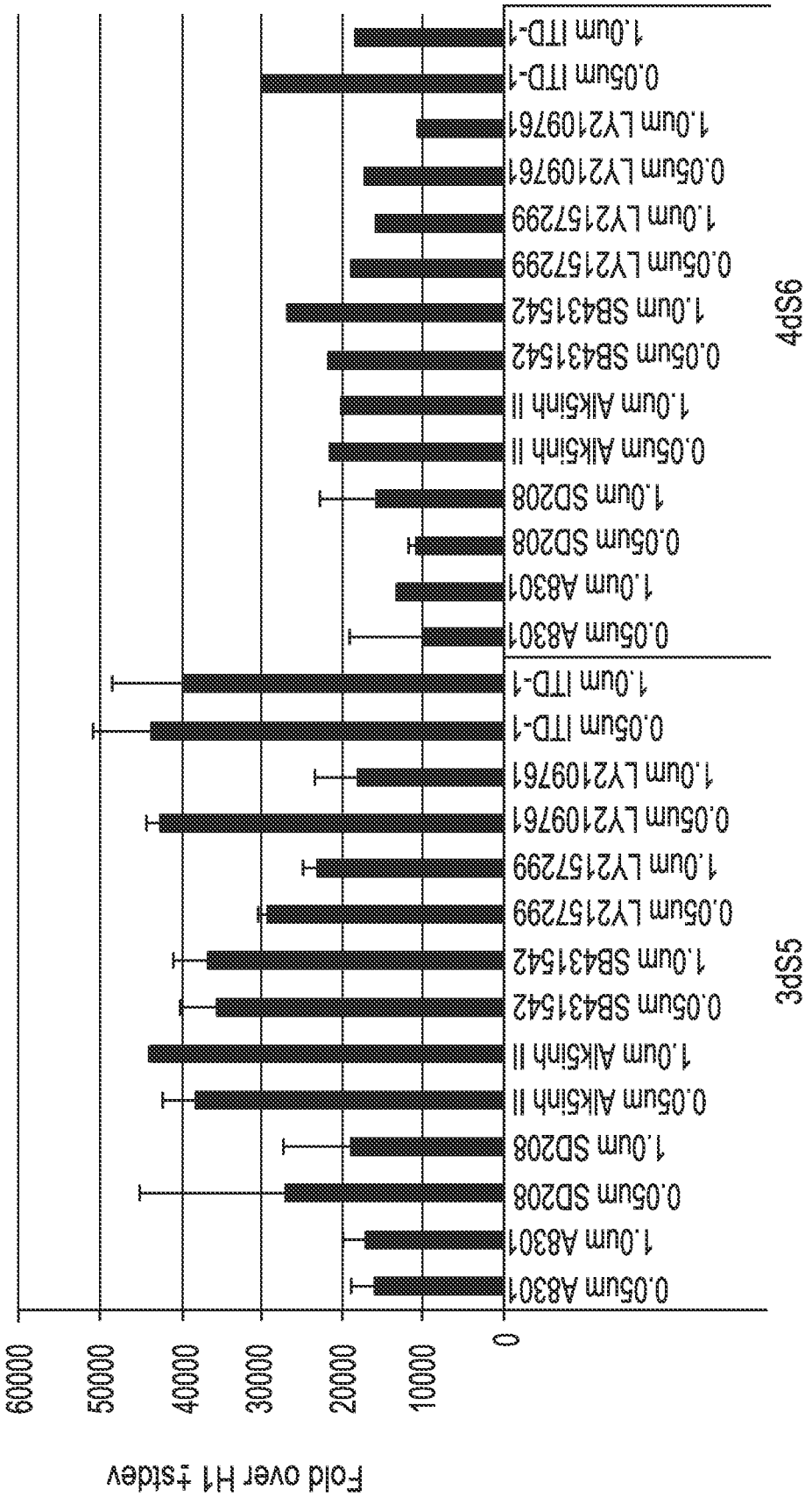

NKX6.1
Fold over H1 ±stdev
60000
50000
40000
30000
20000
10000
0
0.05um A8301
1.0um A8301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
3dS5
0.05um A8301
1.0um A8301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
4dS6

FIG. 9C
NGN3

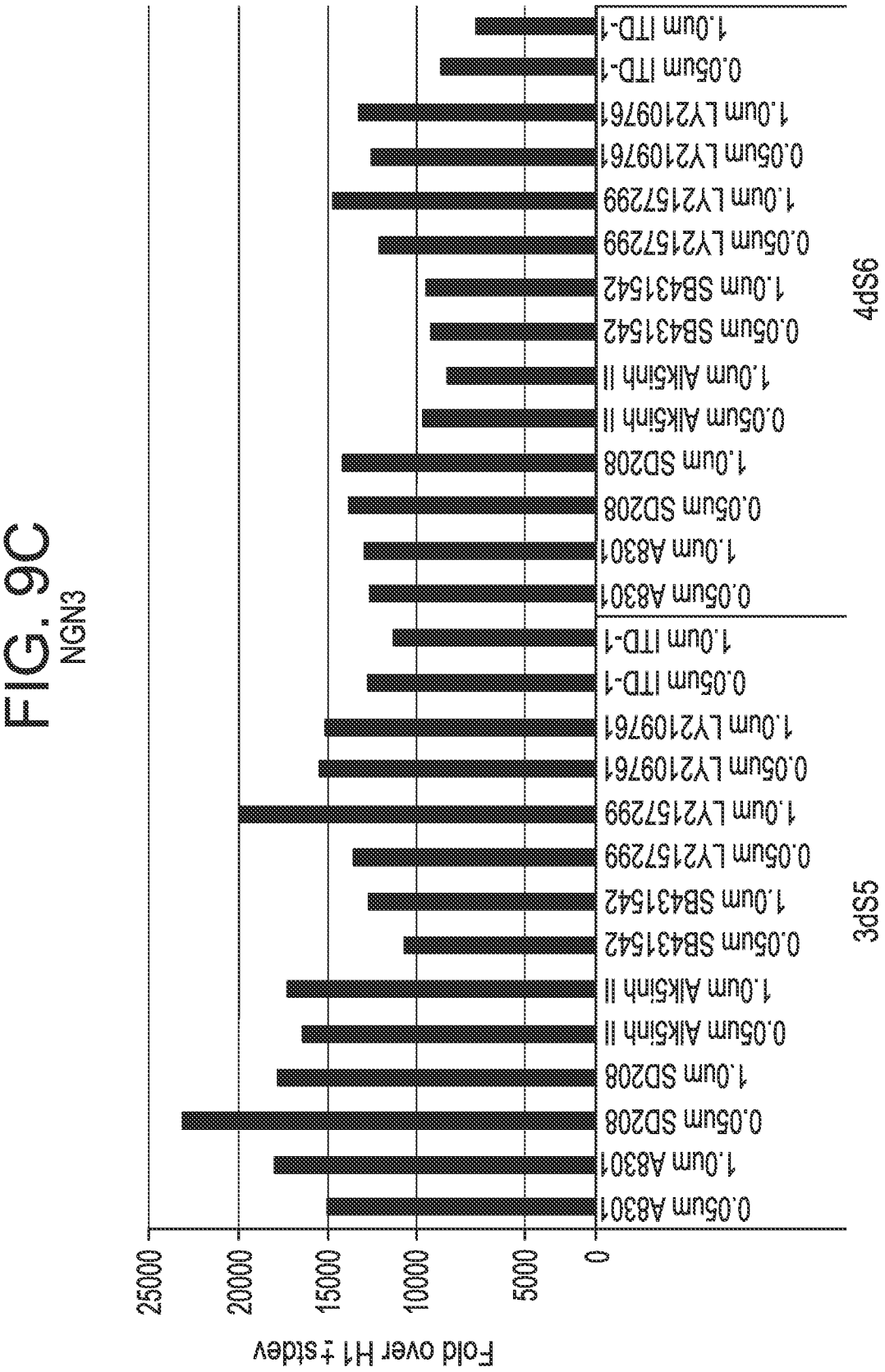

Fold over H1 ± stdev
25000
20000
15000
10000
5000
0
0.05um A8301
1.0um A8301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
3dS5
0.05um A8301
1.0um A8301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
4dS6

FIG. 9D

ABCC8

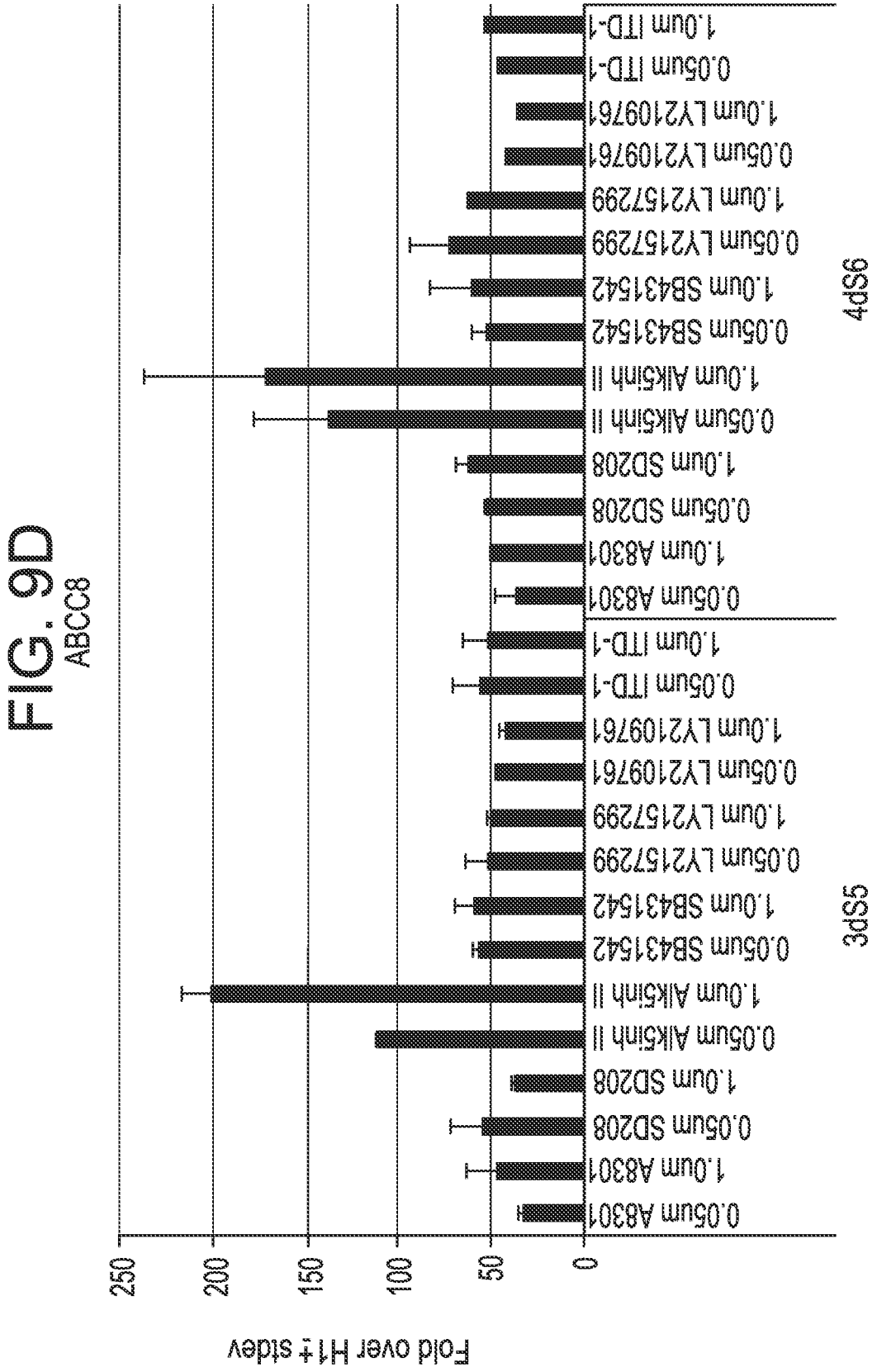

Fold over H1± stdev
250
200
150
100
50
0
0.05um AB301
1.0um AB301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
3dS5
0.05um AB301
1.0um AB301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
4dS6

FIG. 9E

GCG

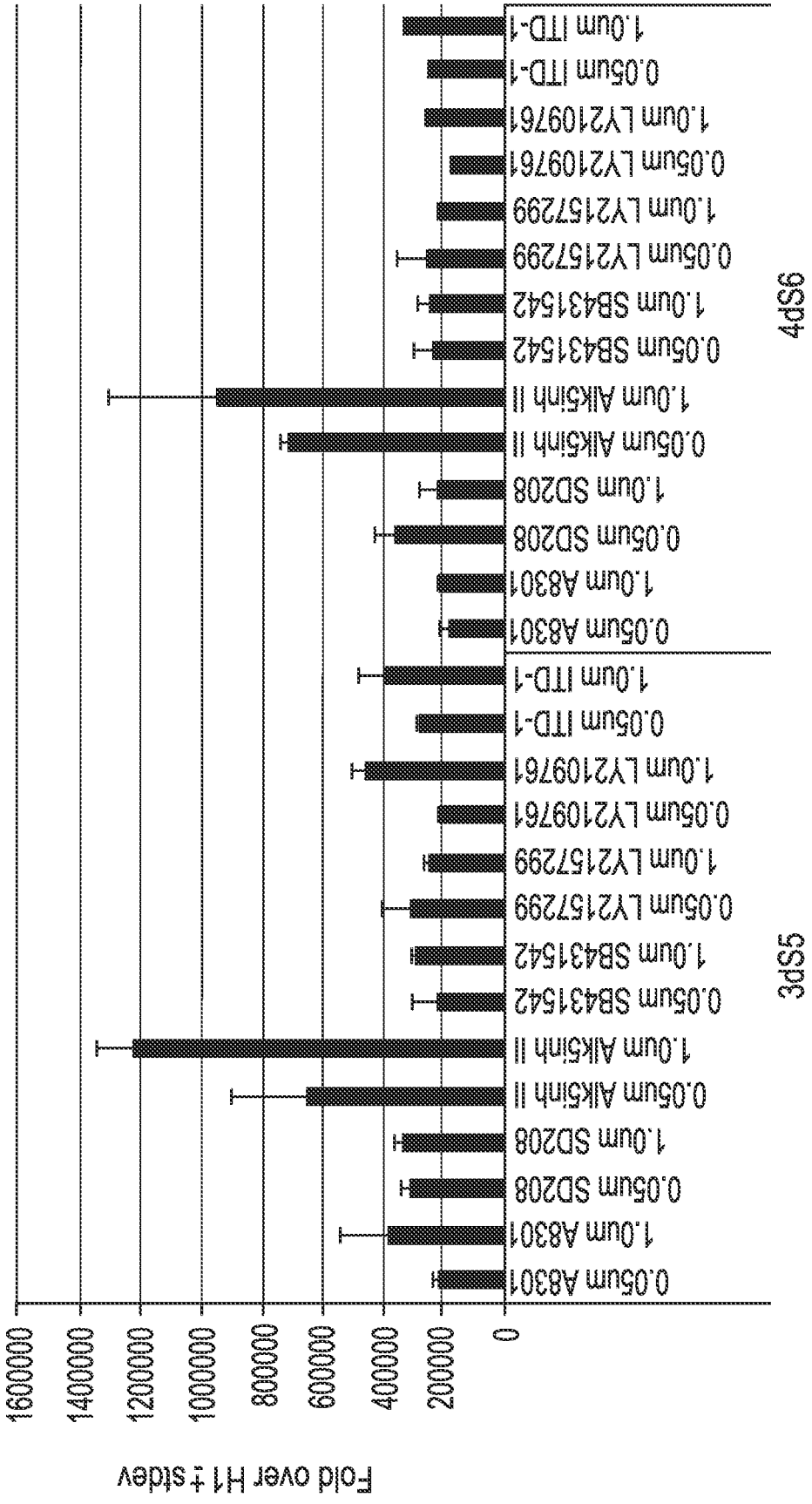

Fold over H1 ± stdev
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
0.05um AB301
1.0um AB301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
3dS5
0.05um AB301
1.0um AB301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
4dS6

FIG. 9F

INS

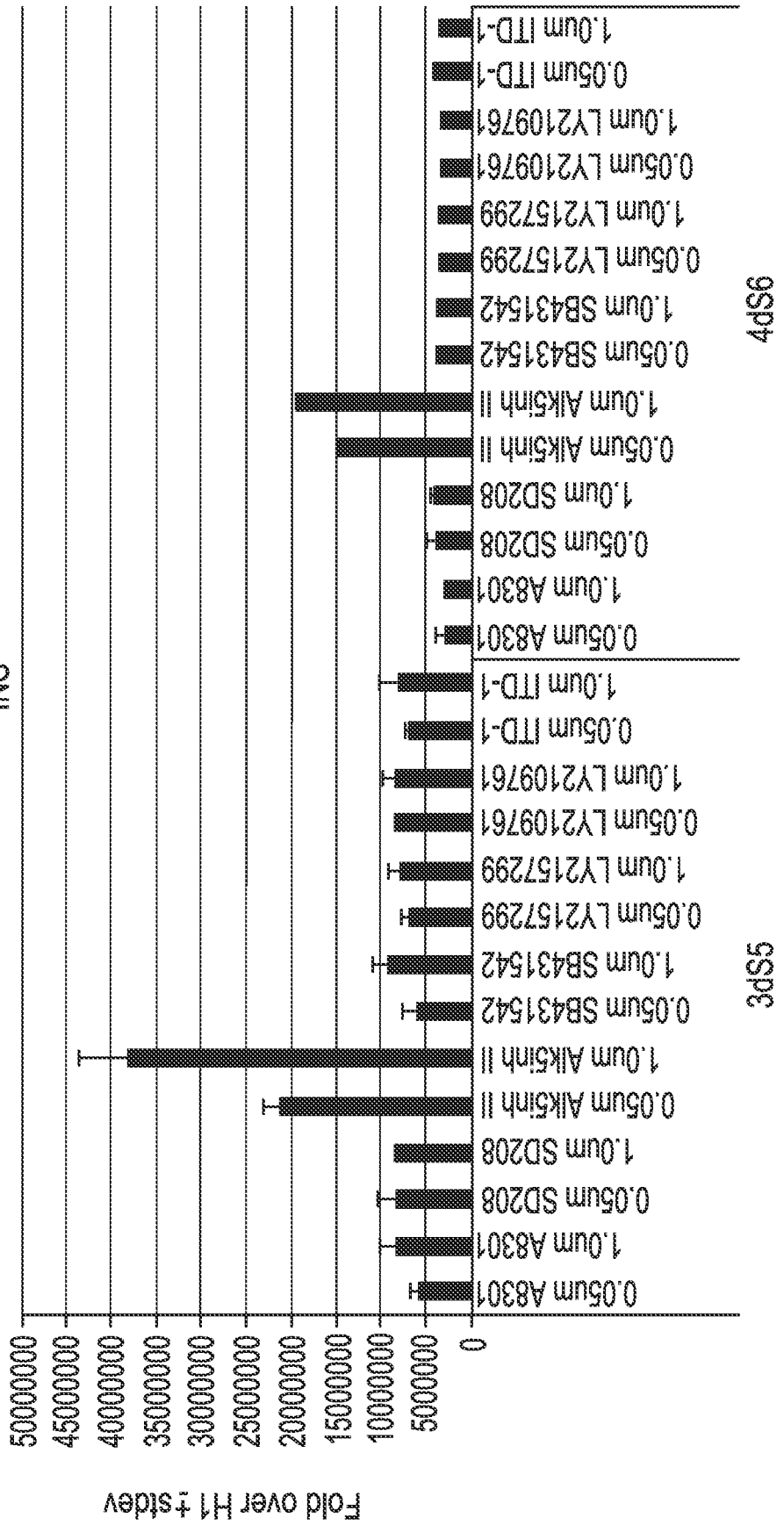

Fold over H1 ± stdev
50000000
45000000
40000000
35000000
30000000
25000000
20000000
15000000
10000000
5000000
0
0.05um A8301
1.0um A8301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
3dS5
0.05um A8301
1.0um A8301
0.05um SD208
1.0um SD208
0.05um Alk5inh II
1.0um Alk5inh II
0.05um SB431542
1.0um SB431542
0.05um LY2157299
1.0um LY2157299
0.05um LY2109761
1.0um LY2109761
0.05um ITD-1
1.0um ITD-1
4dS6

