

FIG. 1A

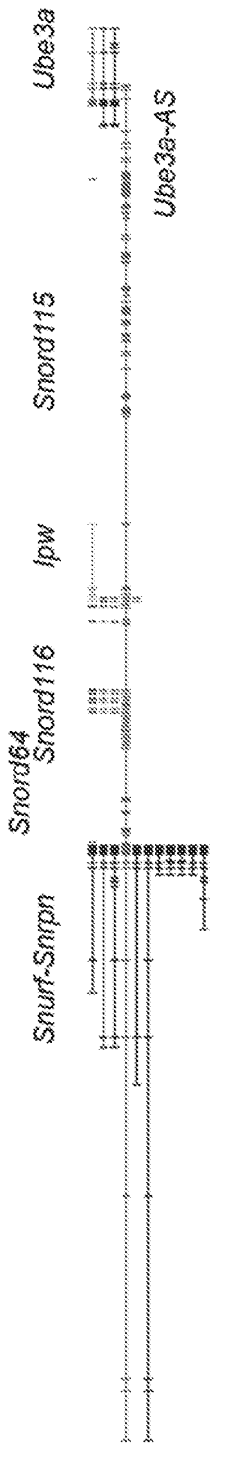


FIG. 1B



FIG. 1C

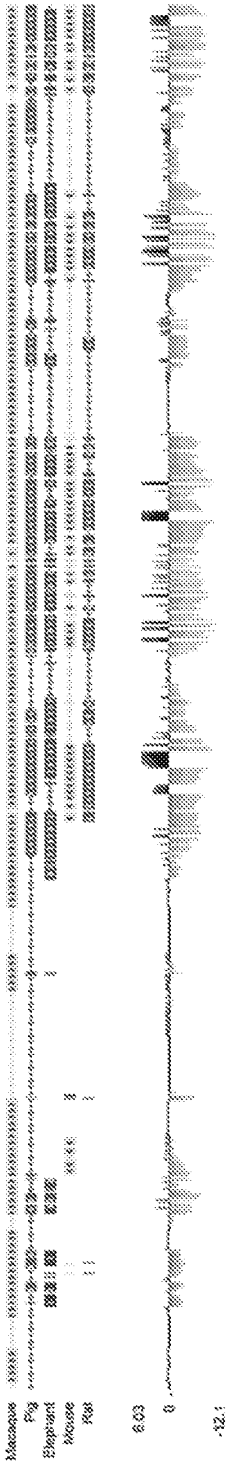

Macaque
Pig
Elephant
Mouse
Rat
6.03
0
-12.1

FIG. 1D

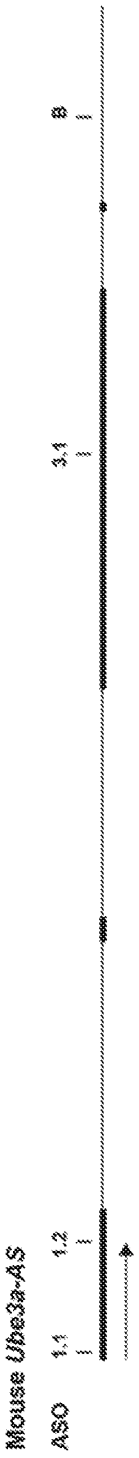

Mouse Ube3a-AS
ASO
1.1
1.2
3.1
8

FIG. 2A

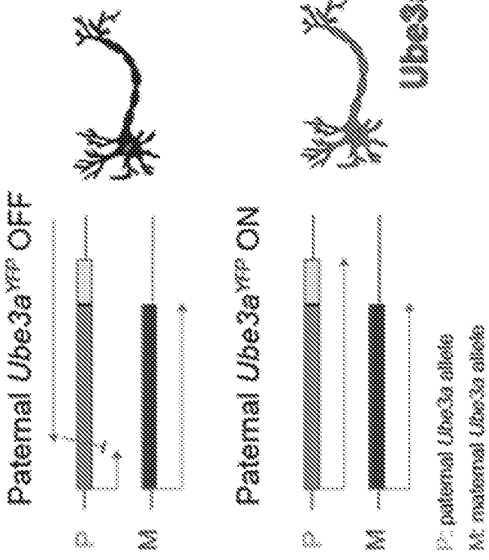

Paternal Ube3a^YFP OFF
P
M
Paternal Ube3a^YFP ON
P
M
Ube3a^YFP
P: paternal Ube3a allele
M: maternal Ube3a allele