FIG. 10A

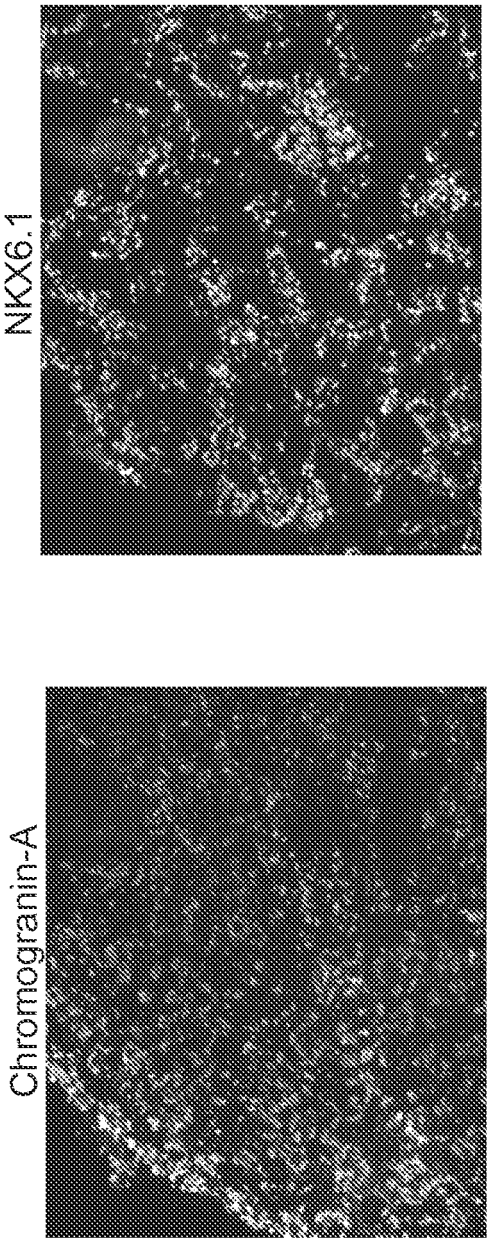


FIG. 10B

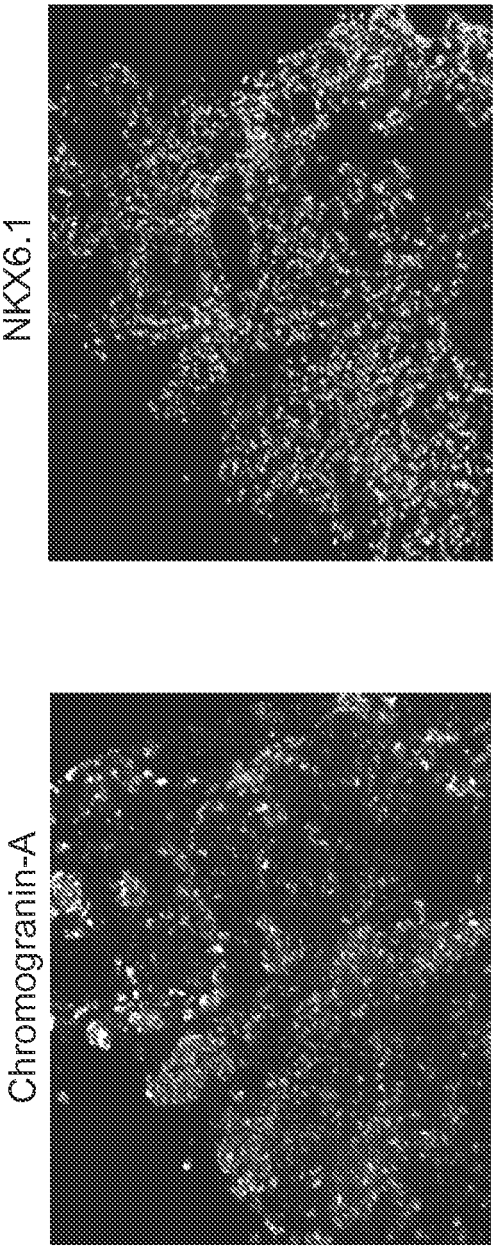


FIG. 11A

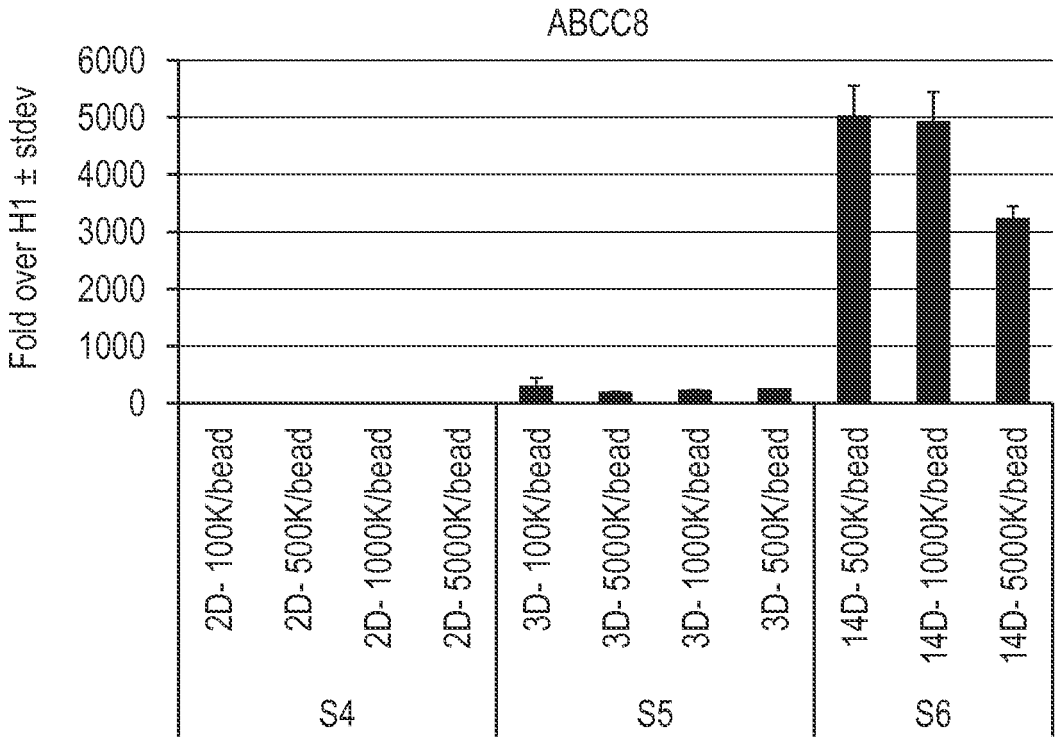


FIG. 11B

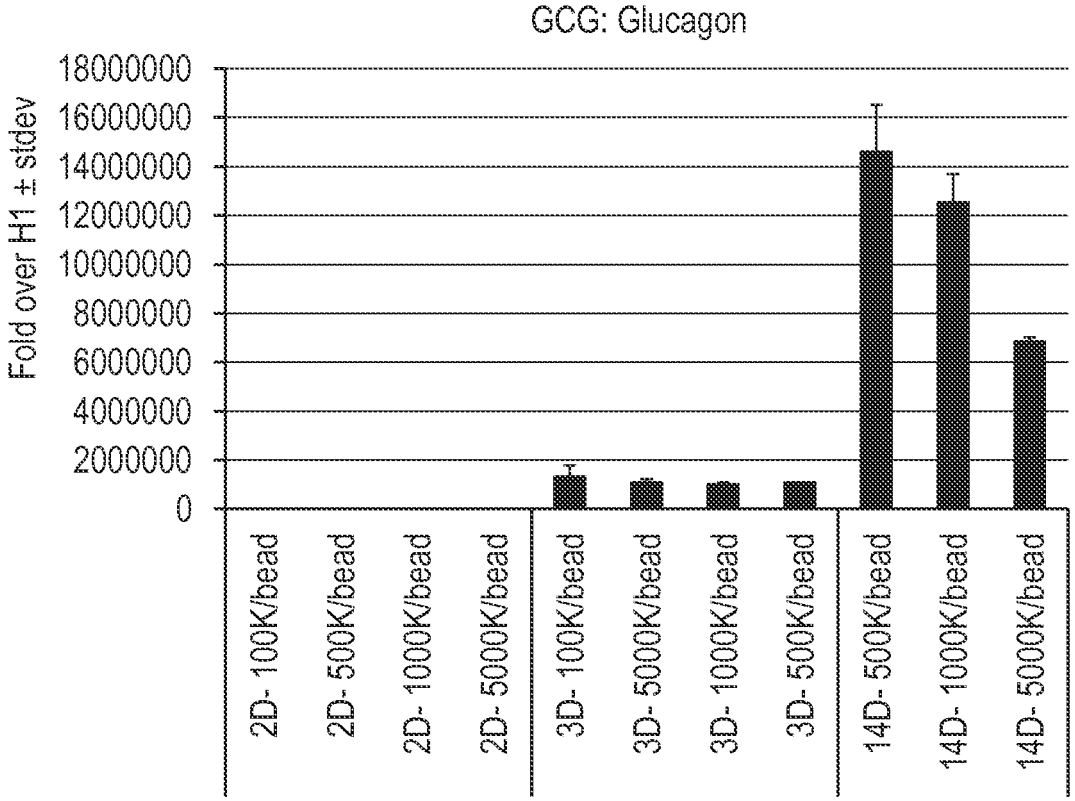


FIG. 11C

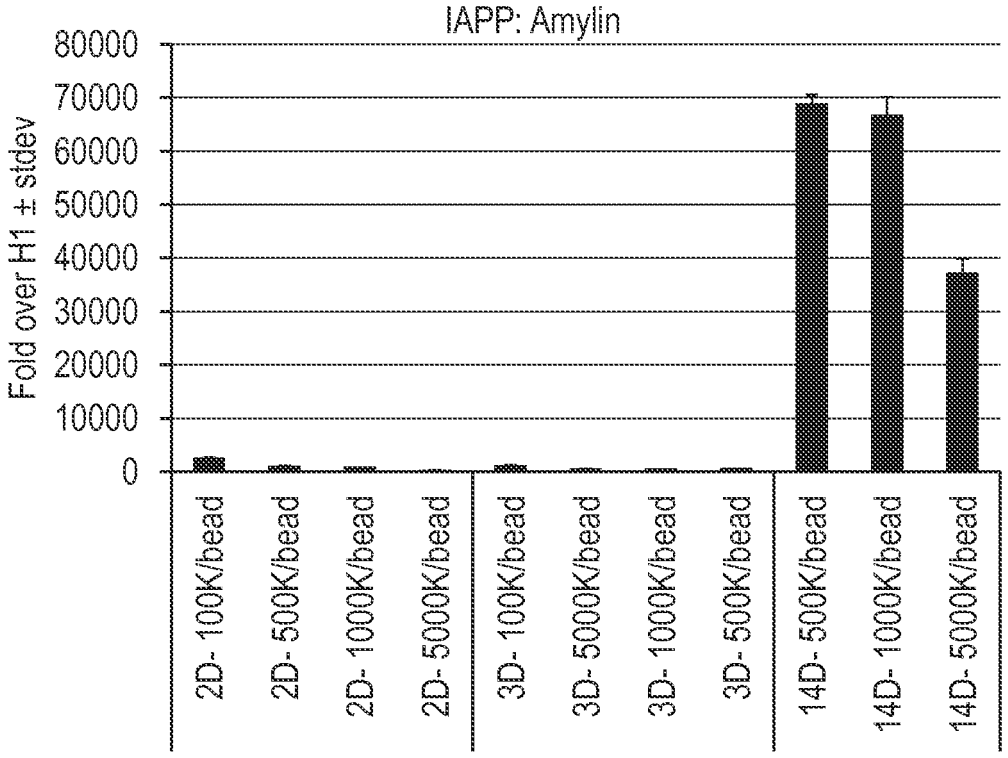


FIG. 11D

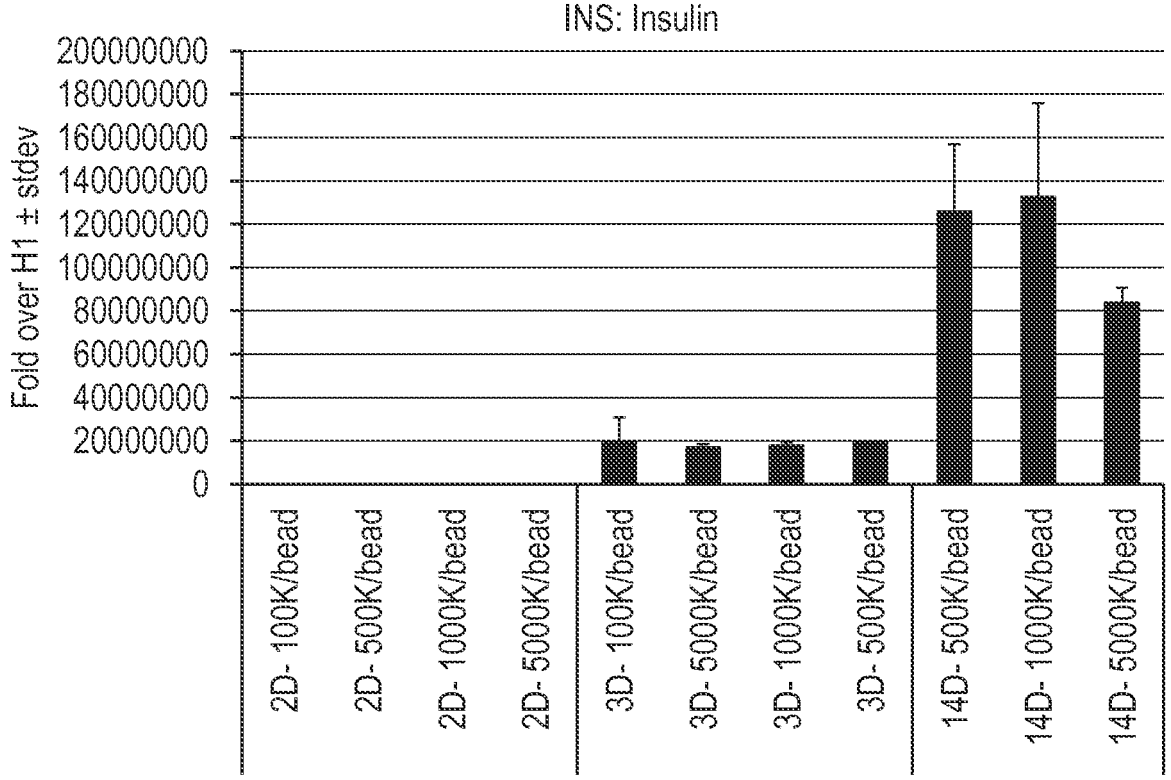


FIG. 11E

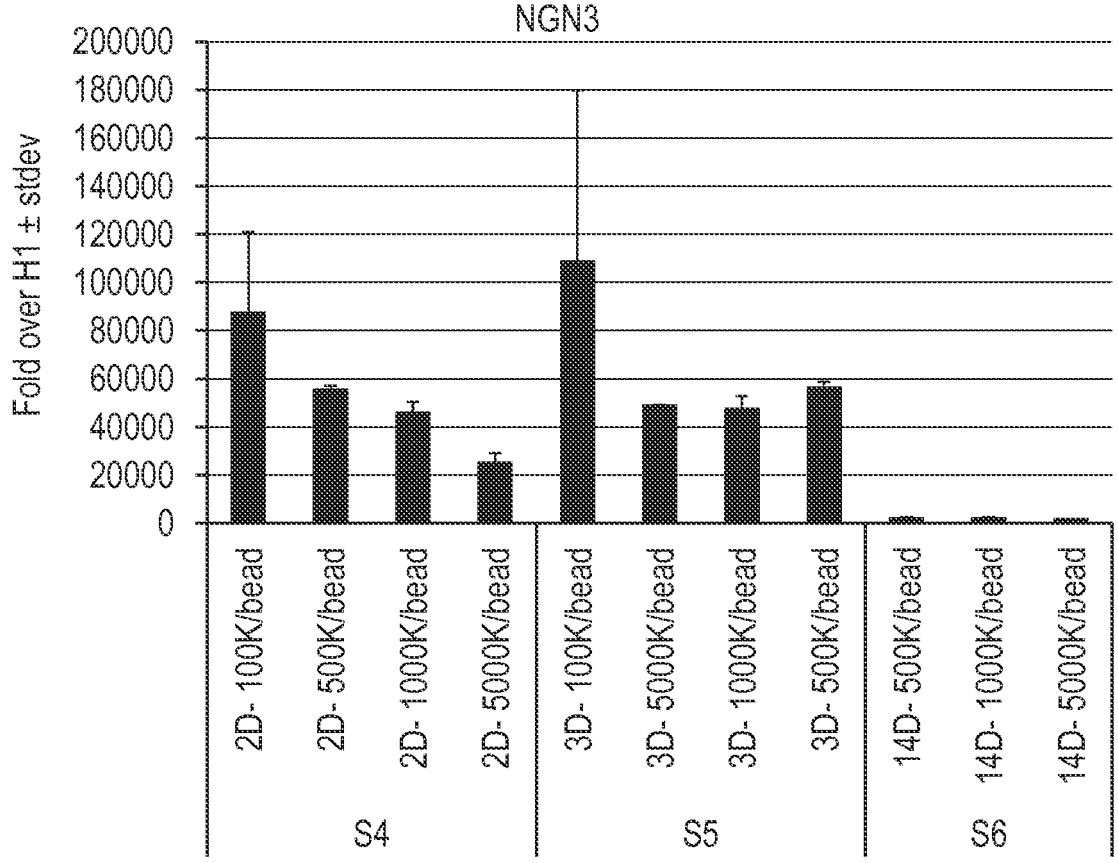


FIG. 11F

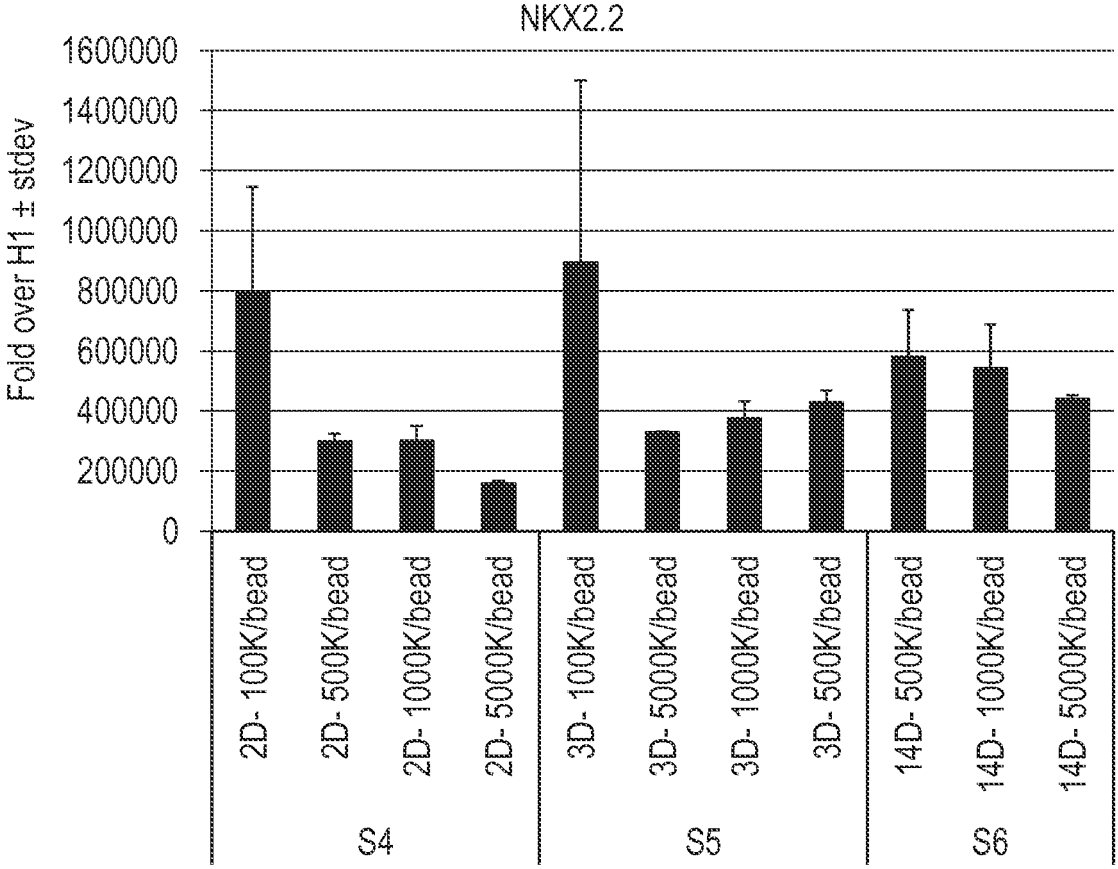


FIG. 11G

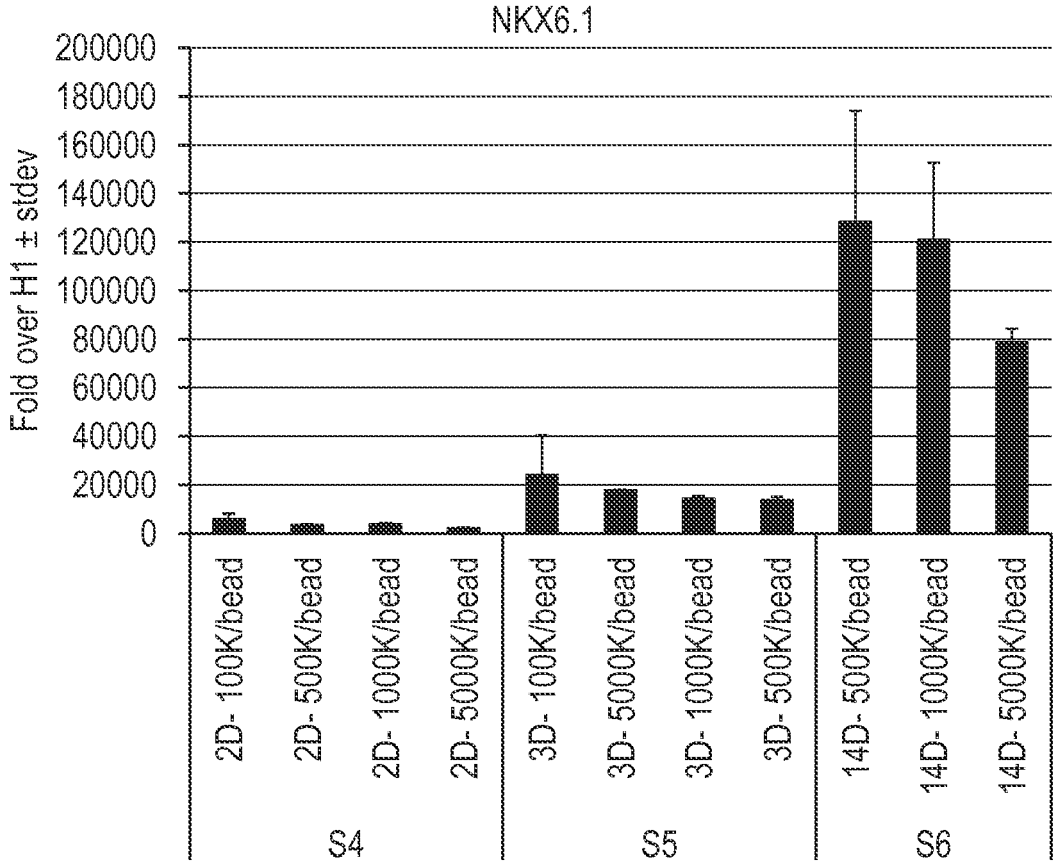


FIG. 11H

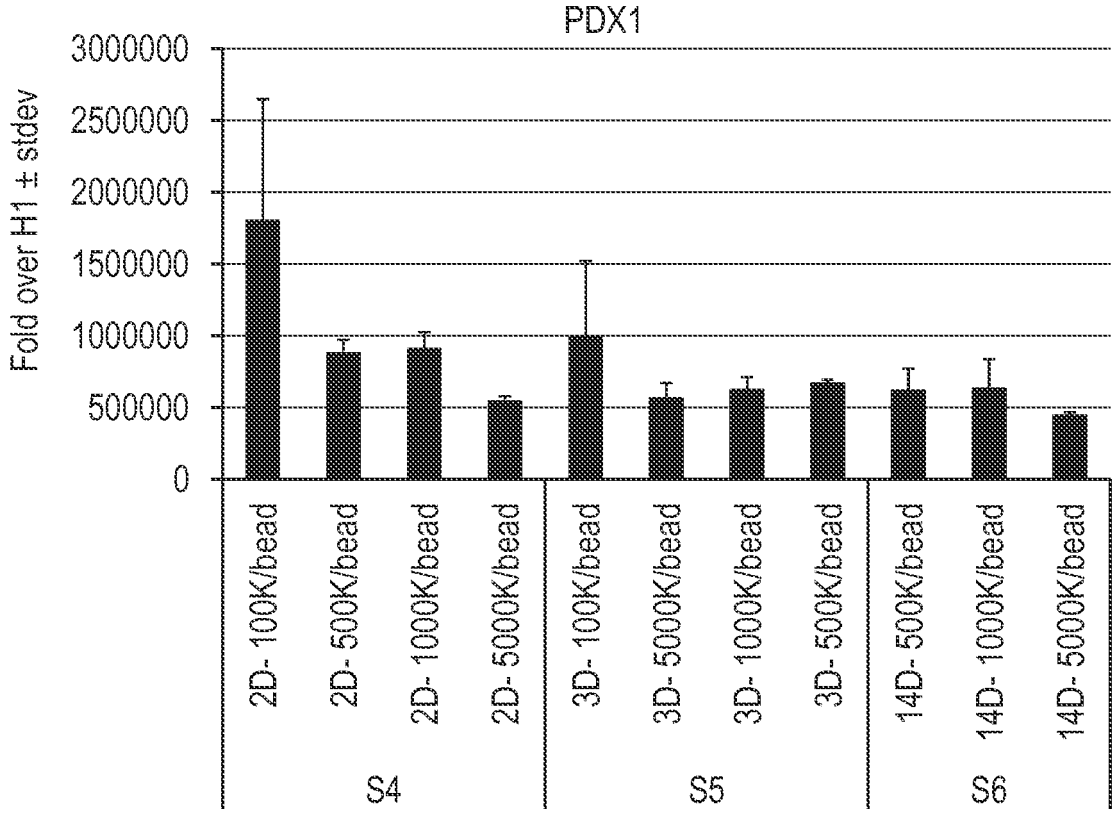


FIG. 12A

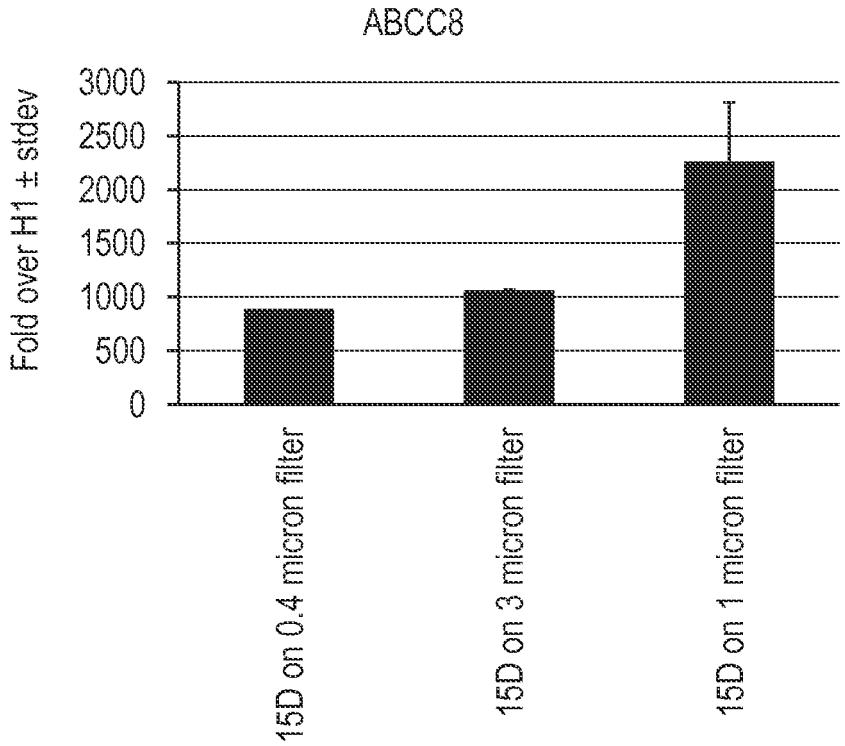


FIG. 12B

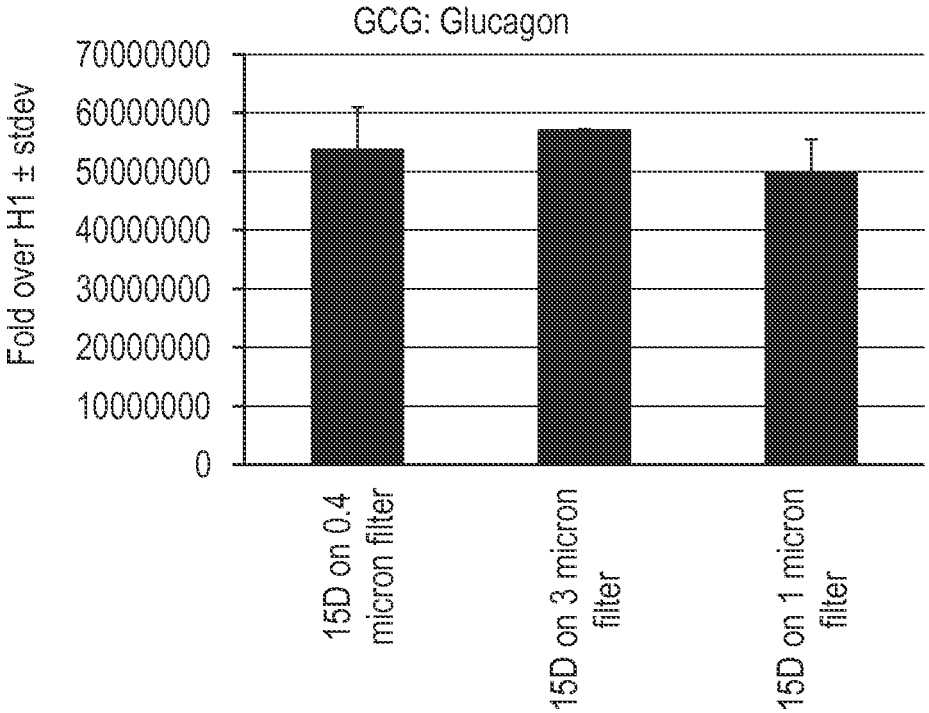


FIG. 12C

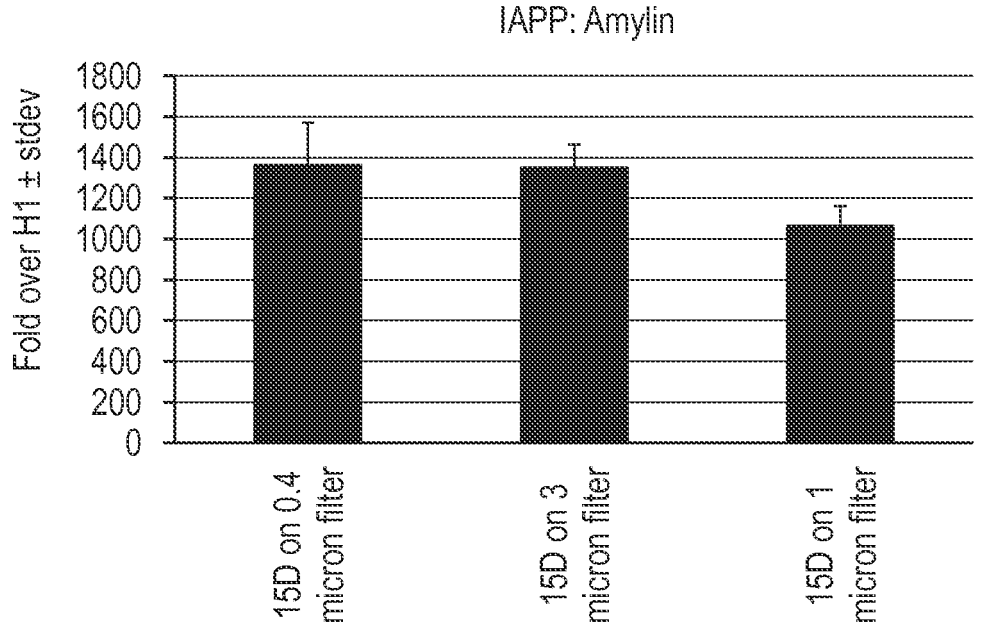


FIG. 12D

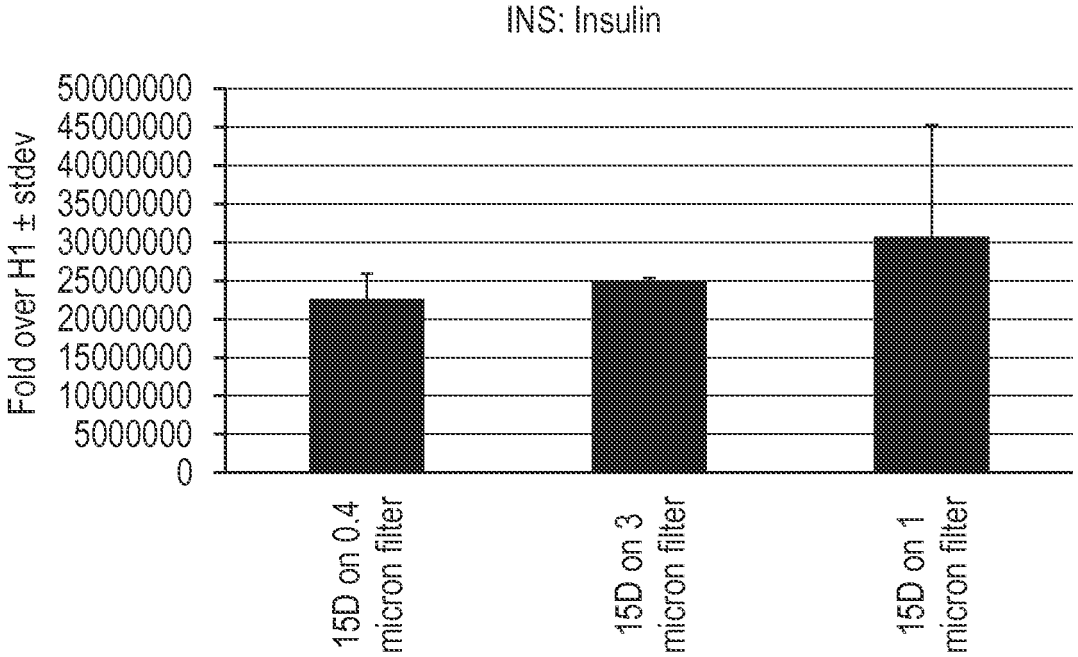


FIG. 12E

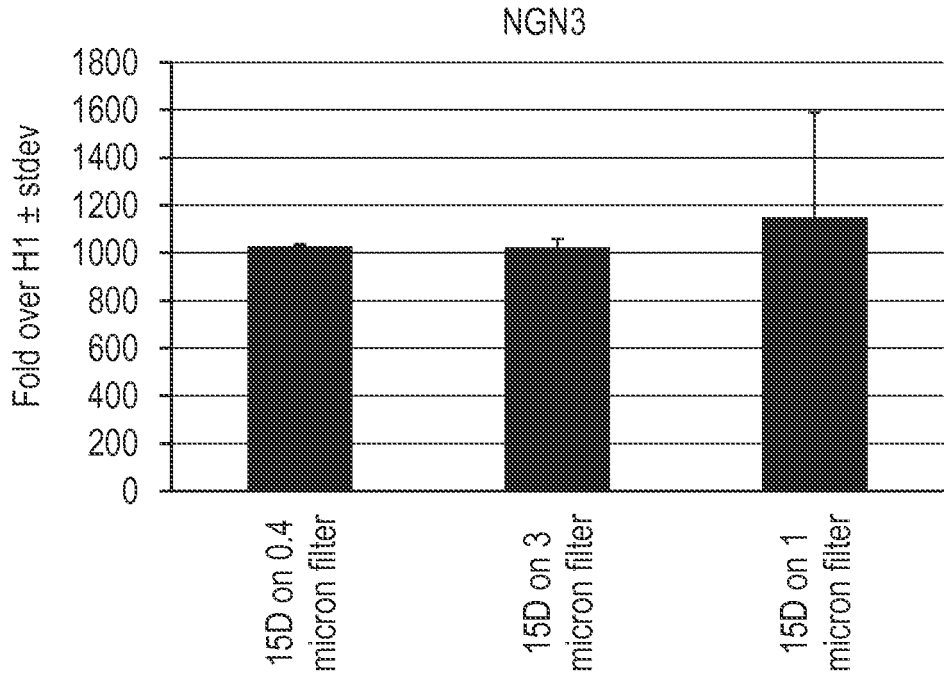


FIG. 12F

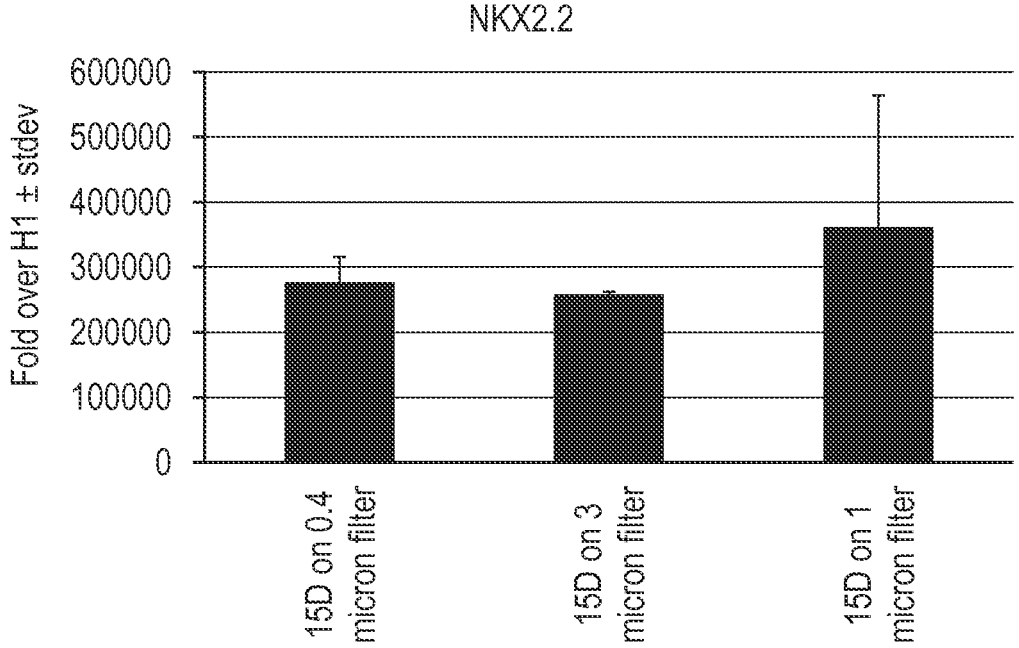


FIG. 12G

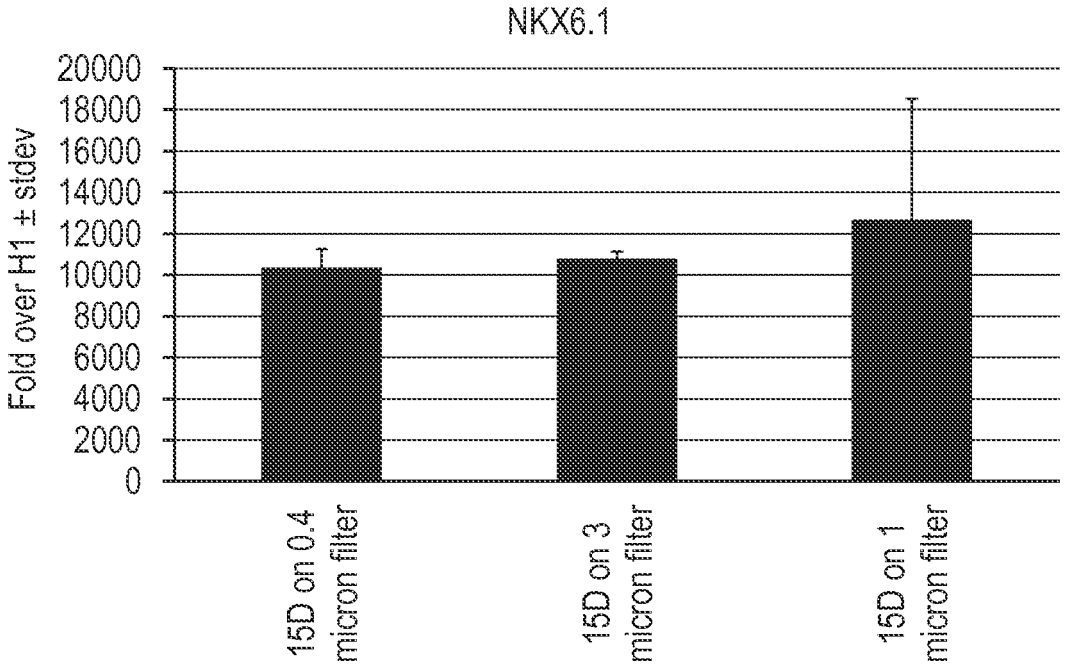


FIG. 12H

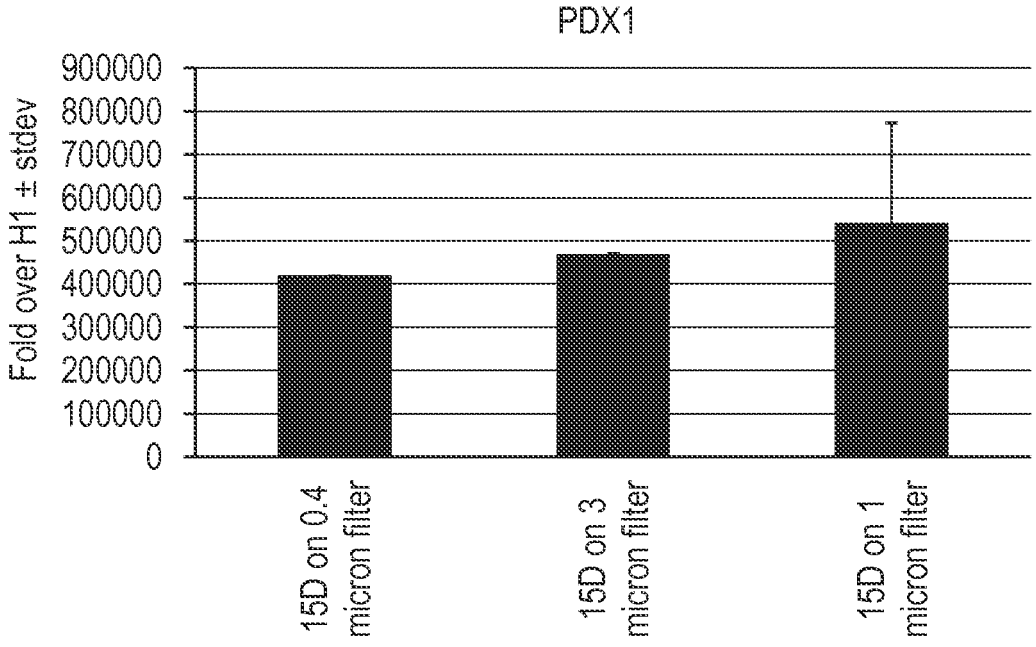


FIG. 13A

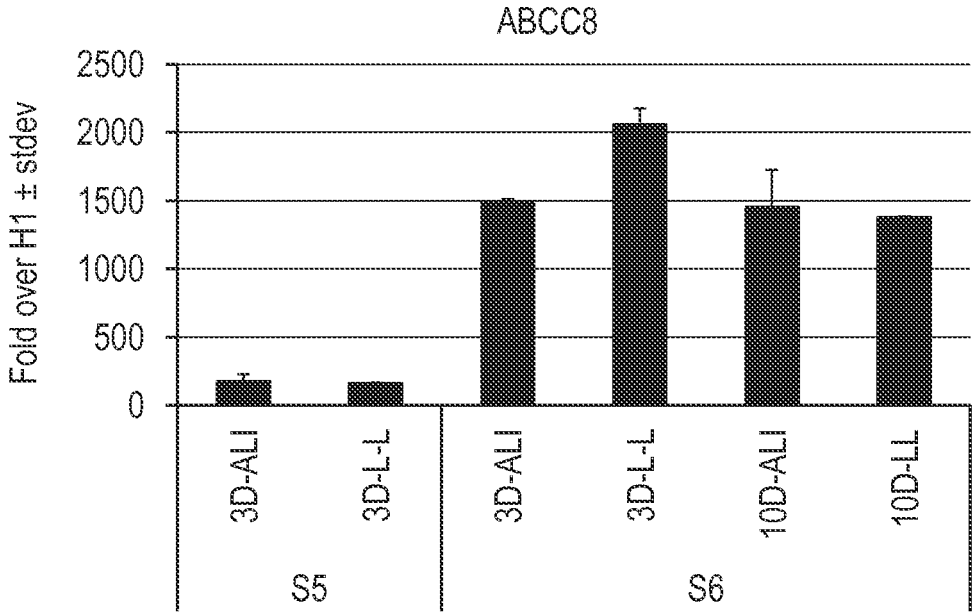


FIG. 13B

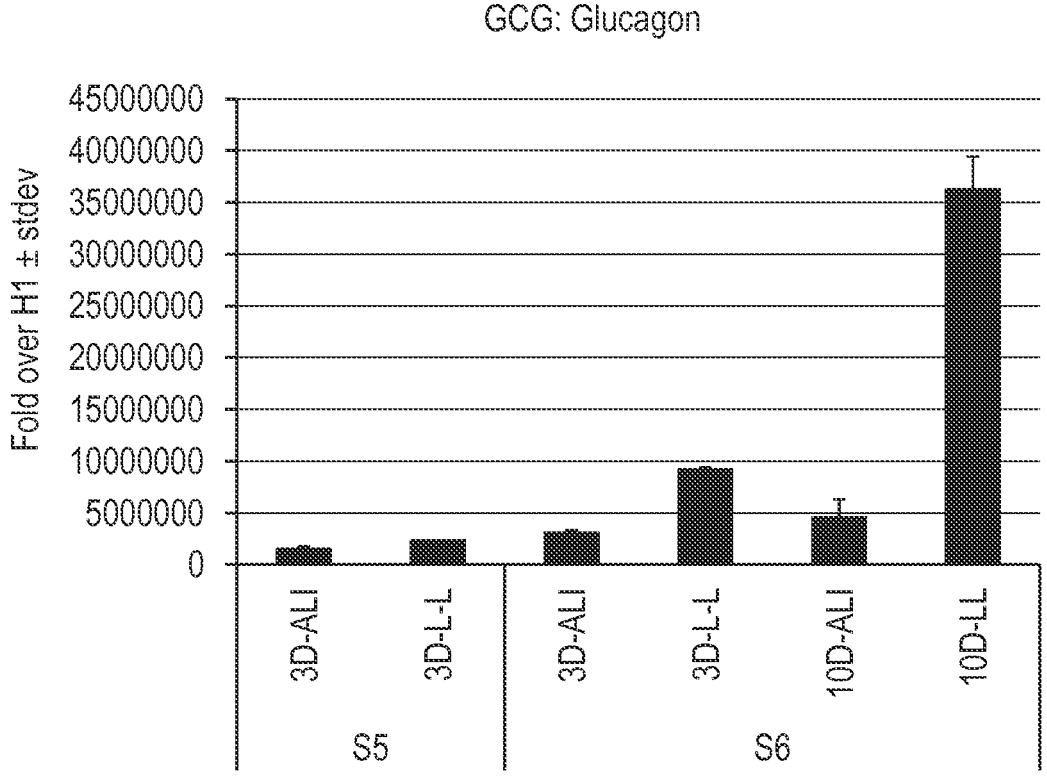


FIG. 13C

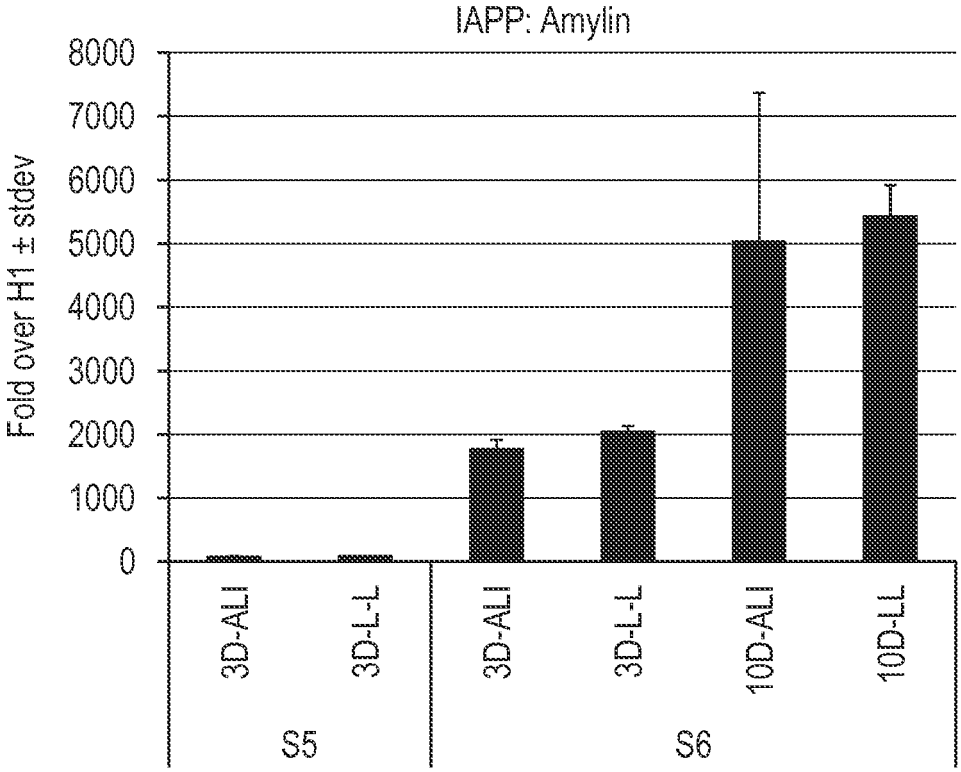


FIG. 13D

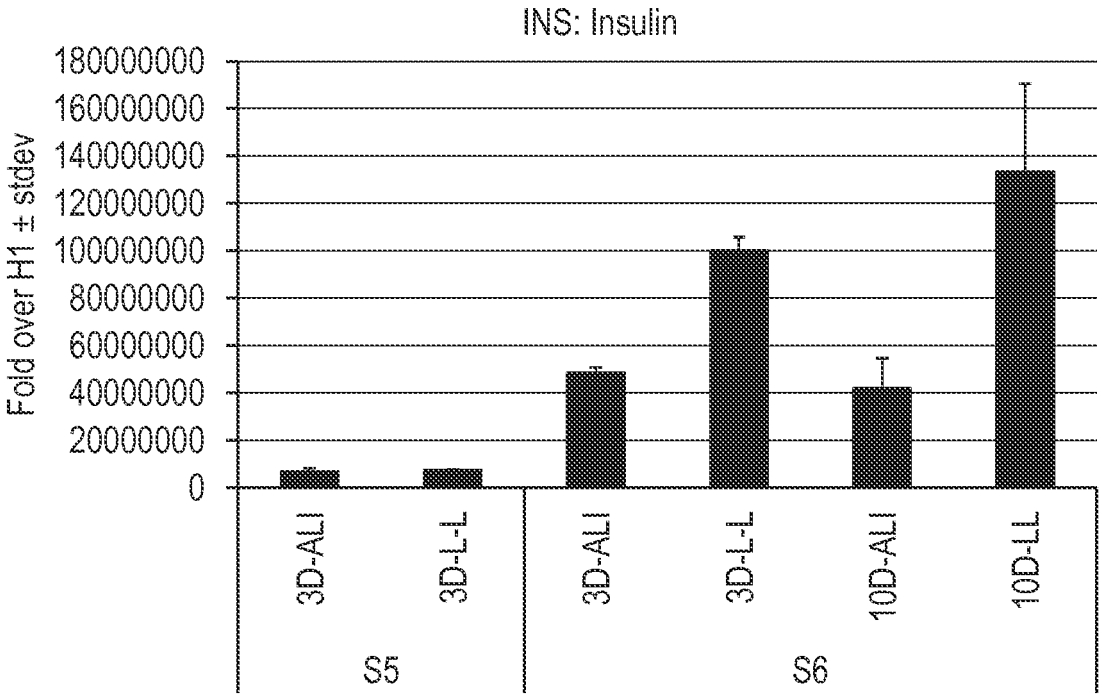


FIG. 13E

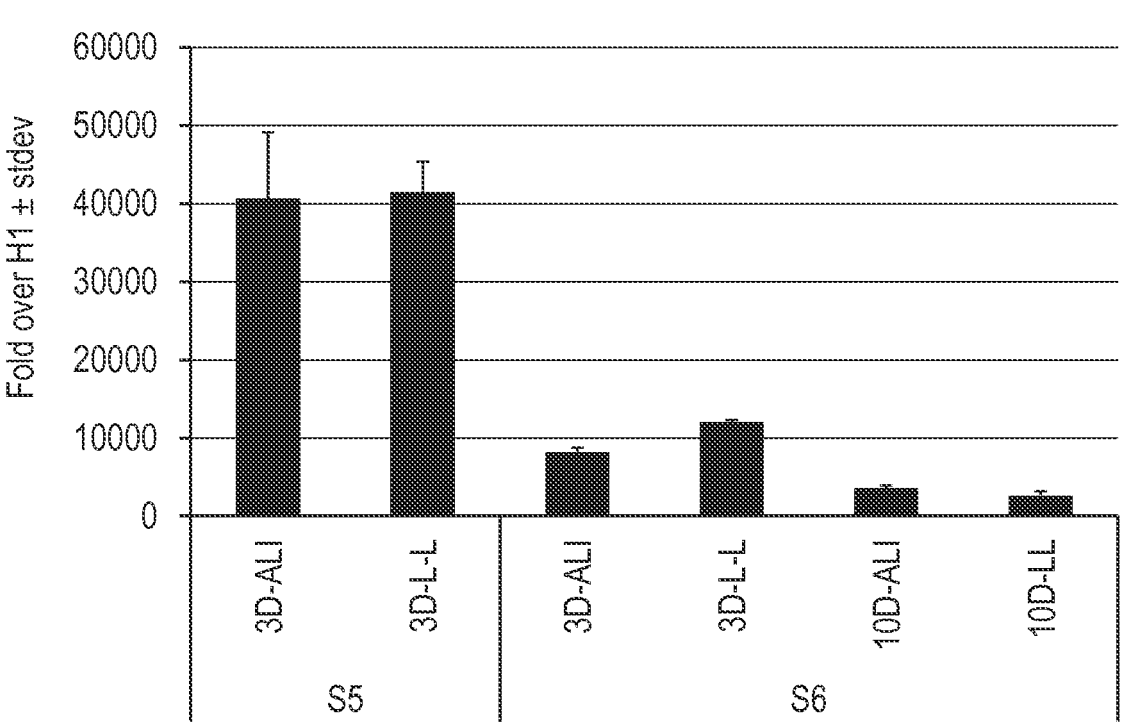


FIG. 13F

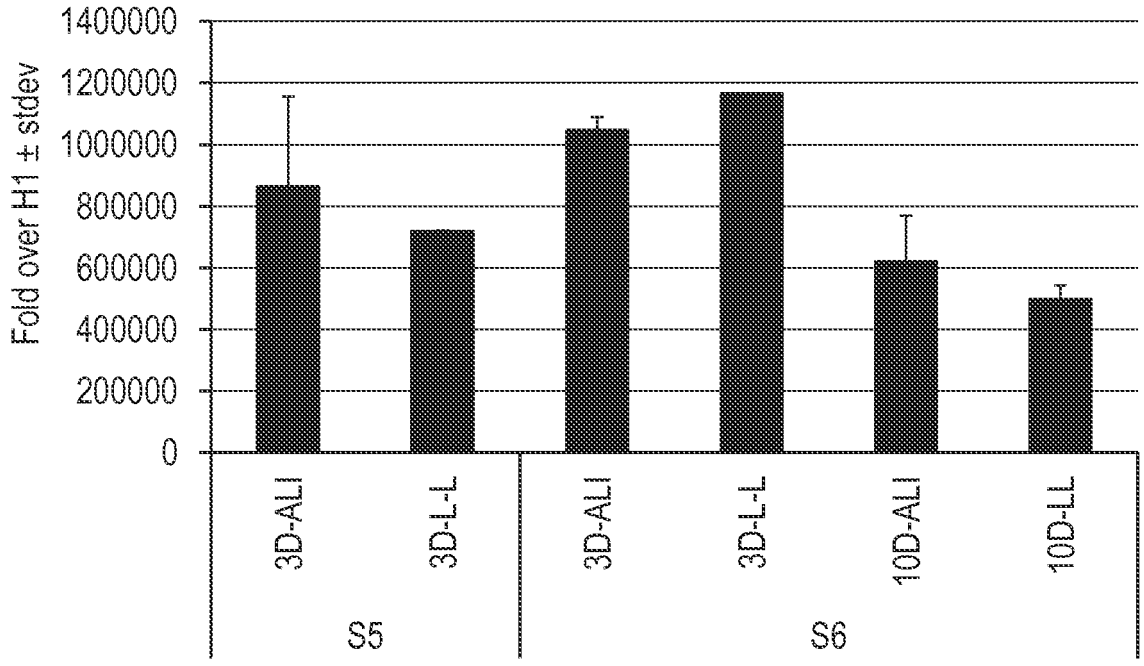


FIG. 13G

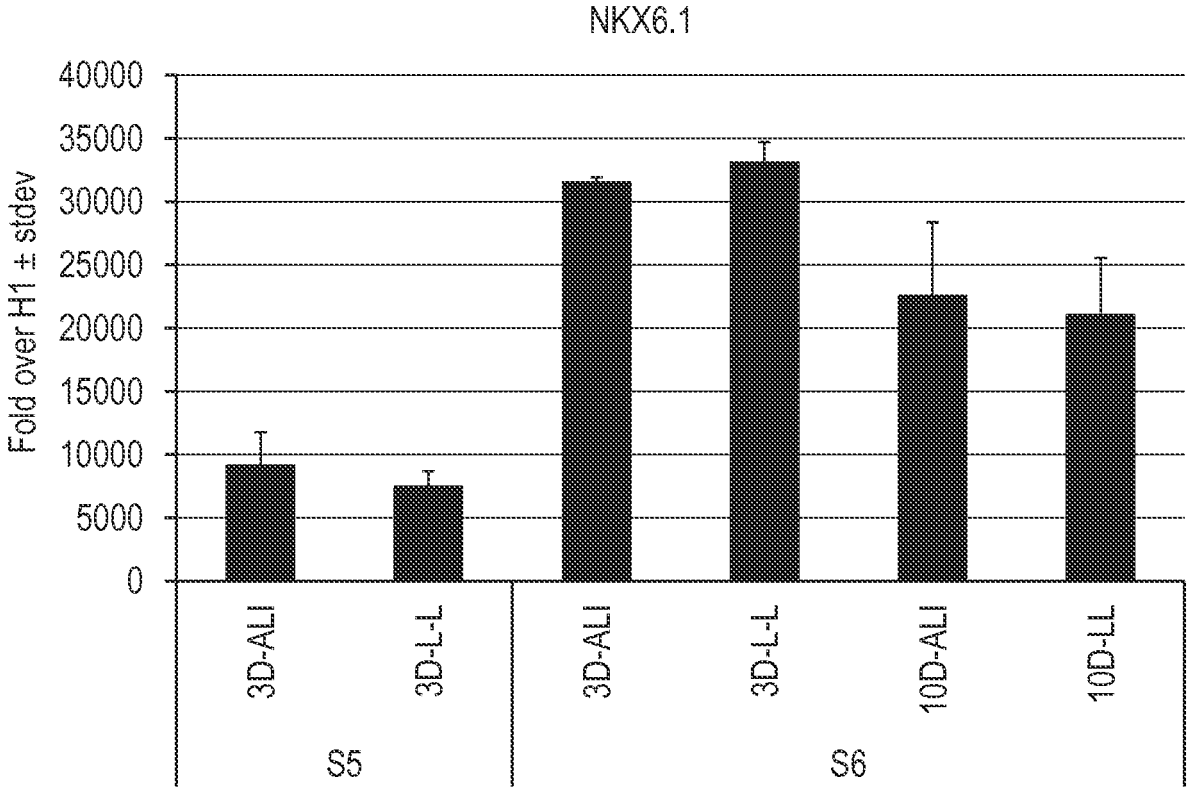


FIG. 13H