FIG. 2B

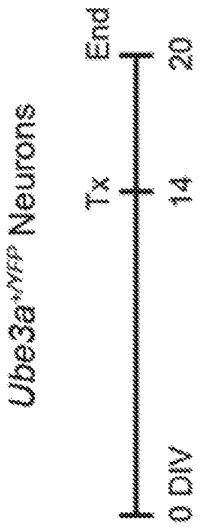

Ube3a^YFP Neurons
Tx
End
0 DIV
14
20

FIG. 2C

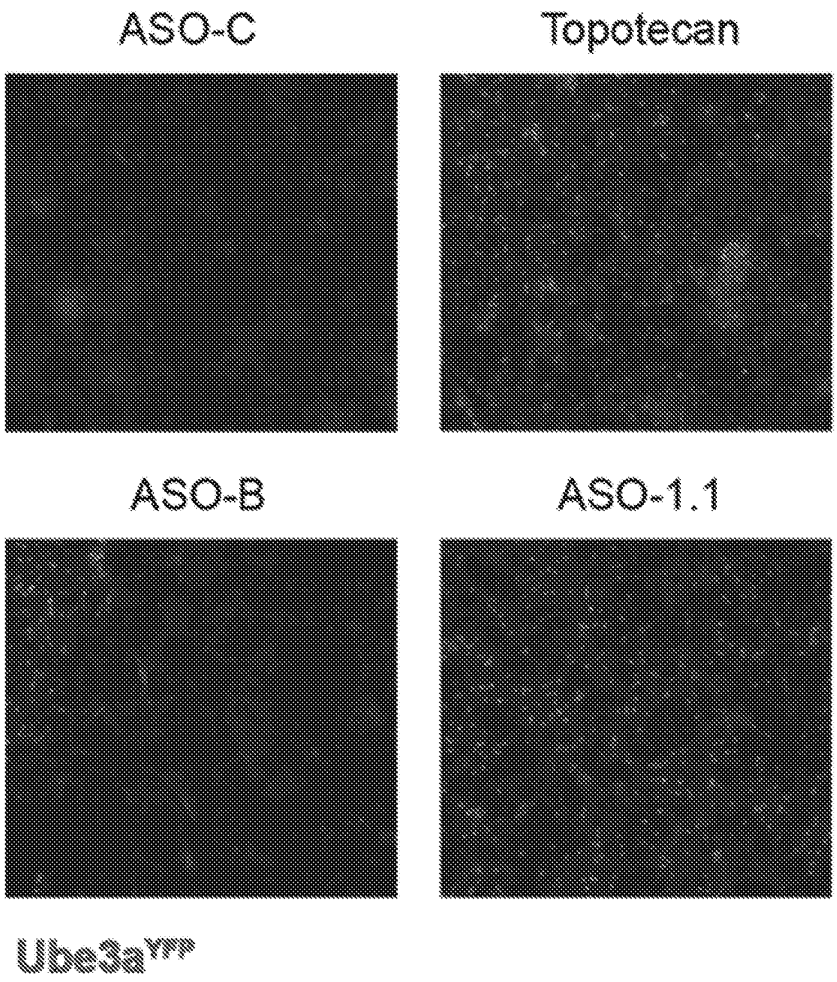


FIG. 2D

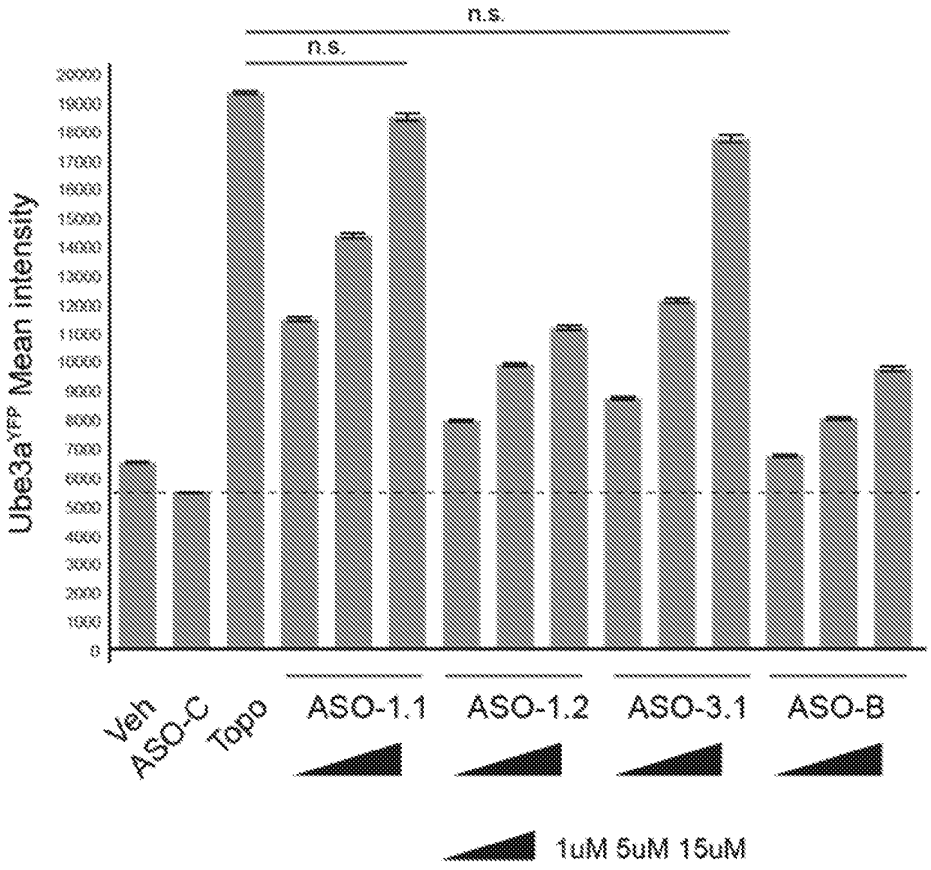

n.s.
n.s.
Ube3a^YFP Mean intensity
Veh
ASO-C
Topo
ASO-1.1
ASO-1.2
ASO-3.1
ASO-B
1uM 5uM 15uM