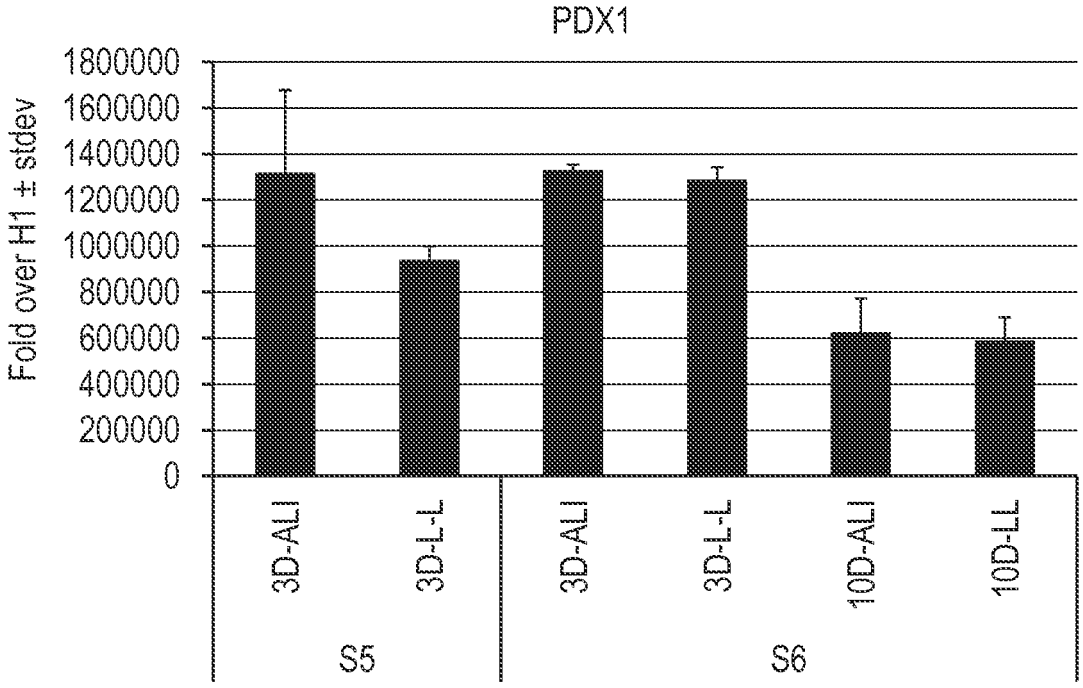


FIG. 14A

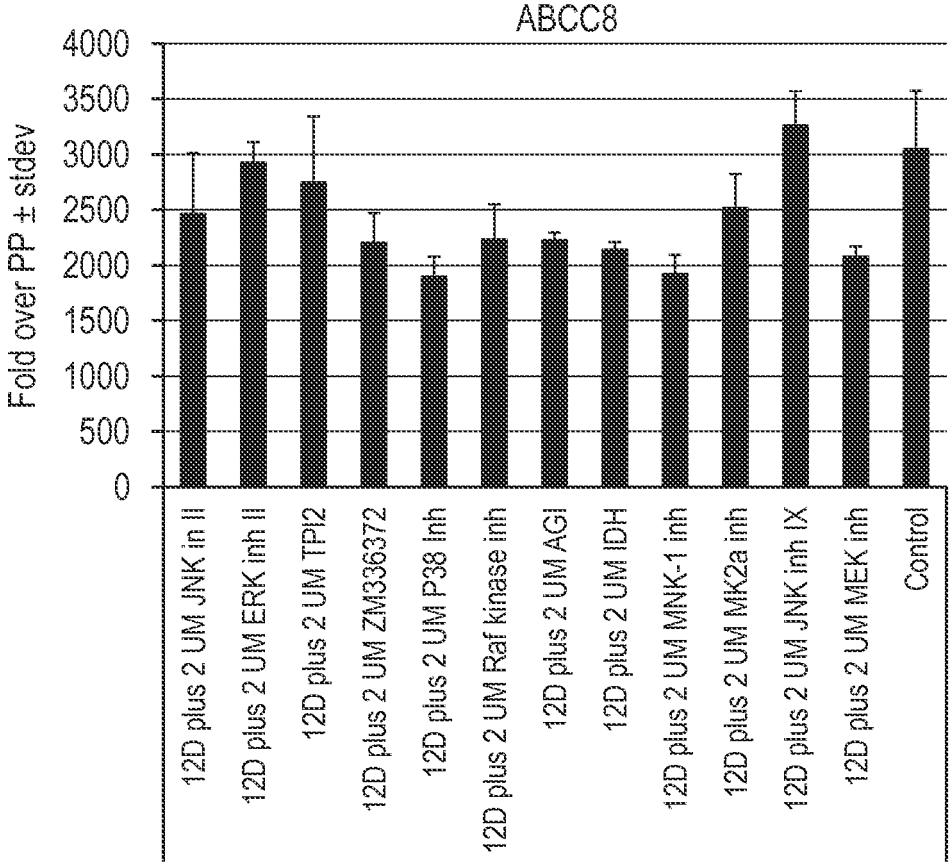


FIG. 14B

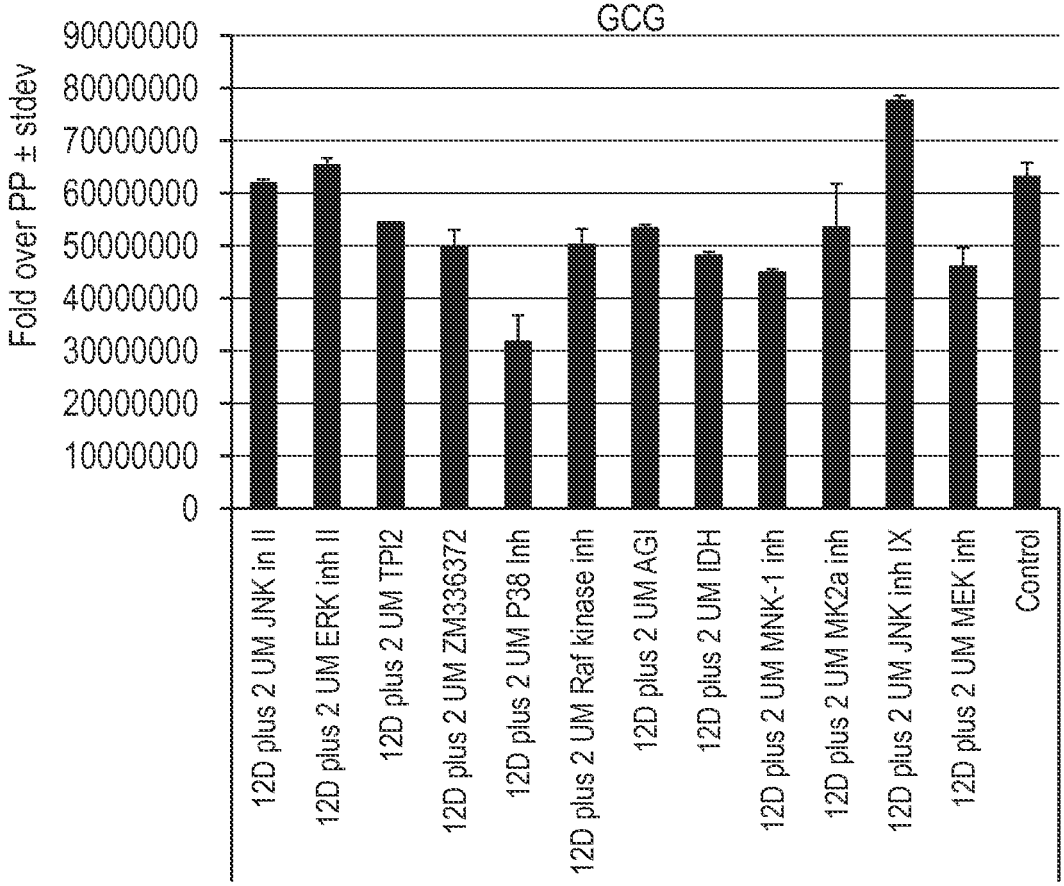


FIG. 14C

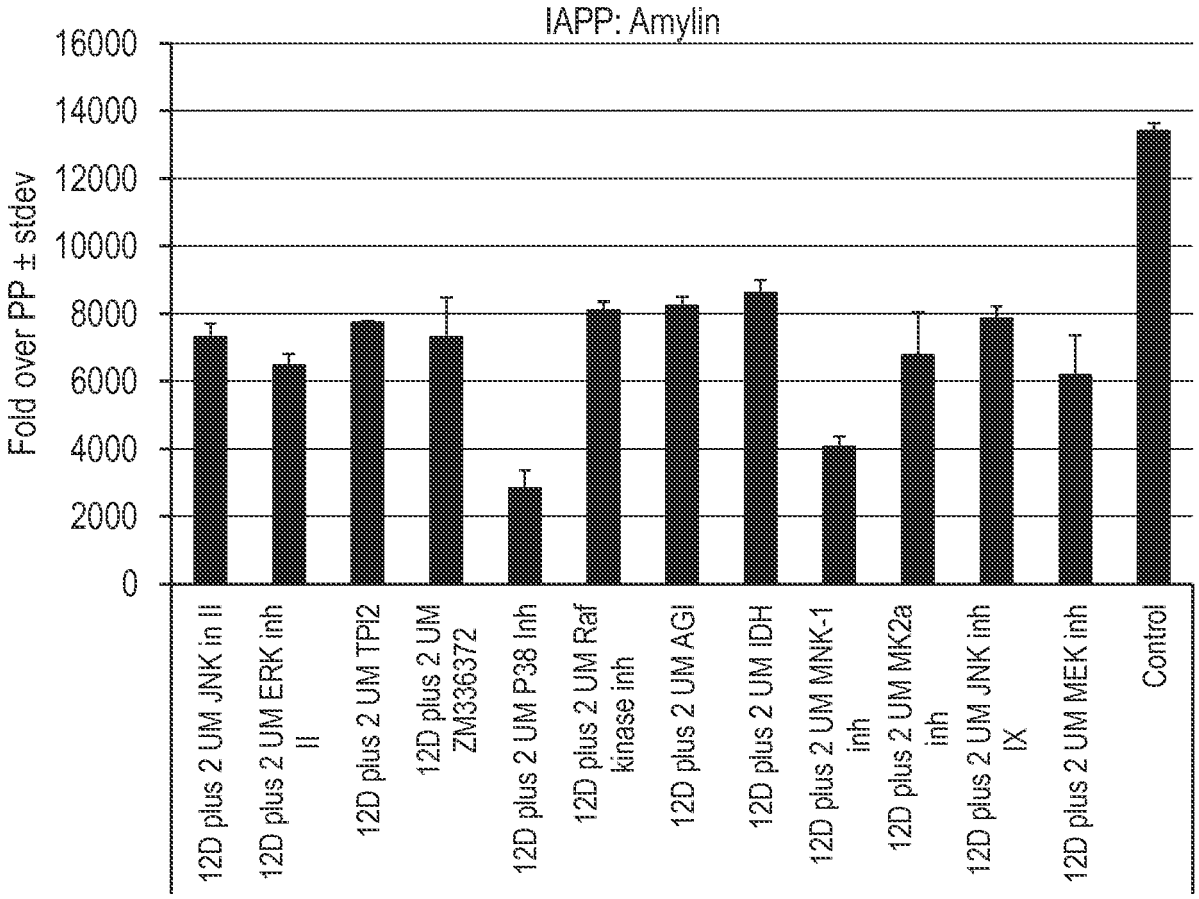


FIG. 14D

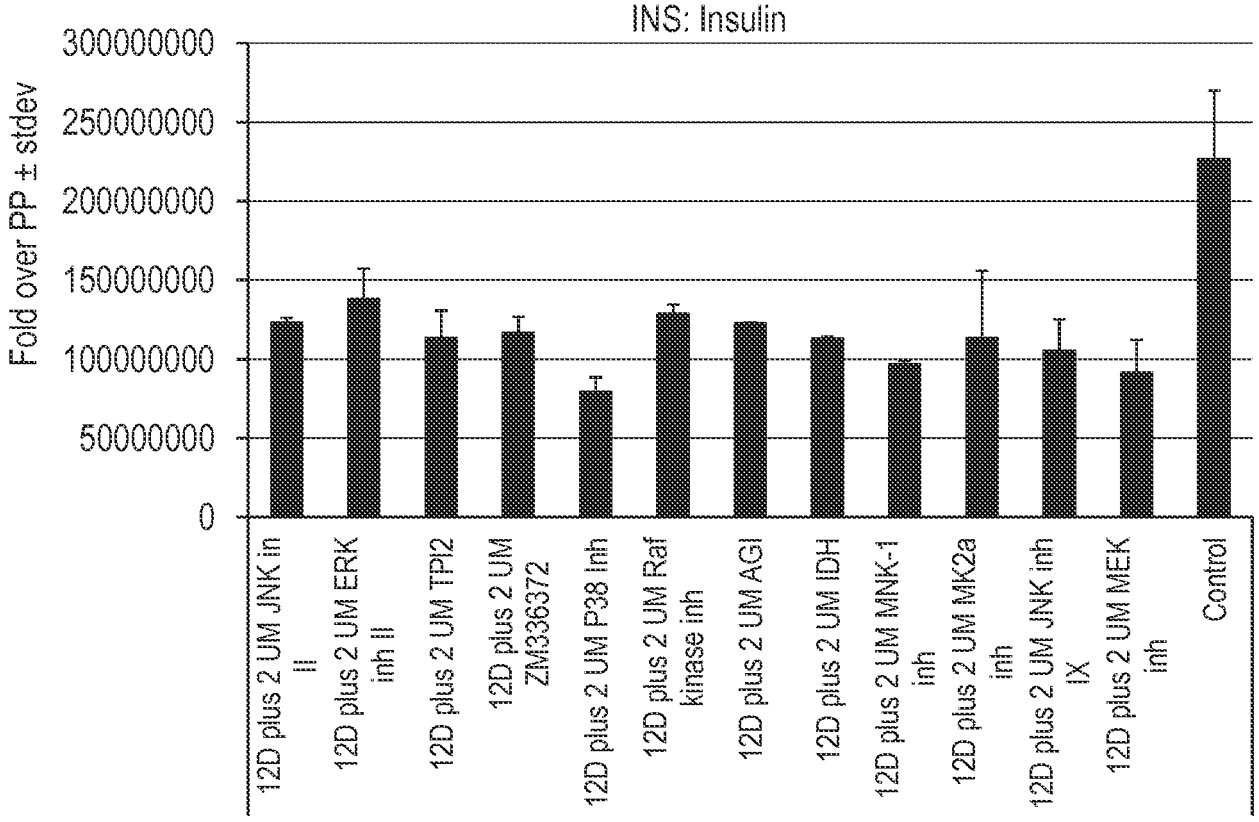


FIG. 14E

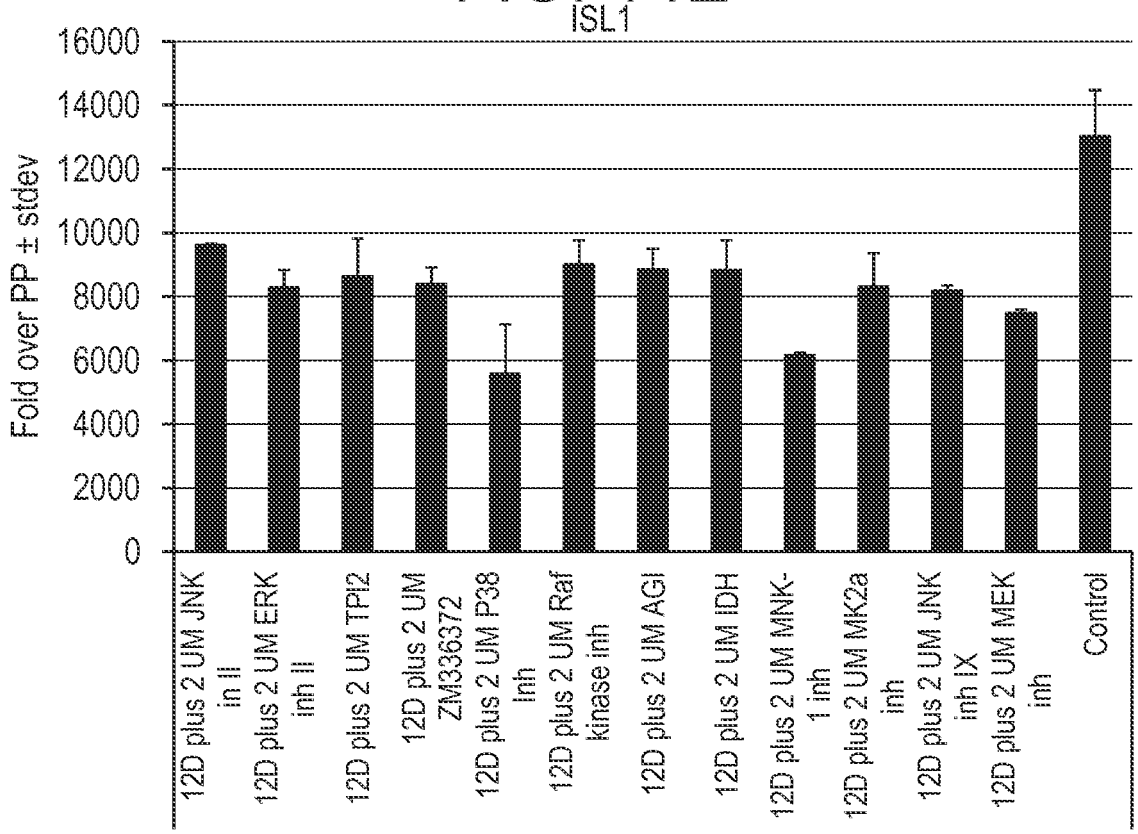


FIG. 14F

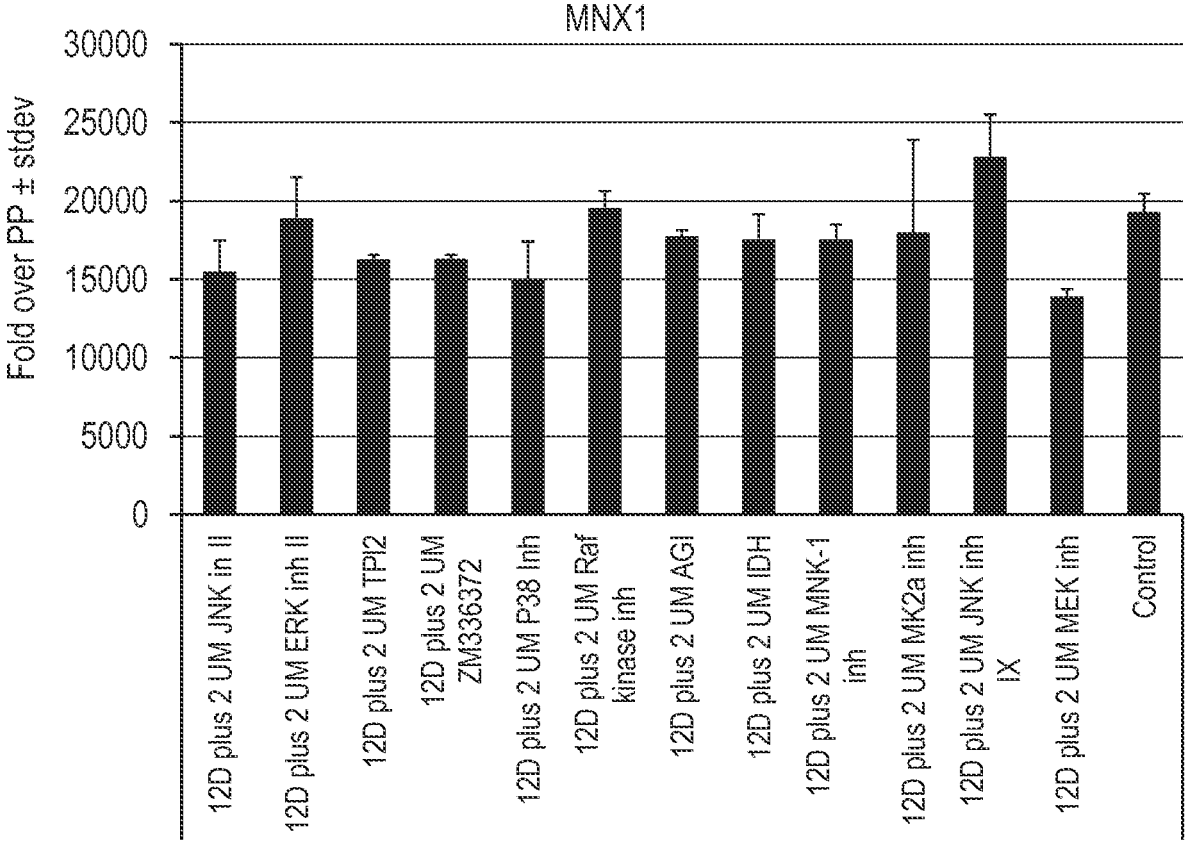


FIG. 14G

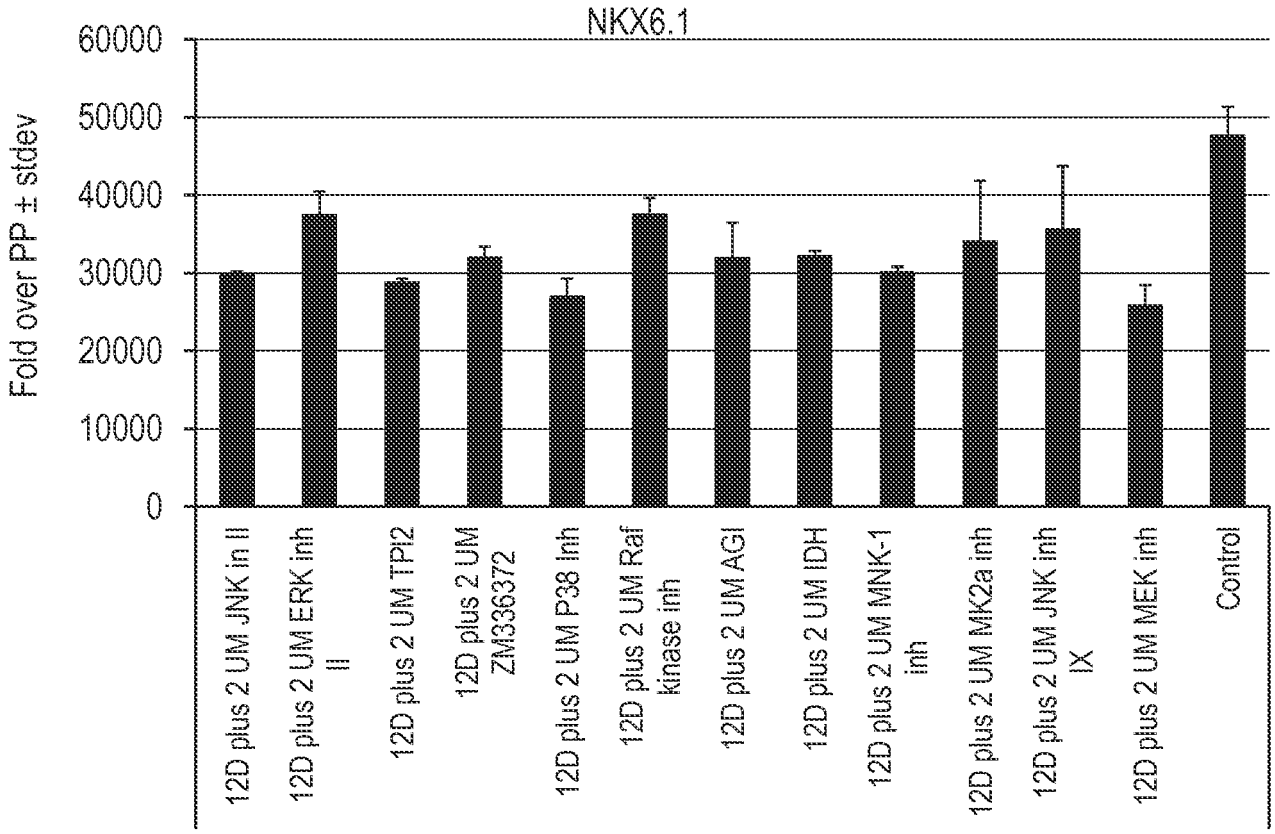


FIG. 14H

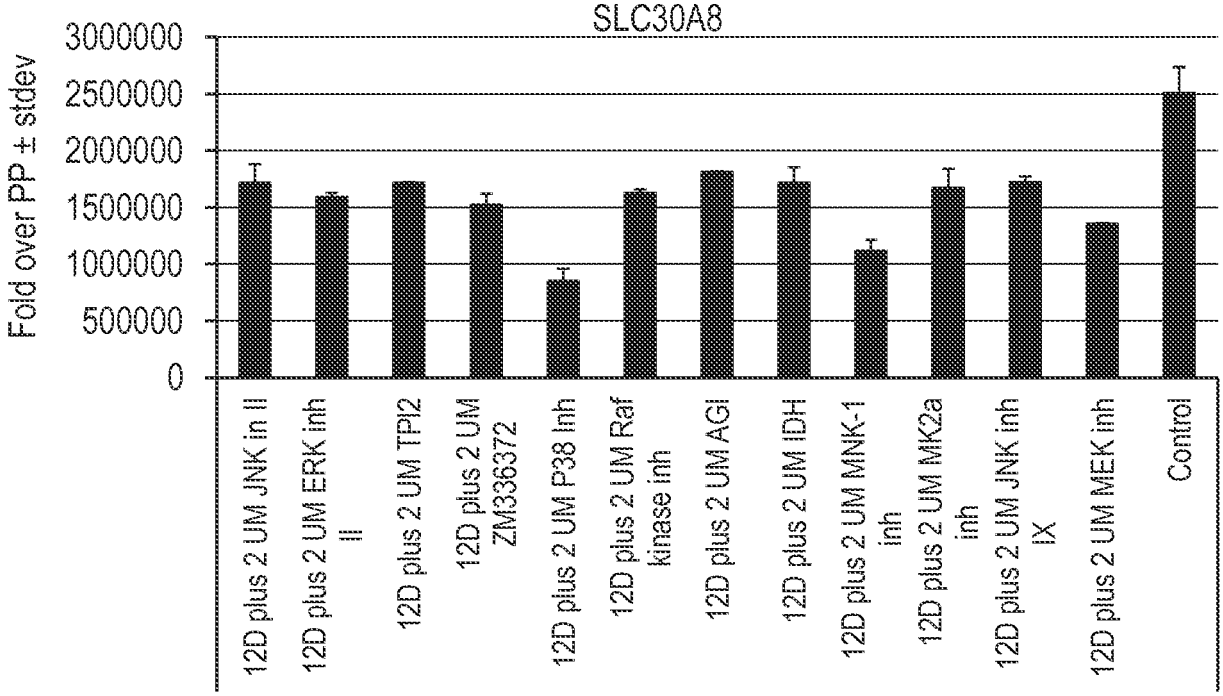


FIG. 15A

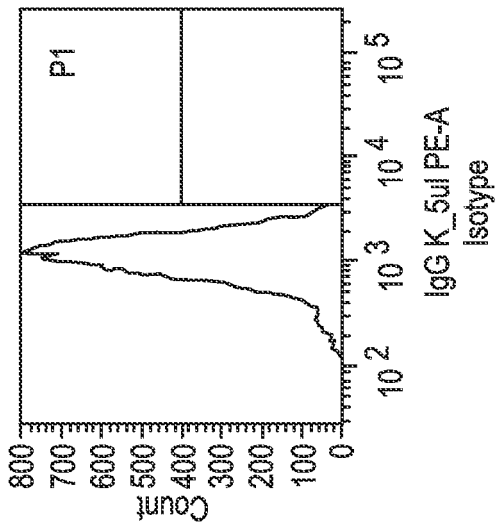


FIG. 15B

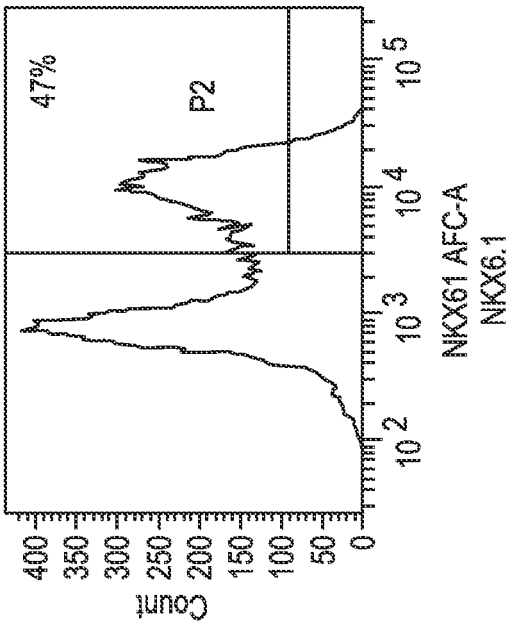


FIG. 15C

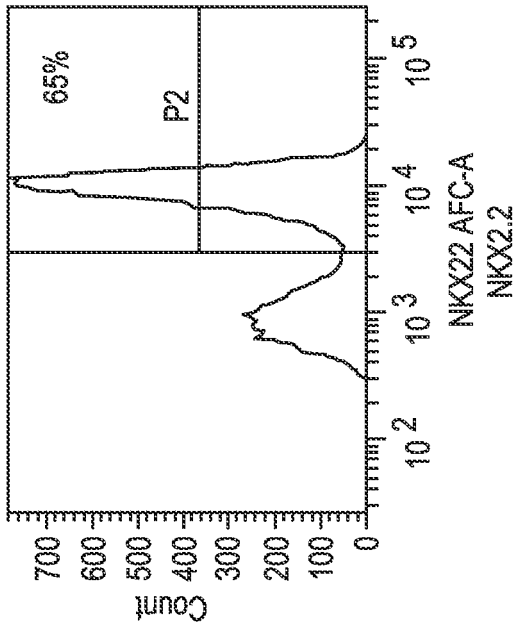


FIG. 15D

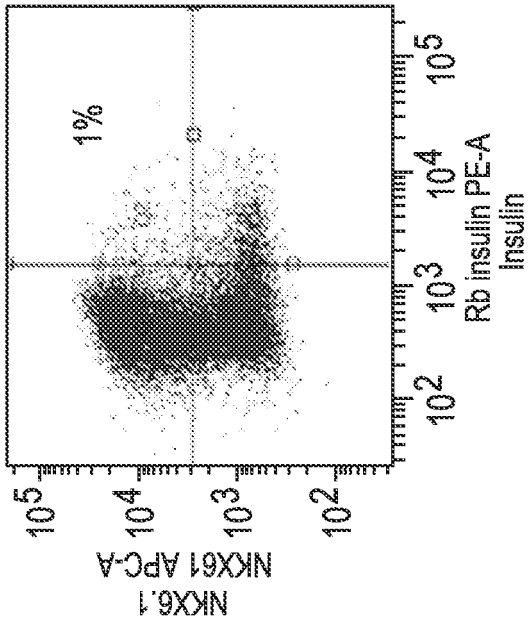


FIG. 15E

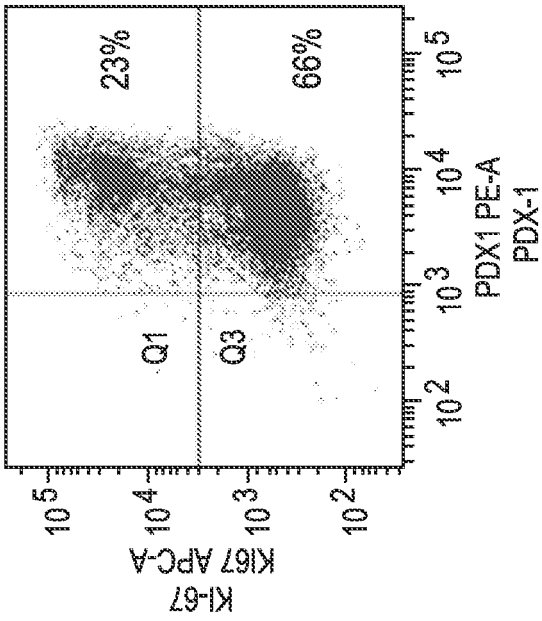


FIG. 15F

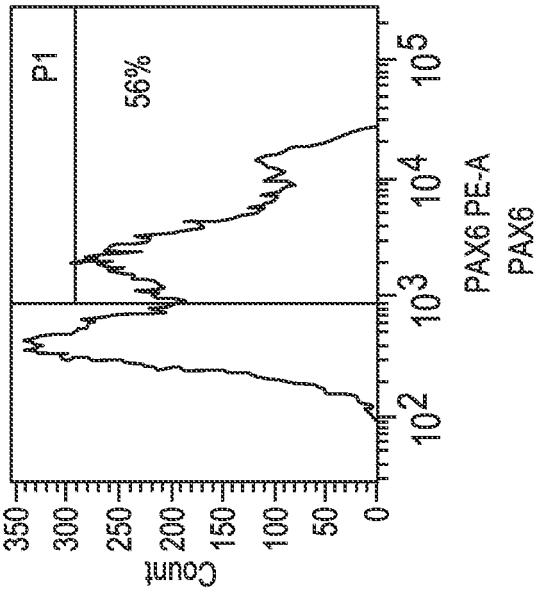


FIG. 15I

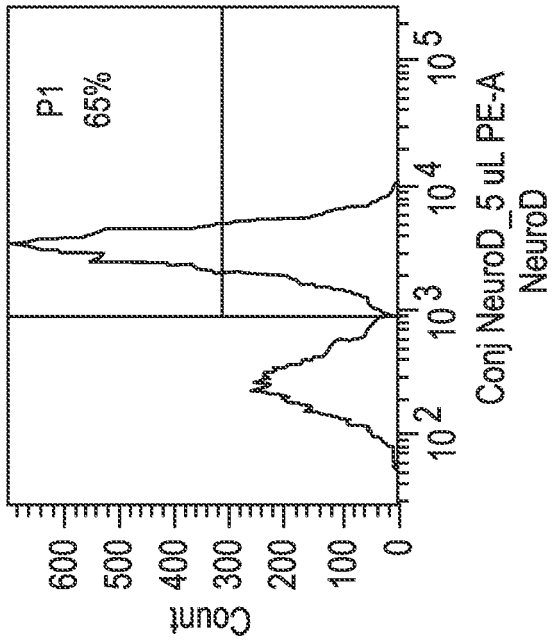


FIG. 15H

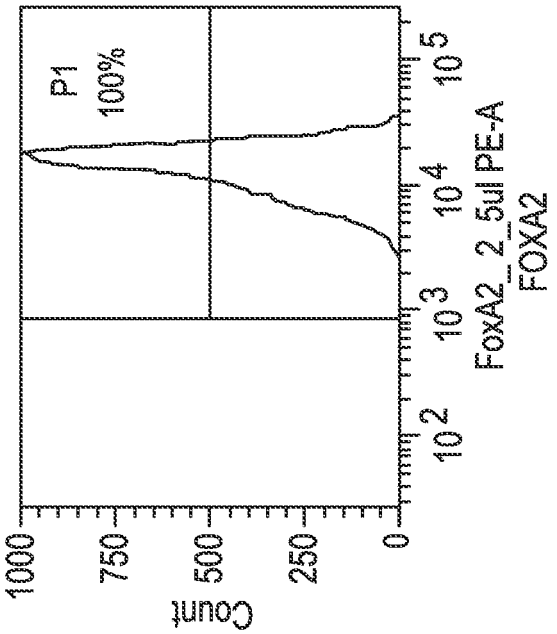


FIG. 15G

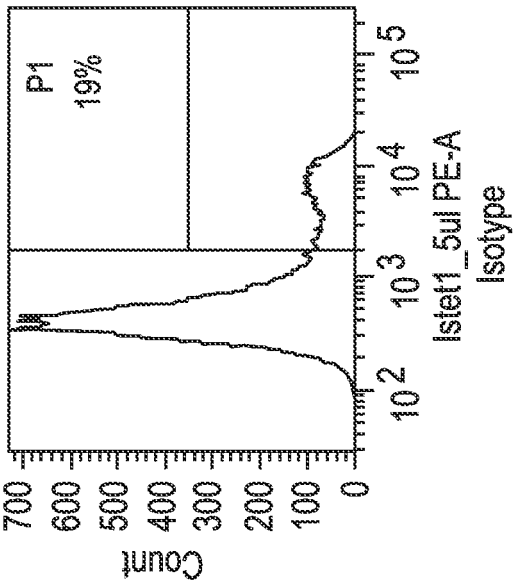


FIG. 15J

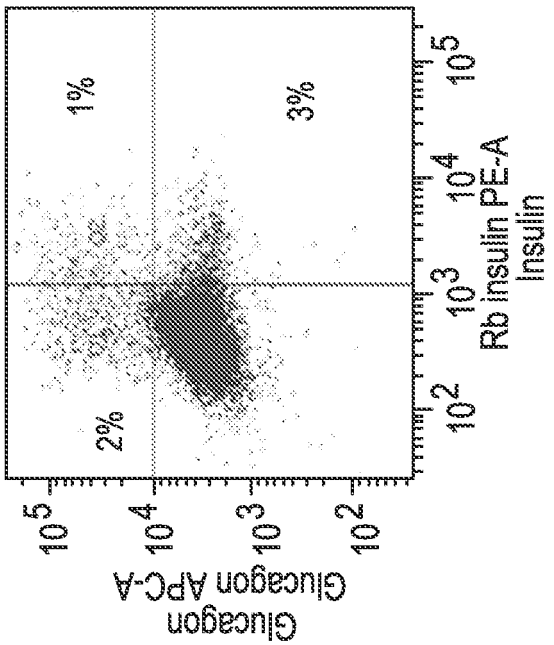


FIG. 16A

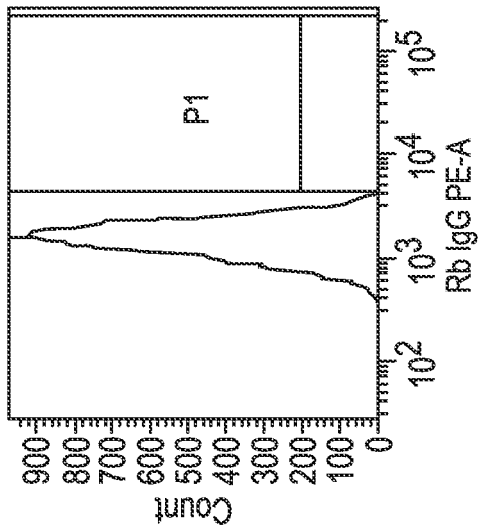


FIG. 16B

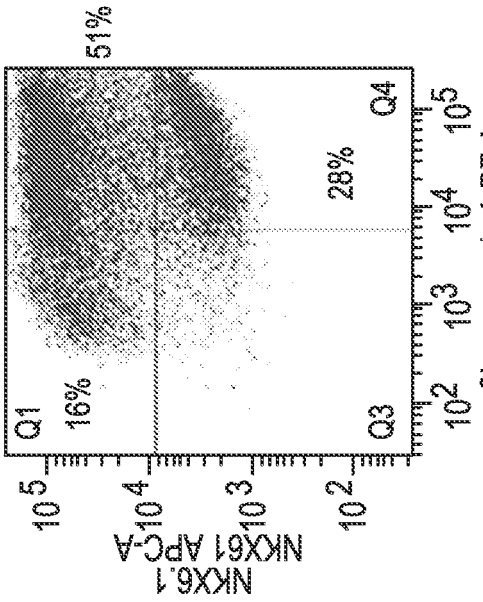


FIG. 16C

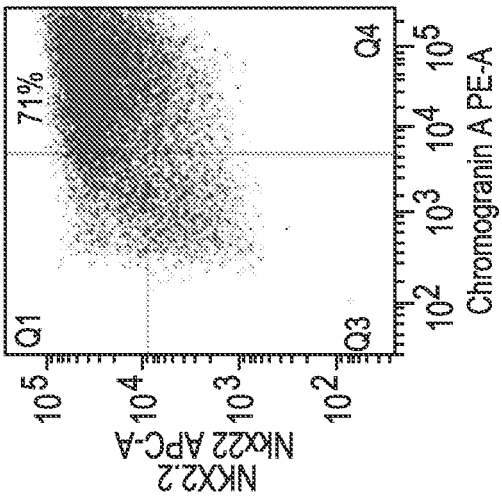


FIG. 16D

FIG. 16E

FIG. 16F

FIG. 16G

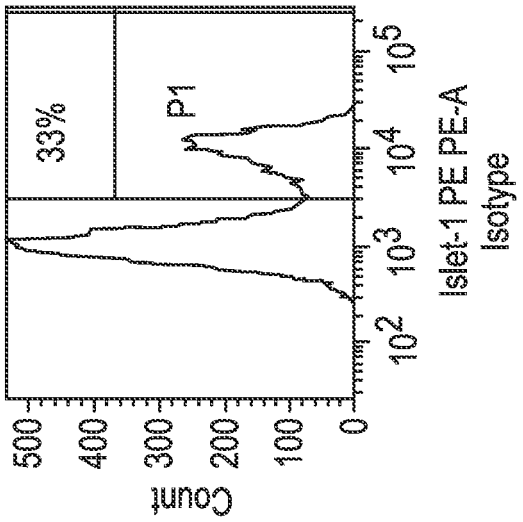


FIG. 16H

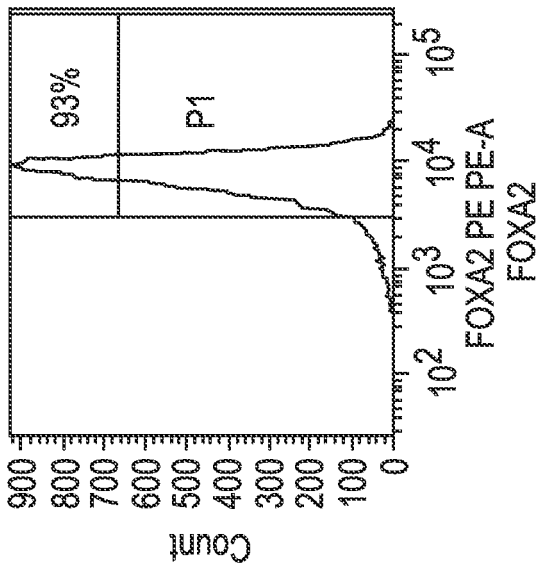


FIG. 16I

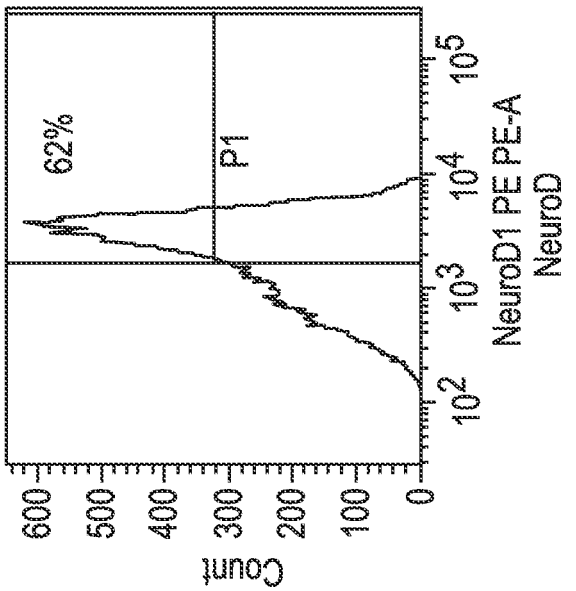


FIG. 17A