FIG. 2E

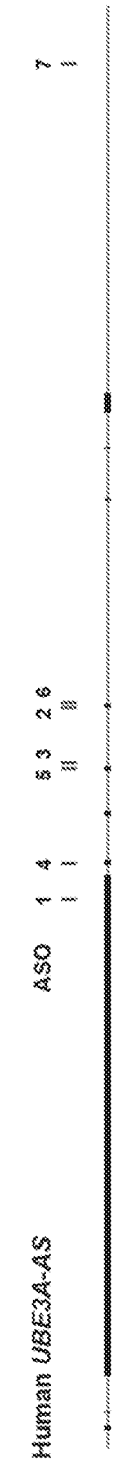

Human UBE3A-AS
ASO
1
4
5
3
2
6
7

FIG. 3A

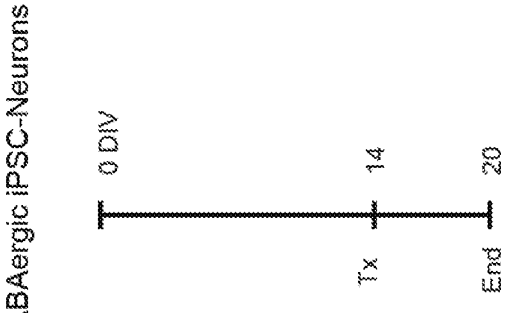

GABAergic iPSC-Neurons
0 DIV
14
20
Tx
End

FIG. 3B

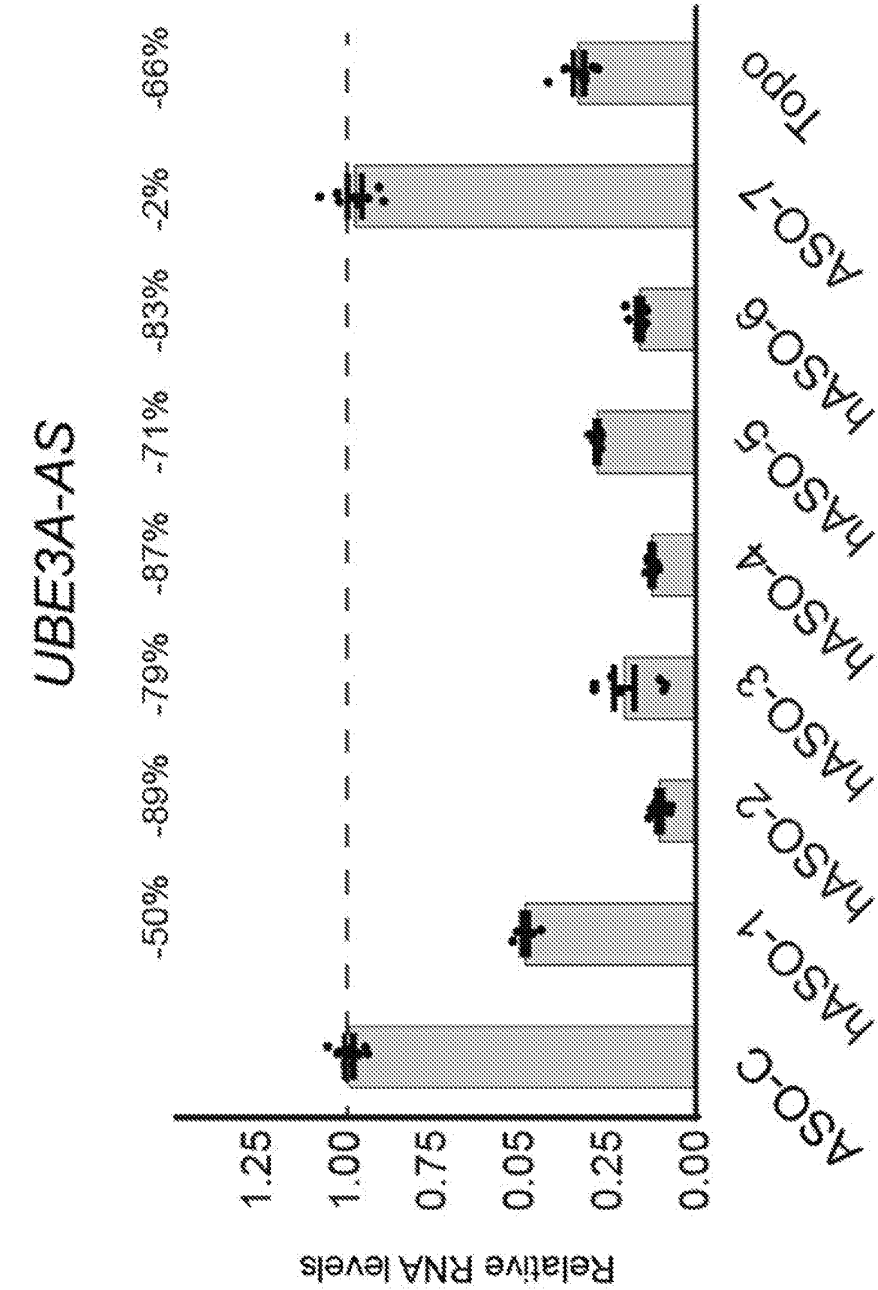

UBE3A-AS
-50%
-89%
-79%
-87%
-71%
-83%
-2%
-66%
1.25
1.00
0.75
0.05
0.25
0.00
Relative RNA levels
ASO-C
hASO-1
hASO-2
hASO-3
hASO-4
hASO-5
hASO-6
ASO-7
Topo