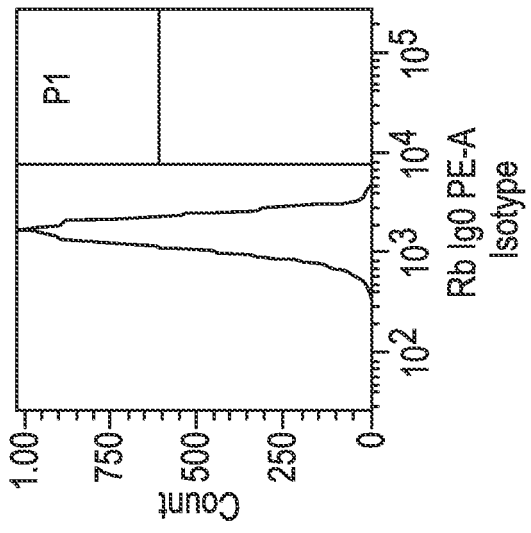


FIG. 17B

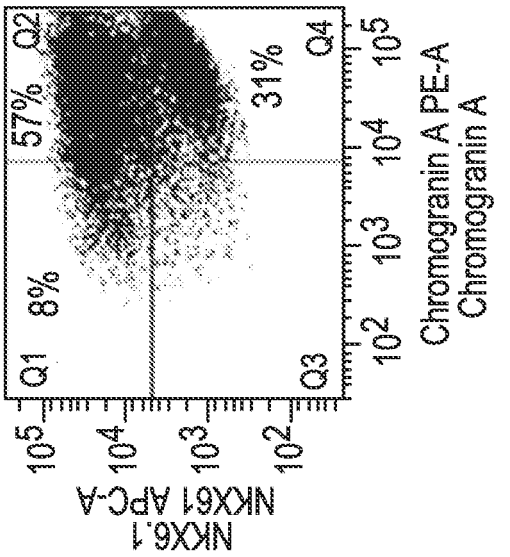


FIG. 17C

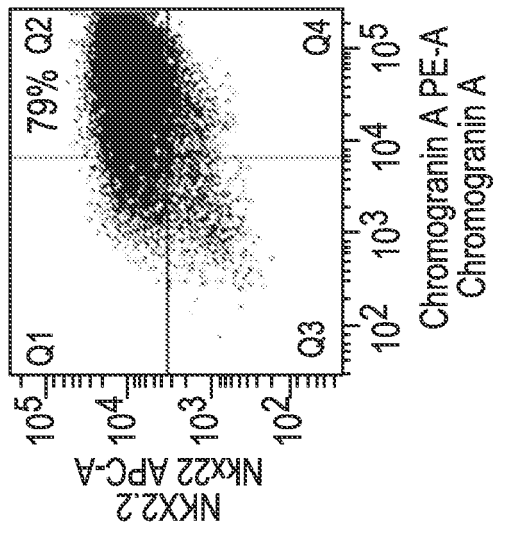


FIG. 17D

FIG. 17E

FIG. 17F

FIG. 17I

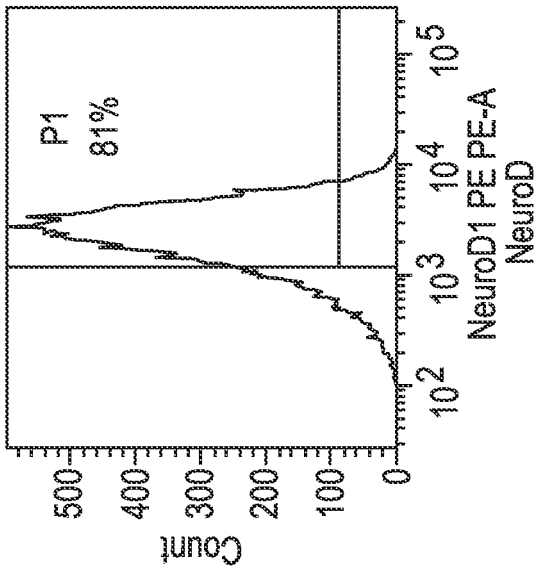


FIG. 17H

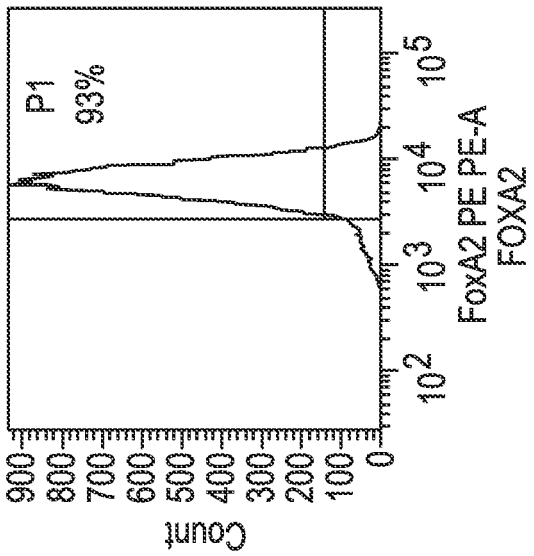


FIG. 17G

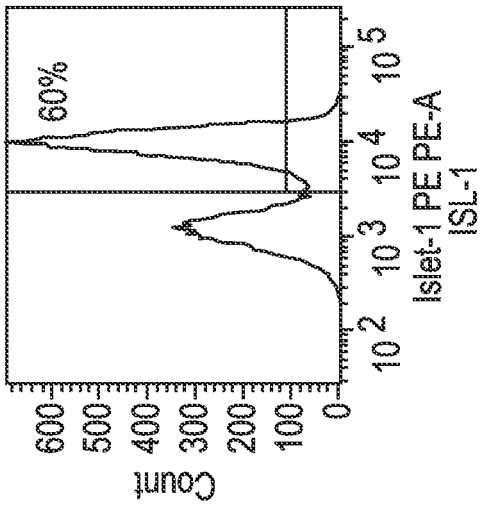


FIG. 18A

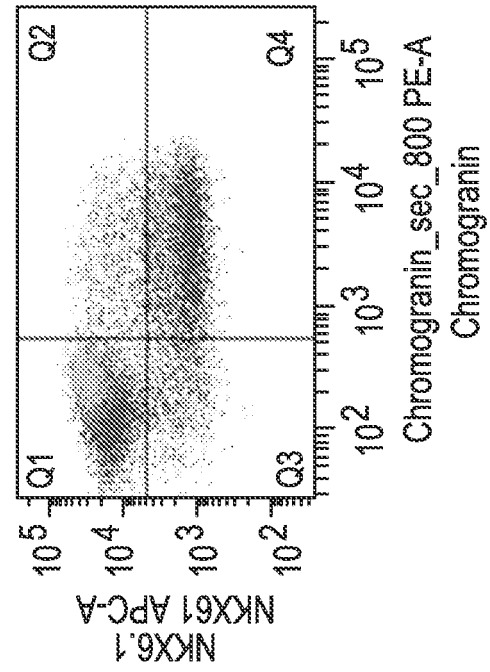


FIG. 18B

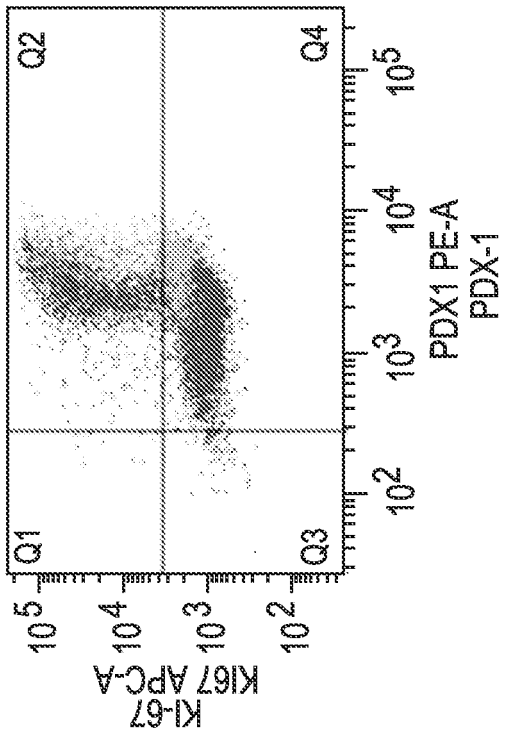


FIG. 18C

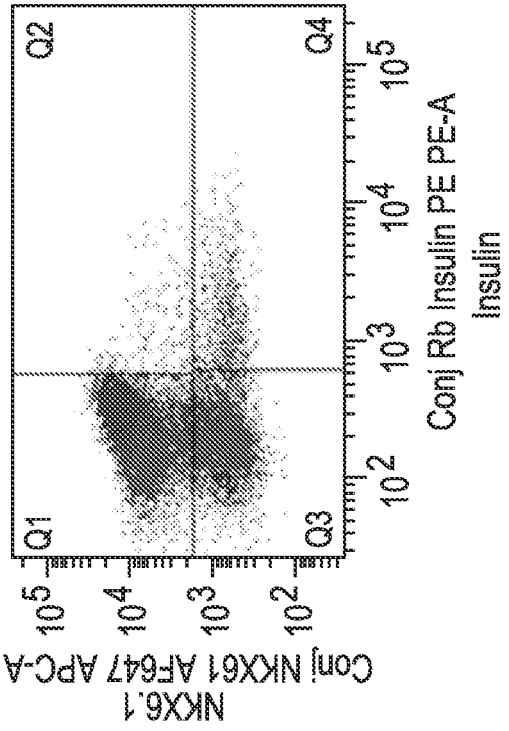


FIG. 19B

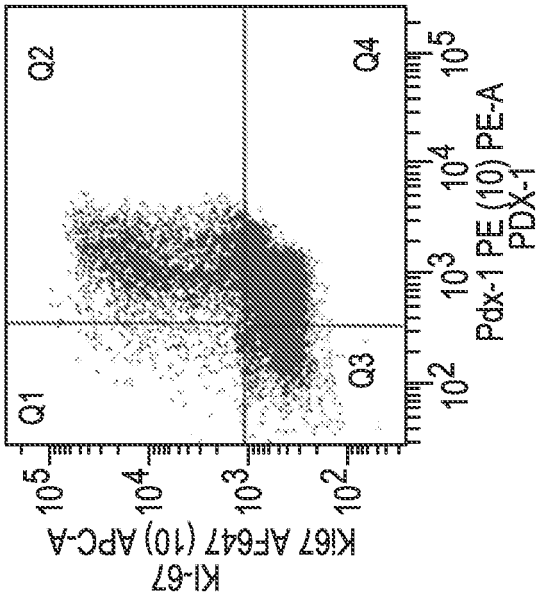


FIG. 19A

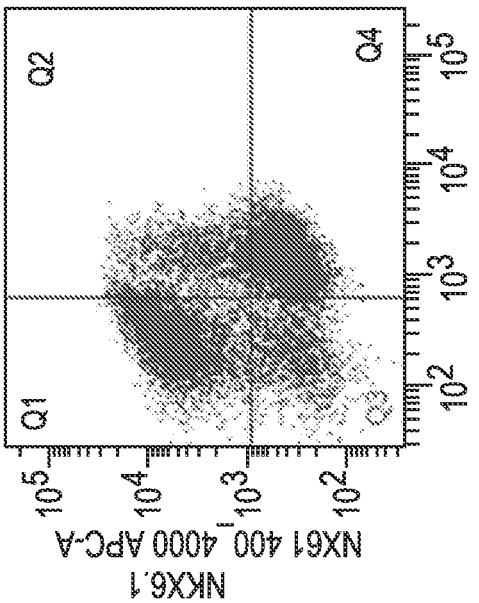


FIG. 19C

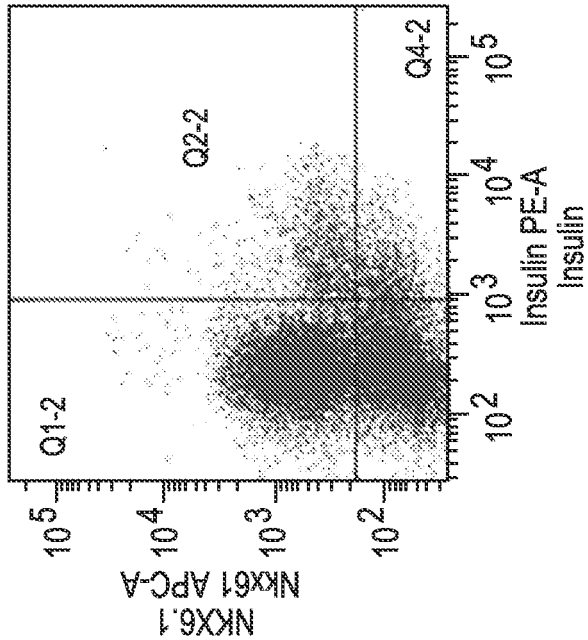
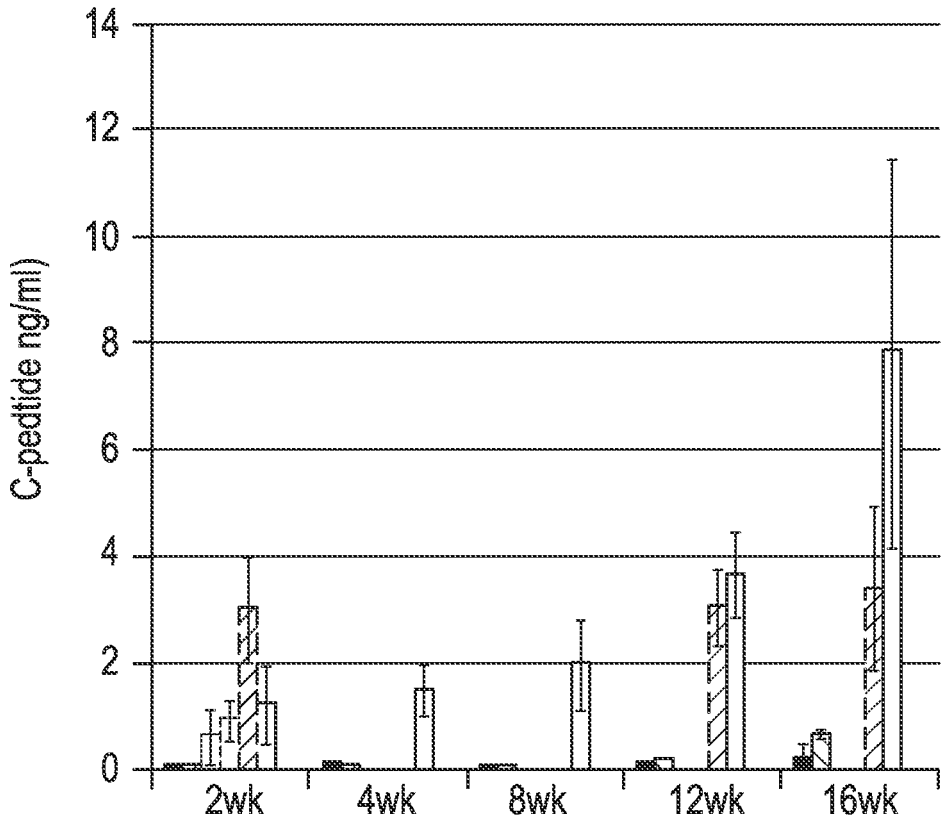