FIG. 3C

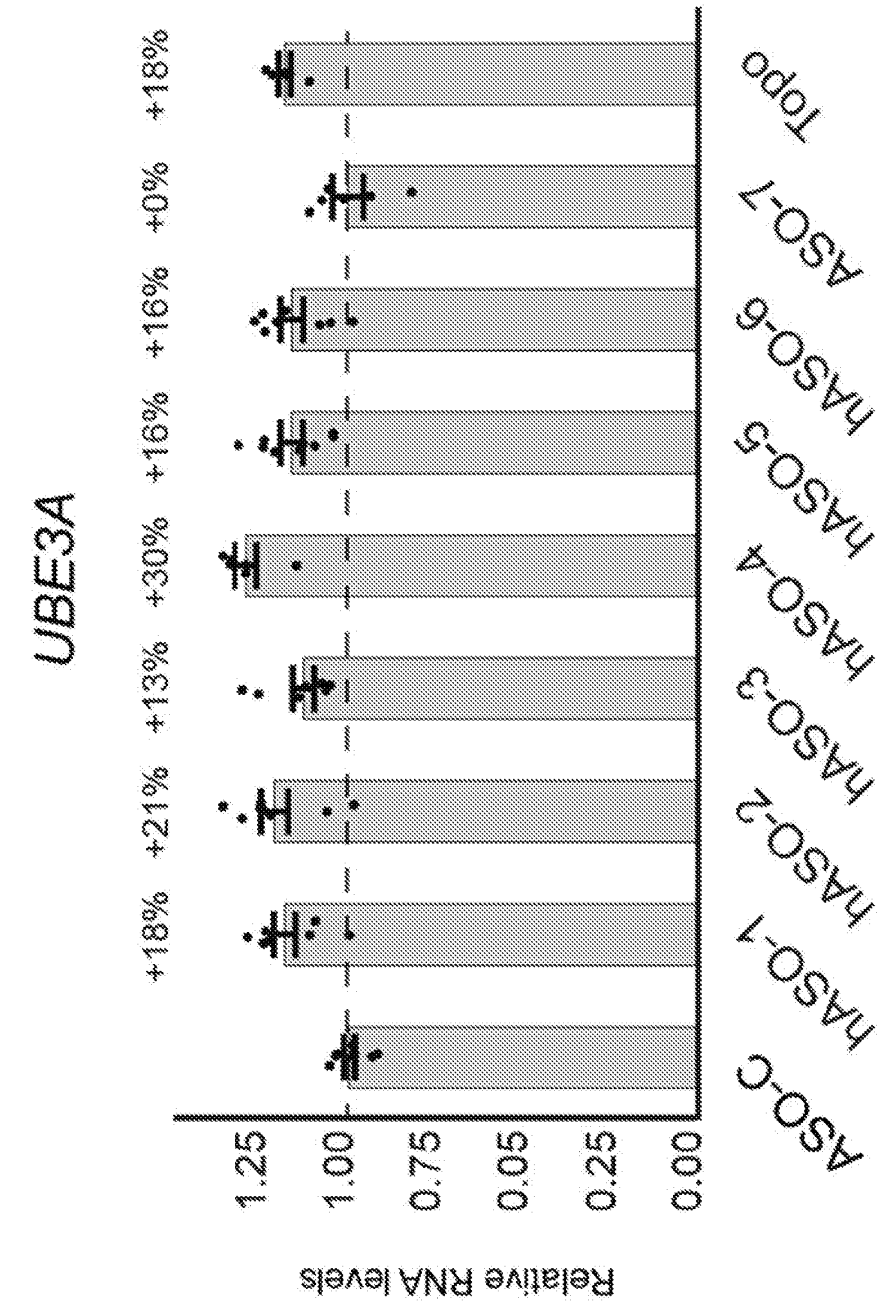

UBE3A
+18%
+21%
+13%
+30%
+16%
+16%
+0%
+18%
1.25
1.00
0.75
0.05
0.25
0.00
Relative RNA levels
ASO-C
hASO-1
hASO-2
hASO-3
hASO-4
hASO-5
hASO-6
ASO-7
Topo