FIG. 20



Pancreatic precursor cells as described in Example 1, Stage 4 day 4

S6 -Liquid-air interface- Nkx6.1+ Chromogranin- as described in Example 11

Human islets-12000 IEQ

Human islets-3000 IEQ

Human islet-4000 IEQ

S6 -Liquid-air interface- Nkx6.1+ Chomogranin+ as described in Example 10

FIG. 21A

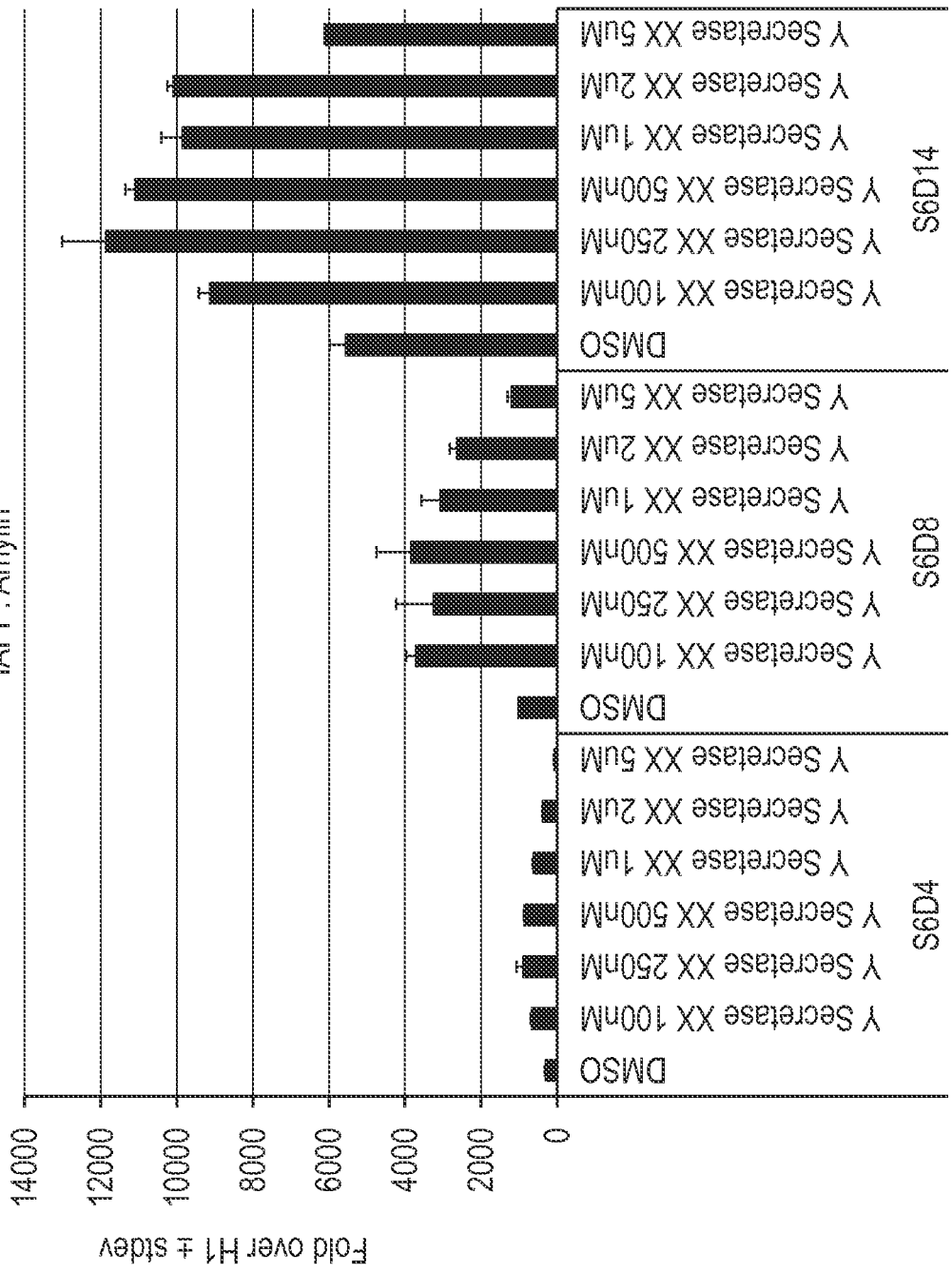

IAPP: Amylin
Fold over H1 ± stdev
14000
12000
10000
8000
6000
4000
2000
0
S6D4
S6D8
S6D14
DMSO
γ Secretase XX 100nM
γ Secretase XX 250nM
γ Secretase XX 500nM
γ Secretase XX 1uM
γ Secretase XX 2uM
γ Secretase XX 5uM

FIG. 21B

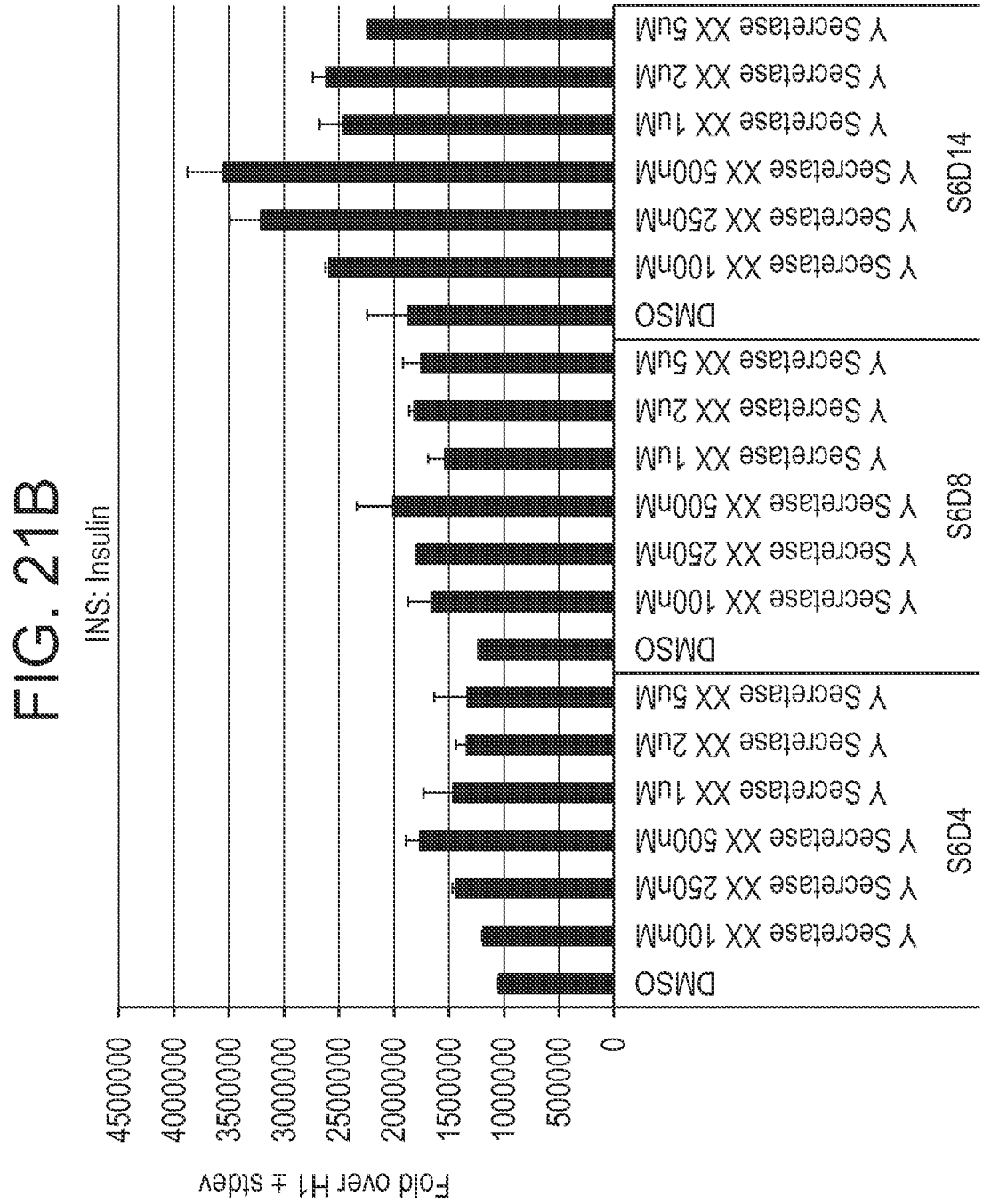

INS: Insulin
Fold over H1 ± stdev
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
DMSO
γ Secretase XX 100nM
γ Secretase XX 250nM
γ Secretase XX 500nM
γ Secretase XX 1uM
γ Secretase XX 2uM
γ Secretase XX 5uM
S6D4
DMSO
γ Secretase XX 100nM
γ Secretase XX 250nM
γ Secretase XX 500nM
γ Secretase XX 1uM
γ Secretase XX 2uM
γ Secretase XX 5uM
S6D8
DMSO
γ Secretase XX 100nM
γ Secretase XX 250nM
γ Secretase XX 500nM
γ Secretase XX 1uM
γ Secretase XX 2uM
γ Secretase XX 5uM
S6D14

FIG. 21C

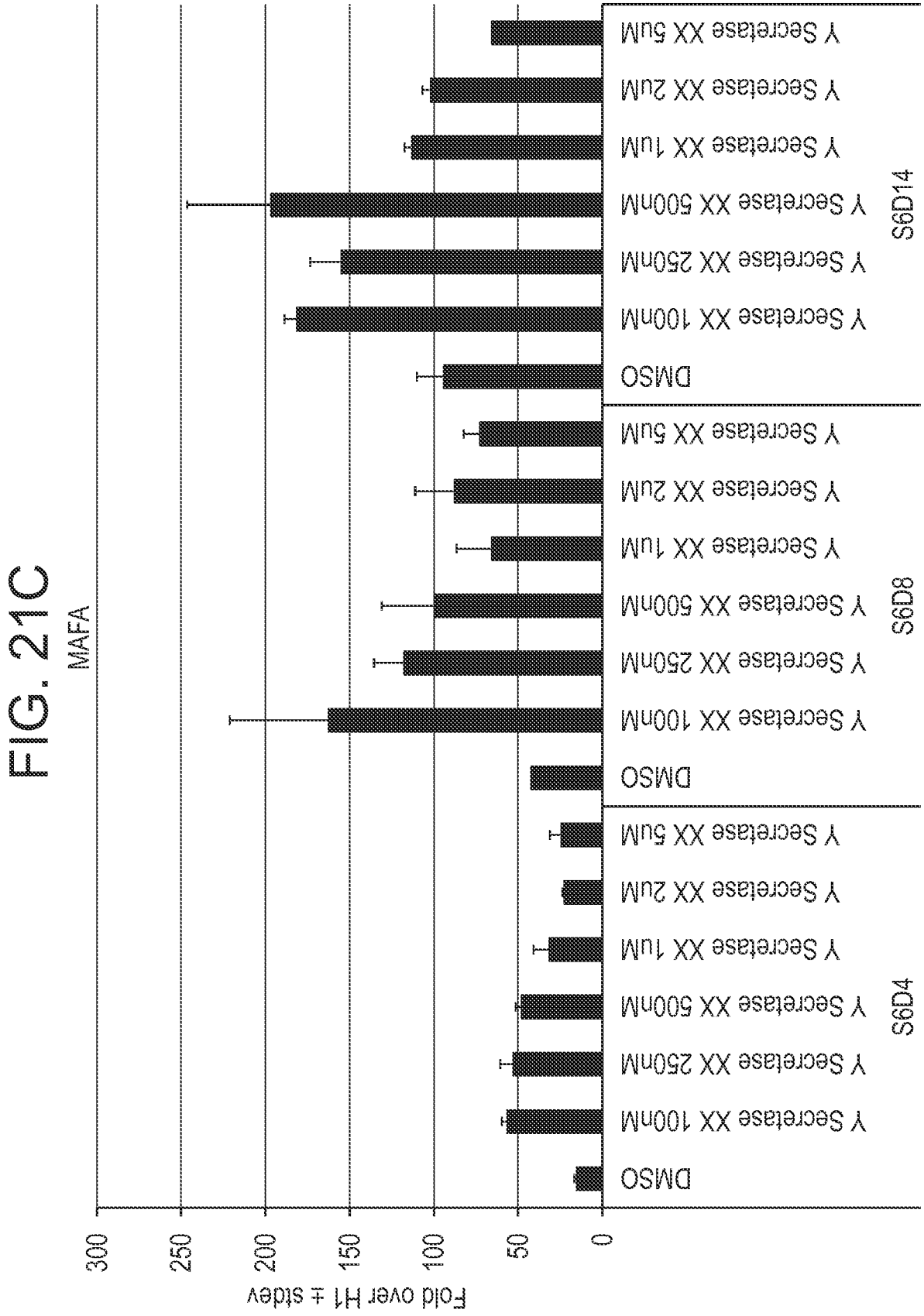

MAFA
Fold over H1 ± stdev
300
250
200
150
100
50
0
S6D4
S6D8
S6D14
DMSO
γ Secretase XX 100nM
γ Secretase XX 250nM
γ Secretase XX 500nM
γ Secretase XX 1uM
γ Secretase XX 2uM
γ Secretase XX 5uM

FIG. 21D

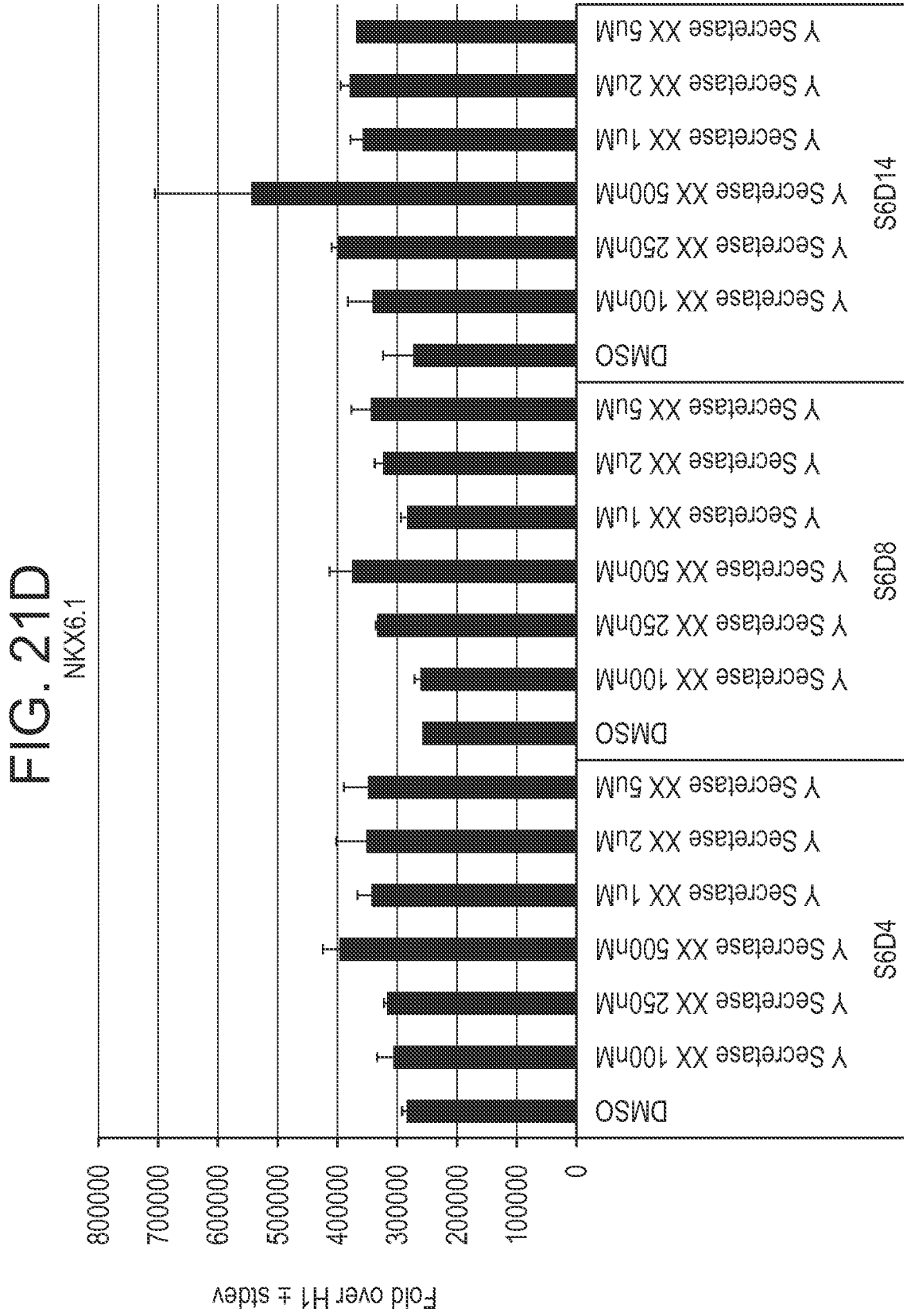

NKX6.1
Fold over H1 ± stdev
800000
700000
600000
500000
400000
300000
200000
100000
0
S6D4
DMSO
γ Secretase XX 100nM
γ Secretase XX 250nM
γ Secretase XX 500nM
γ Secretase XX 1uM
γ Secretase XX 2uM
γ Secretase XX 5uM
S6D8
DMSO
γ Secretase XX 100nM
γ Secretase XX 250nM
γ Secretase XX 500nM
γ Secretase XX 1uM
γ Secretase XX 2uM
γ Secretase XX 5uM
S6D14
DMSO
γ Secretase XX 100nM
γ Secretase XX 250nM
γ Secretase XX 500nM
γ Secretase XX 1uM
γ Secretase XX 2uM
γ Secretase XX 5uM