FIG. 3D

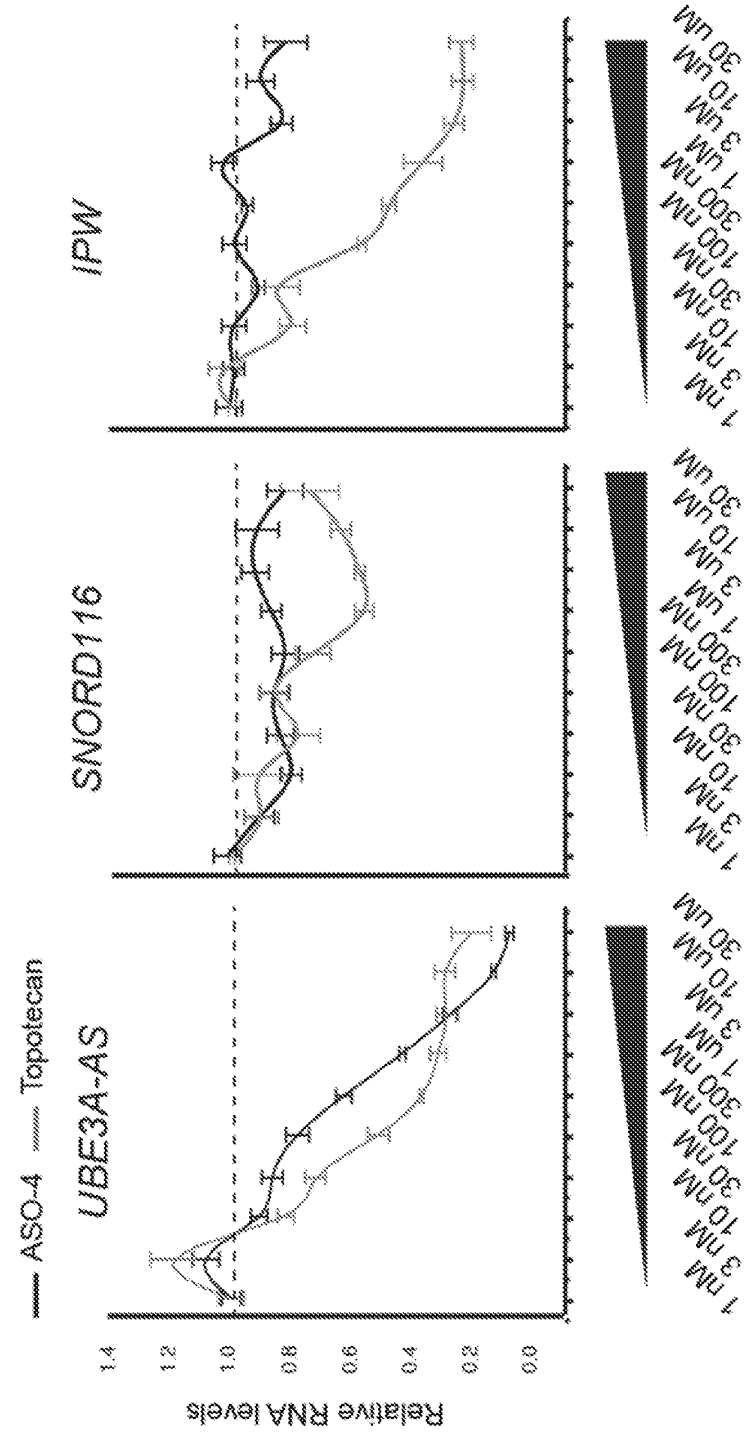


FIG. 4A

FIG. 4B

FIG. 4C

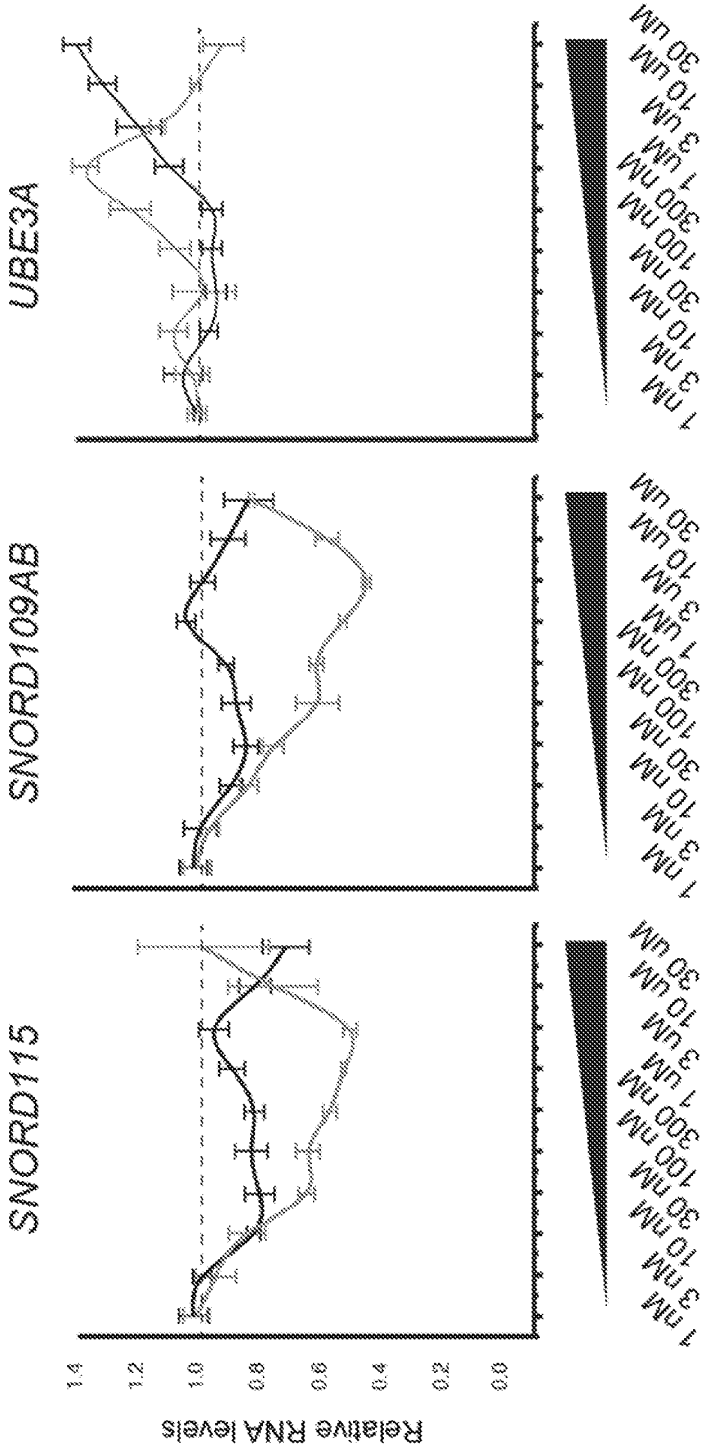


FIG. 4D

FIG. 4E

FIG. 4F

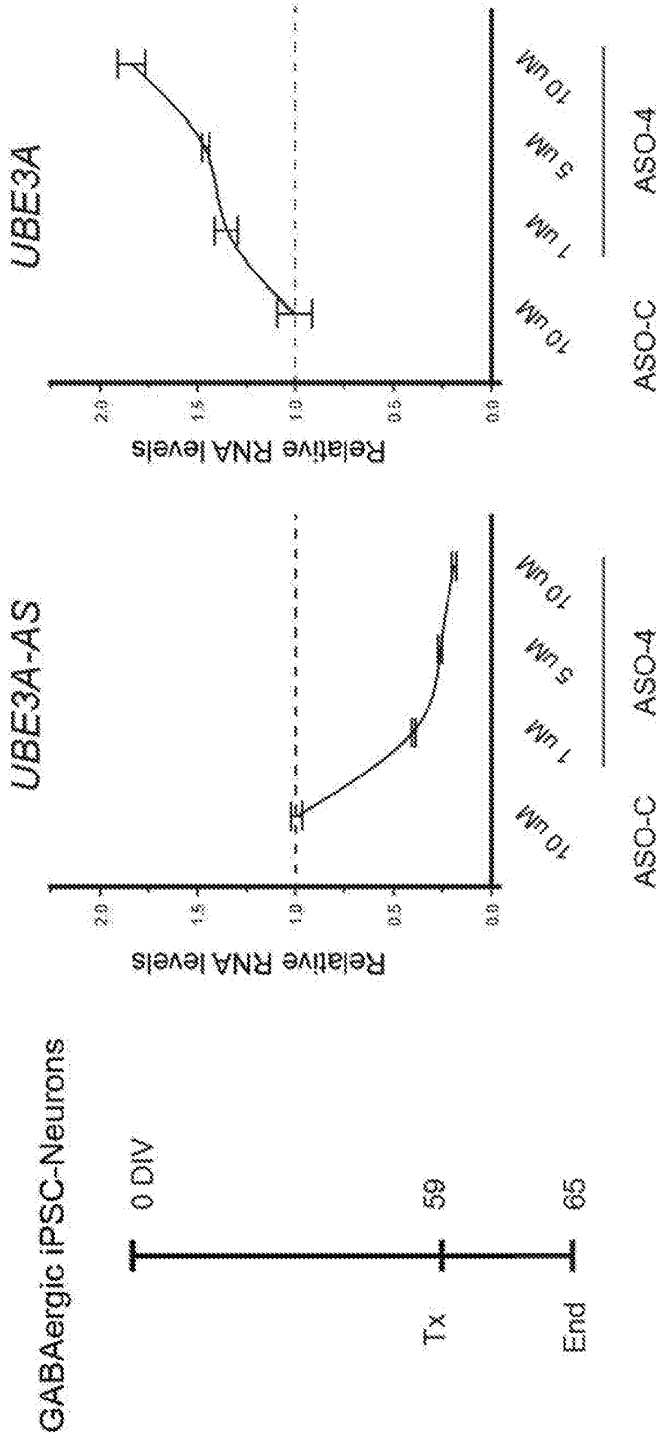


FIG. 4G

FIG. 4H

FIG. 4I

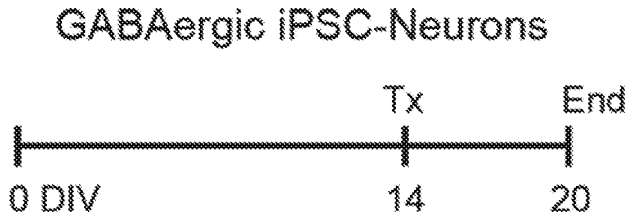

GABAergic iPSC-Neurons
Tx
End
0 DIV
14
20

FIG. 5A

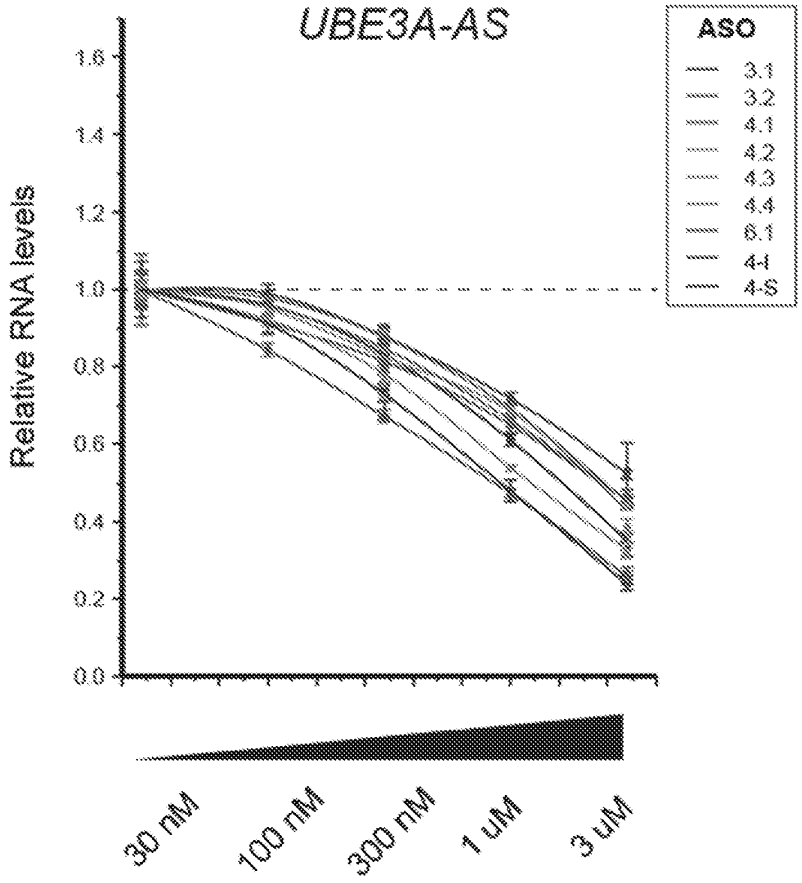

UBE3A-AS
ASO
3.1
3.2
4.1
4.2
4.3
4.4
6.1
4-I
4-S
Relative RNA levels
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
30 nM
100 nM
300 nM
1 uM
3 uM

FIG. 5B