FIG. 21E

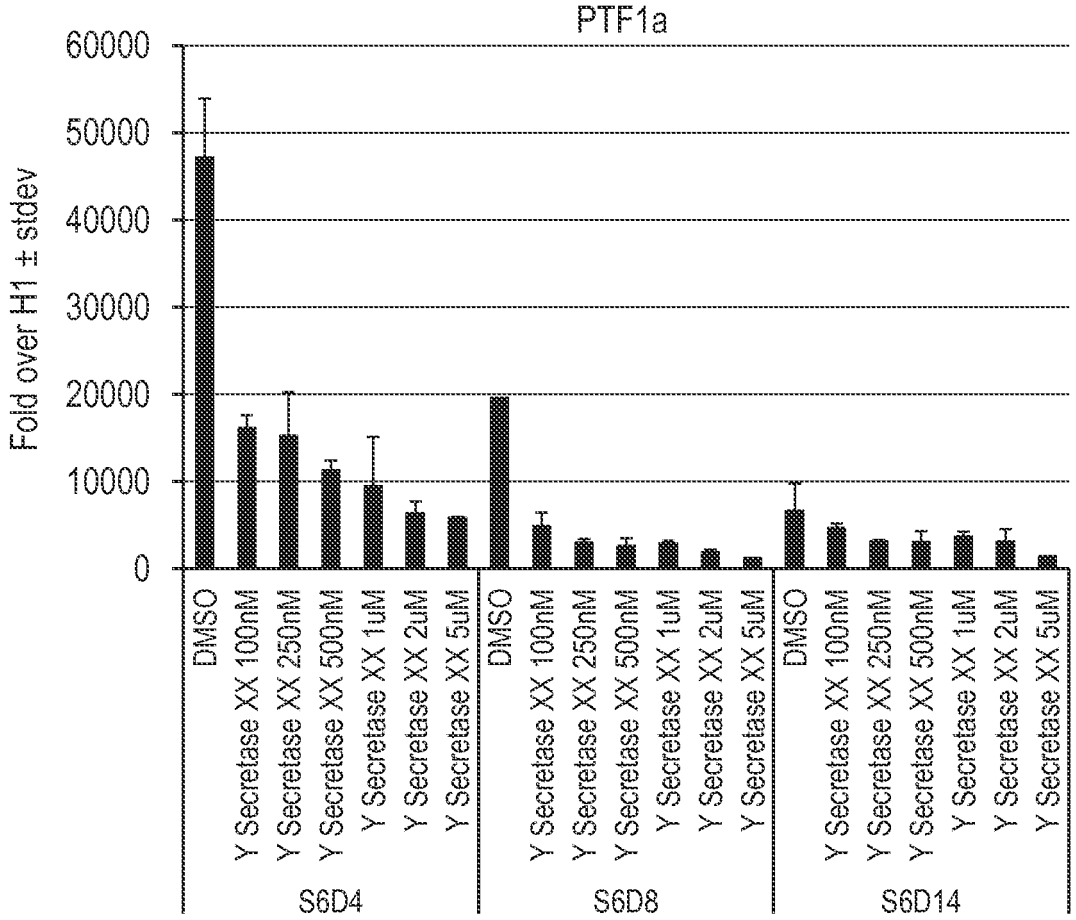


FIG. 21F

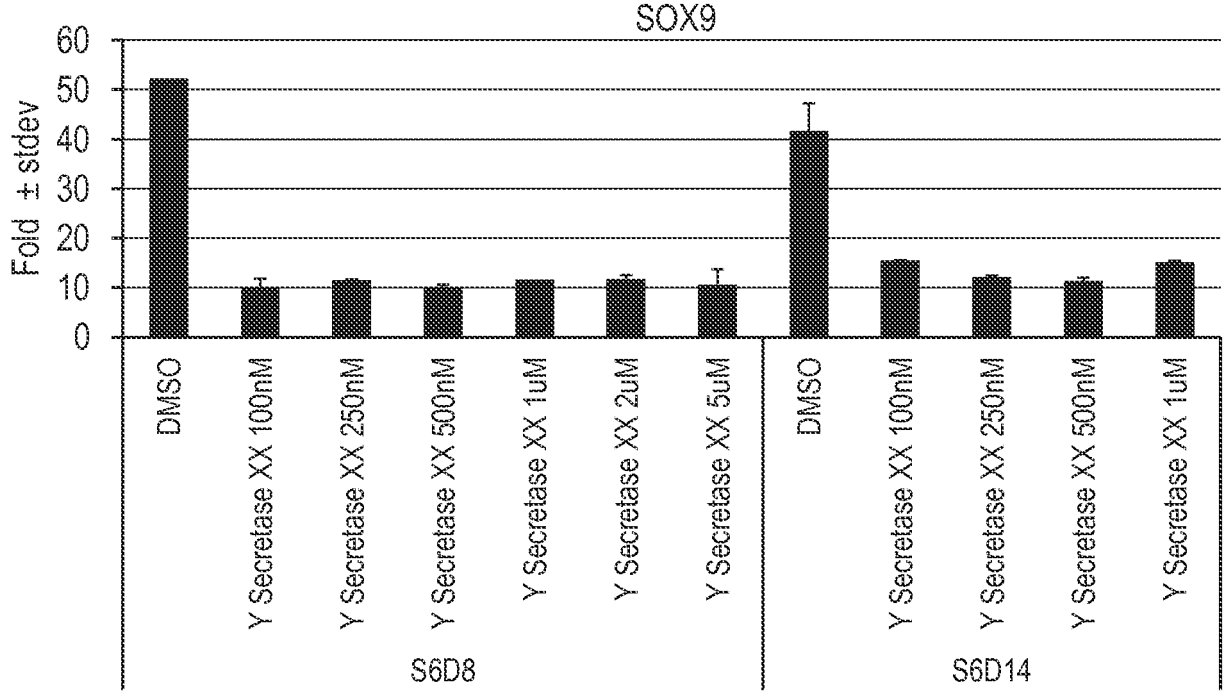


FIG. 22A

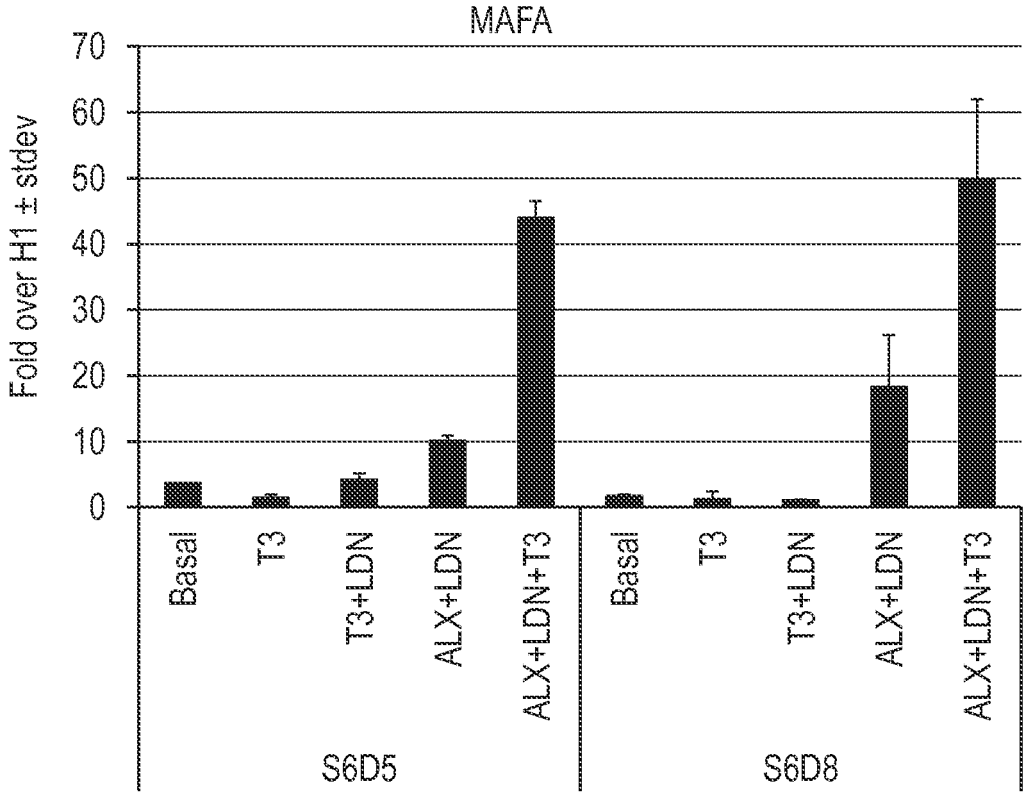


FIG. 22B

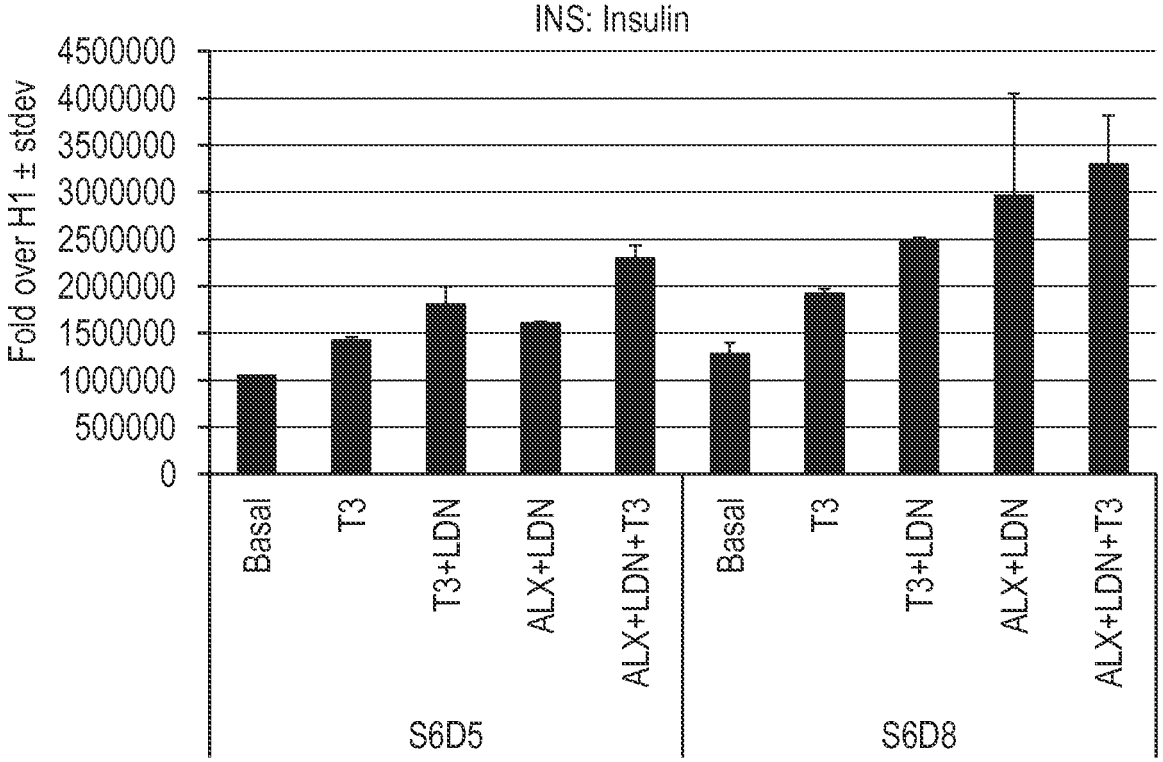


FIG. 22C

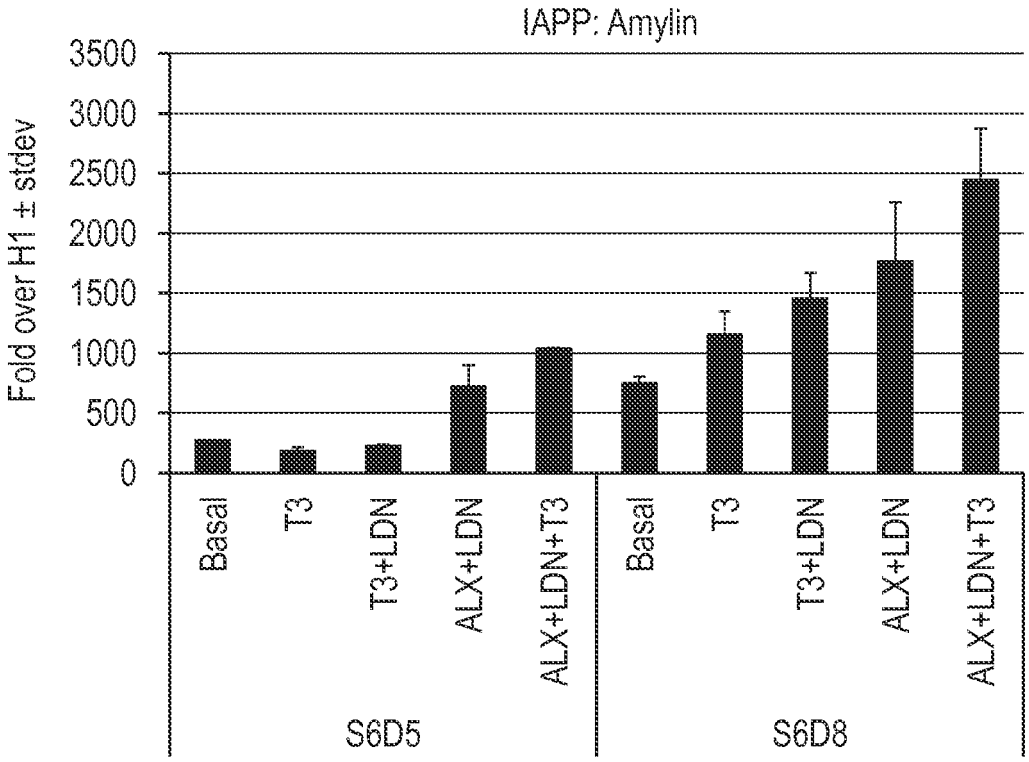


FIG. 22D

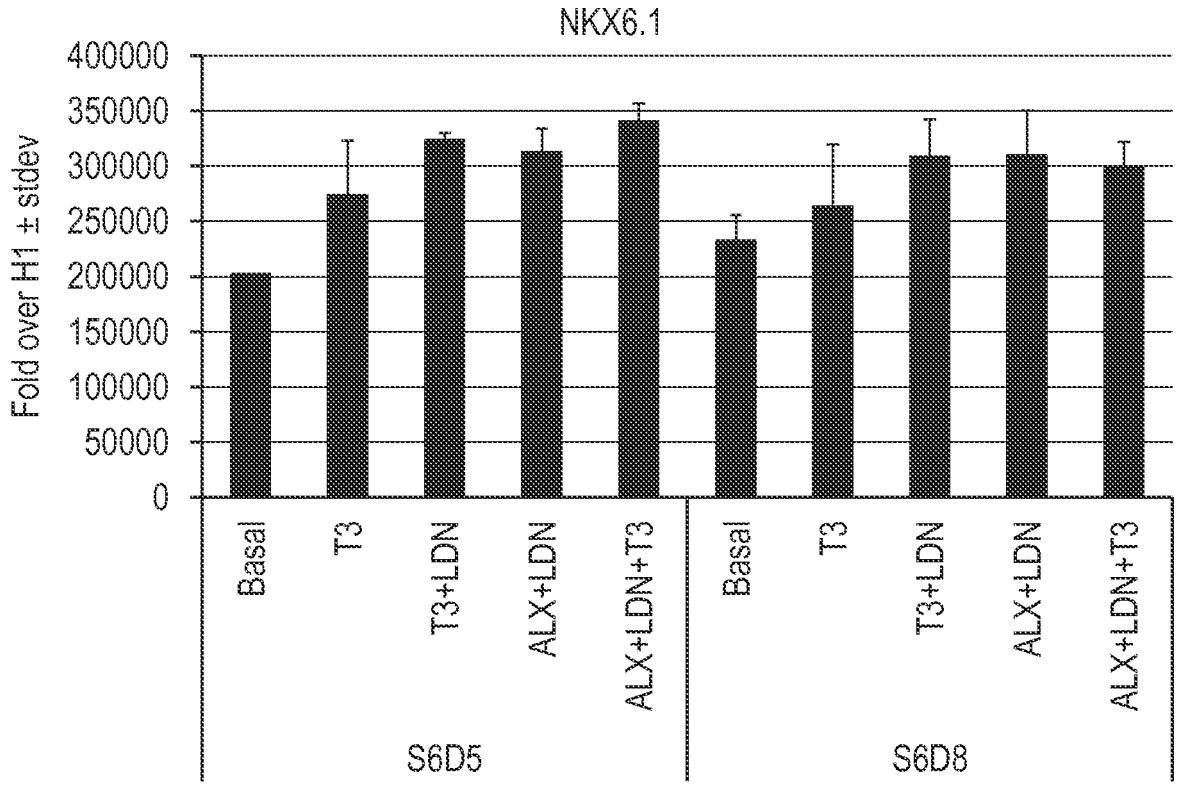


FIG. 23A

PDX1

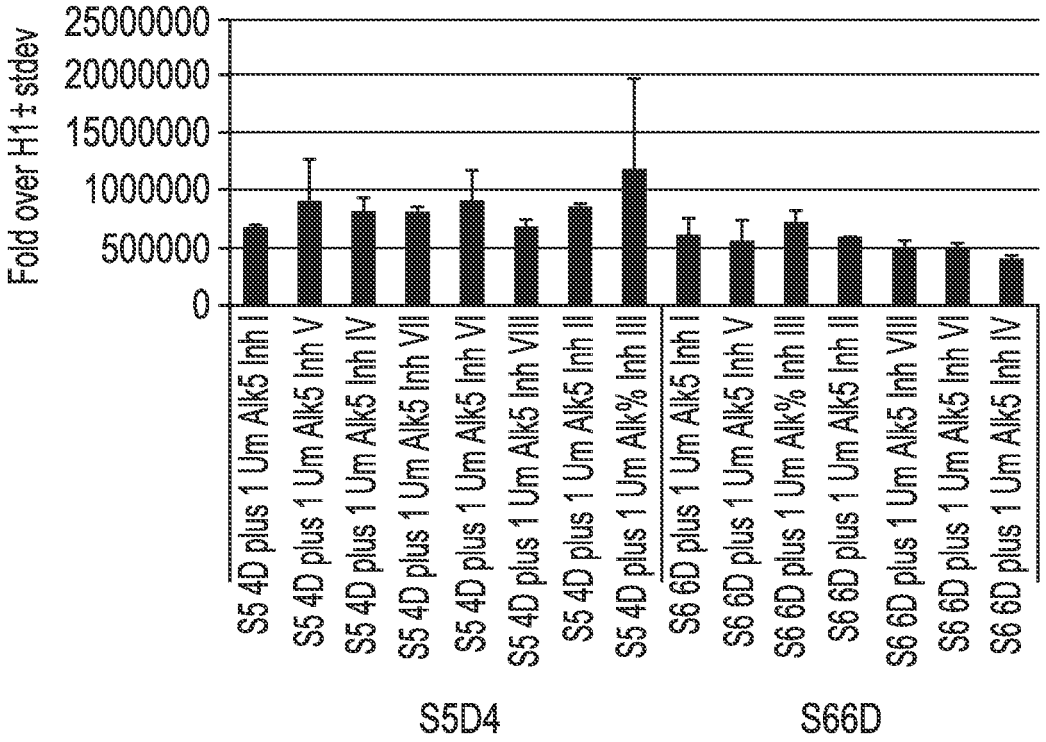


FIG. 23B

NKX6.1

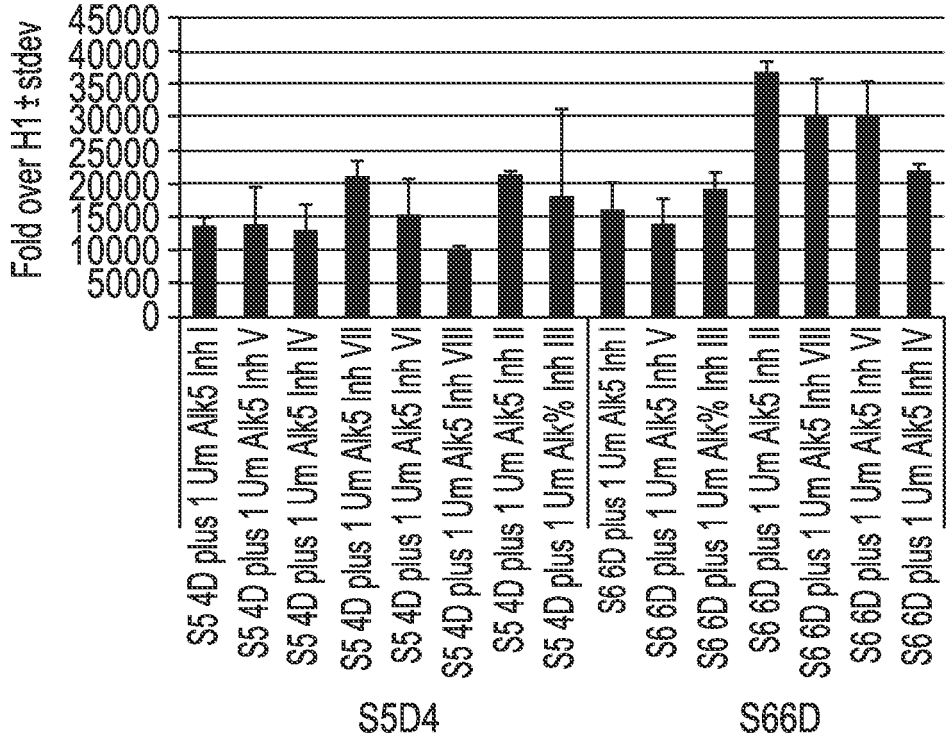


FIG. 23C

NGN3

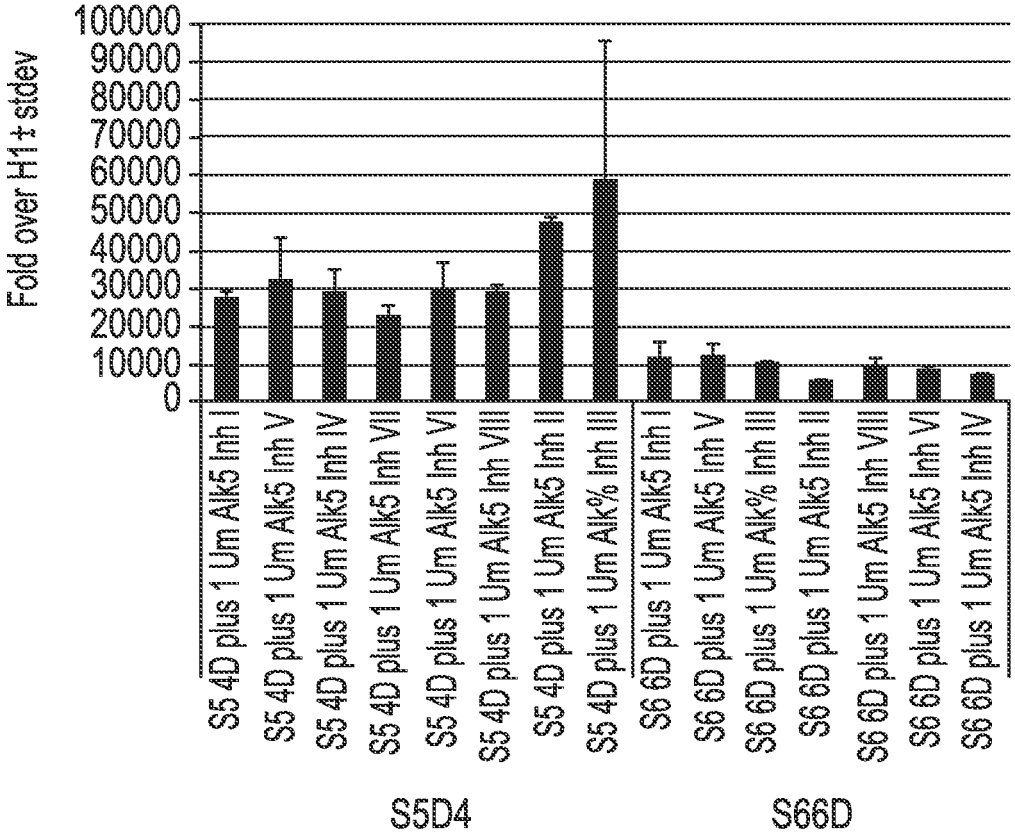


FIG. 23D

ABCC8

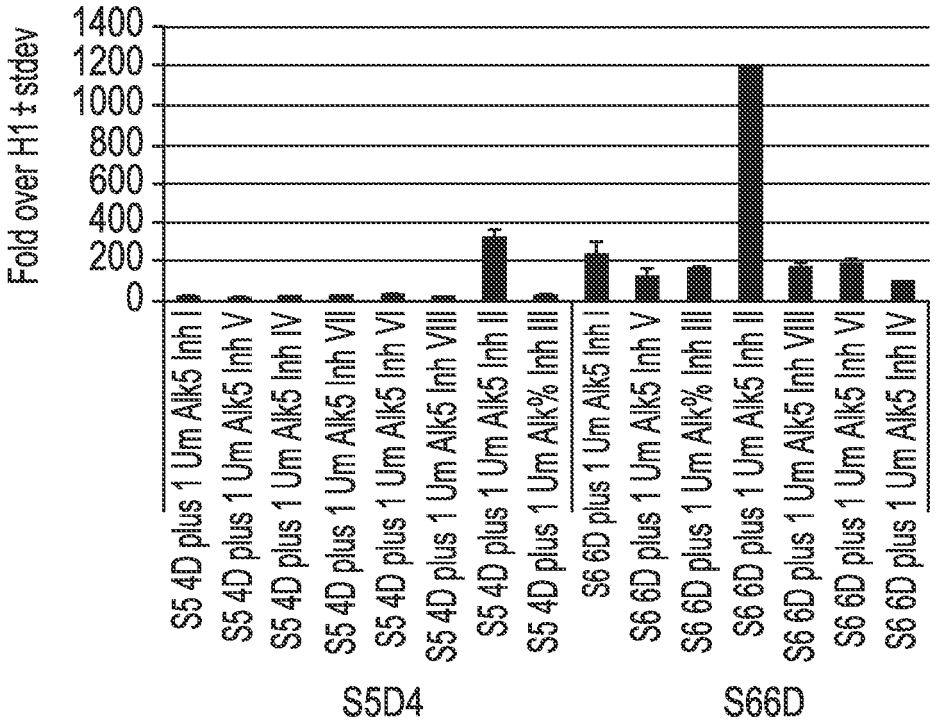


FIG. 23E

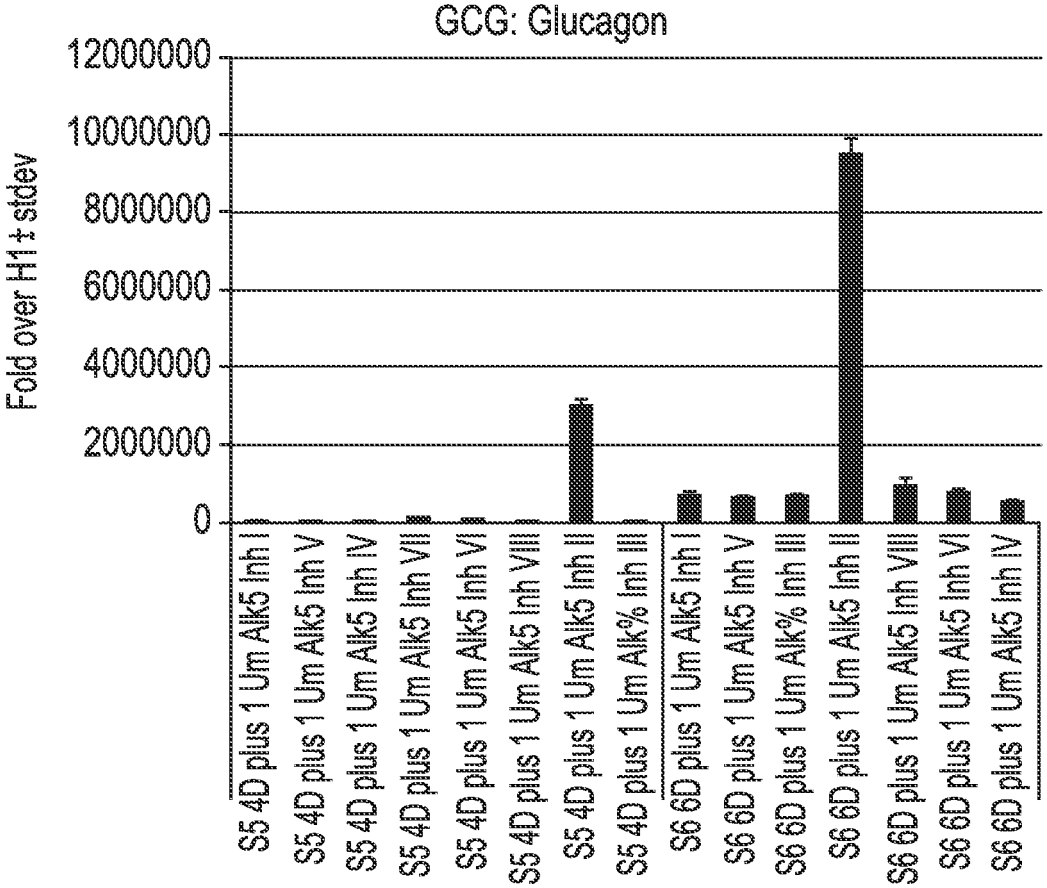


FIG. 23F