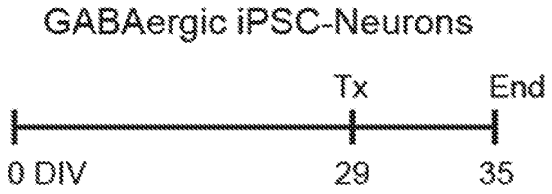

GABAergic iPSC-Neurons
Tx
End
0 DIV
29
35

FIG. 5C

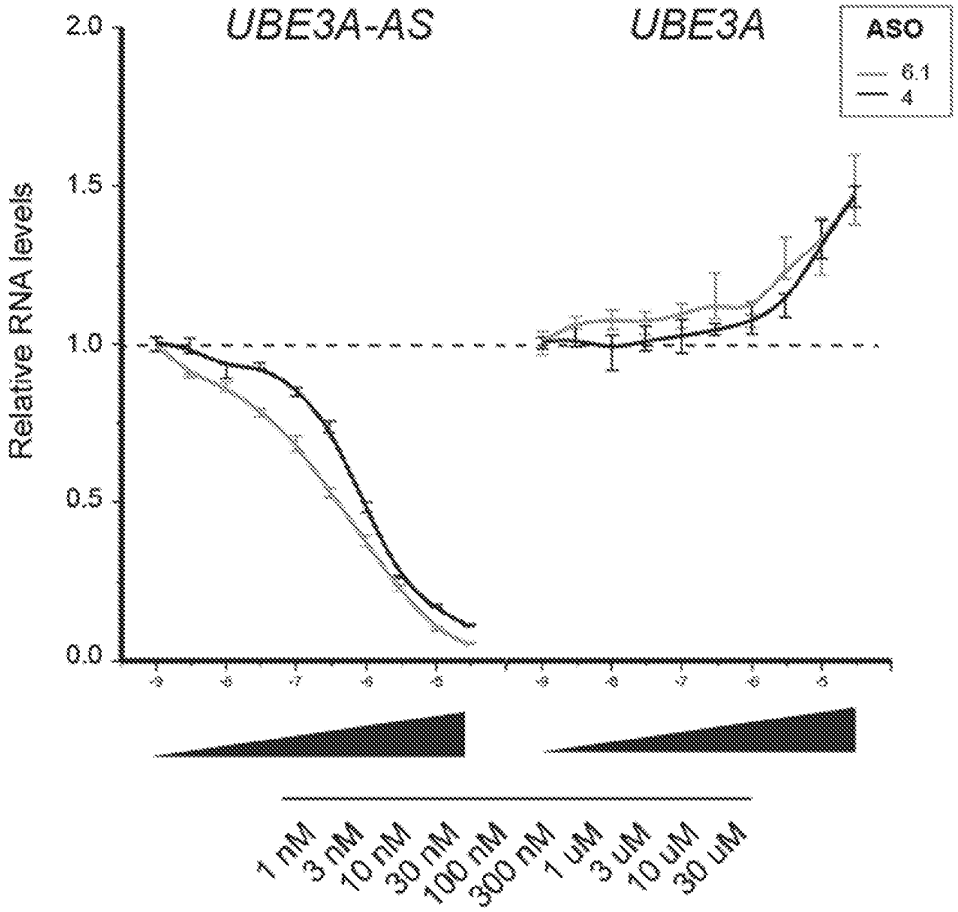

UBE3A-AS
UBE3A
ASO
6.1
4
Relative RNA levels
2.0
1.5
1.0
0.5
0.0
1 nM
3 nM
10 nM
30 nM
100 nM
300 nM
1 uM
3 uM
10 uM
30 uM

FIG. 5D

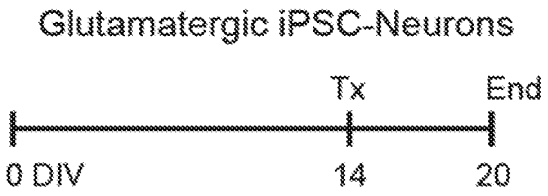

Glutamatergic iPSC-Neurons
Tx
End
0 DIV
14
20

FIG. 5E

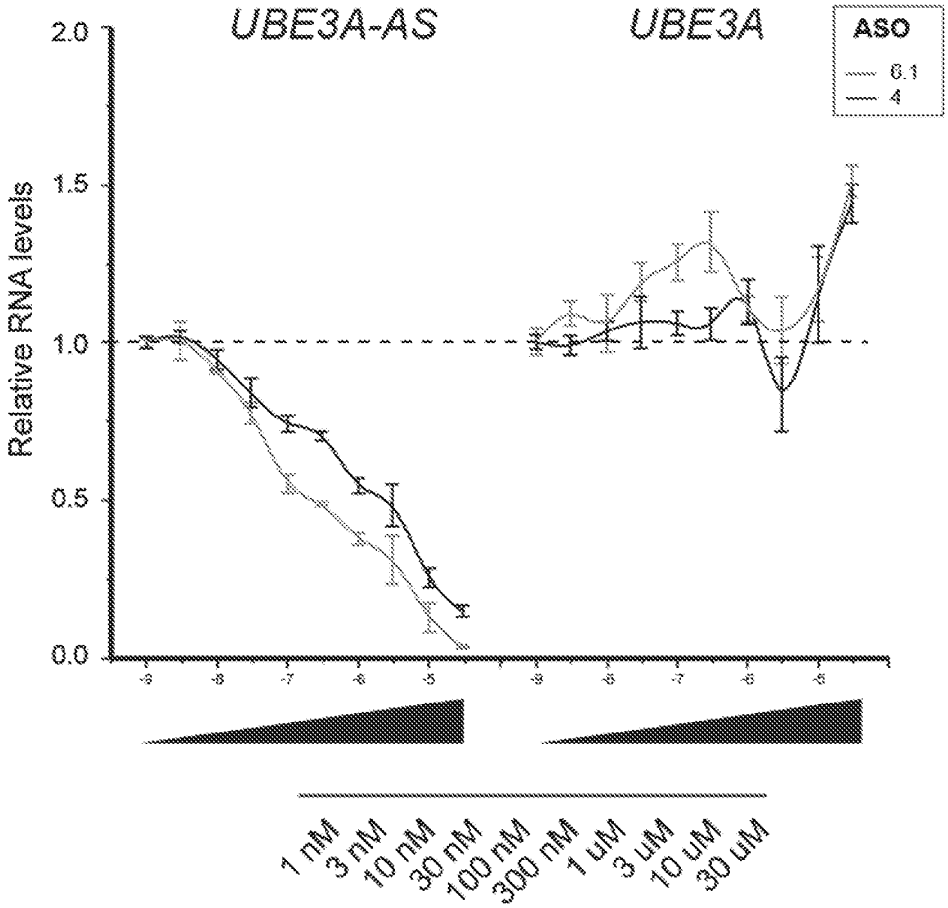

UBE3A-AS
UBE3A
ASO
6.1
4
Relative RNA levels
2.0
1.5
1.0
0.5
0.0
1 nM
3 nM
10 nM
30 nM
100 nM
300 nM
1 uM
3 uM
10 uM
30 uM

FIG. 5F



FIG. 6A

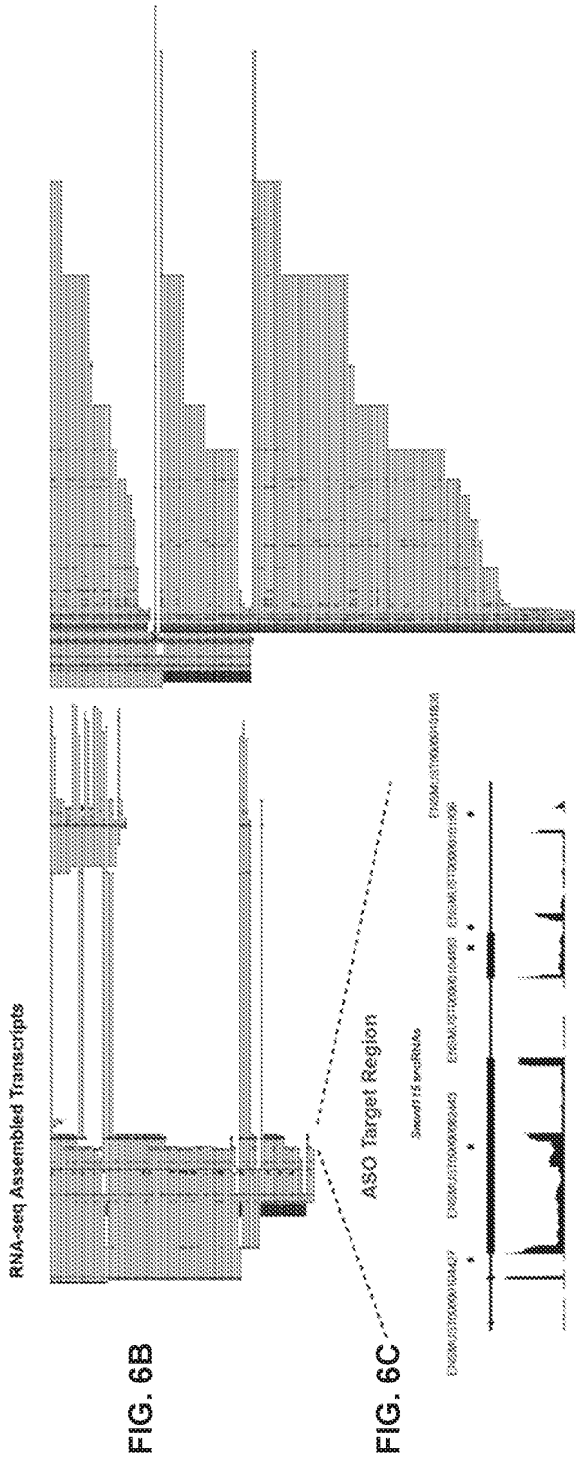


FIG. 6B

FIG. 6C

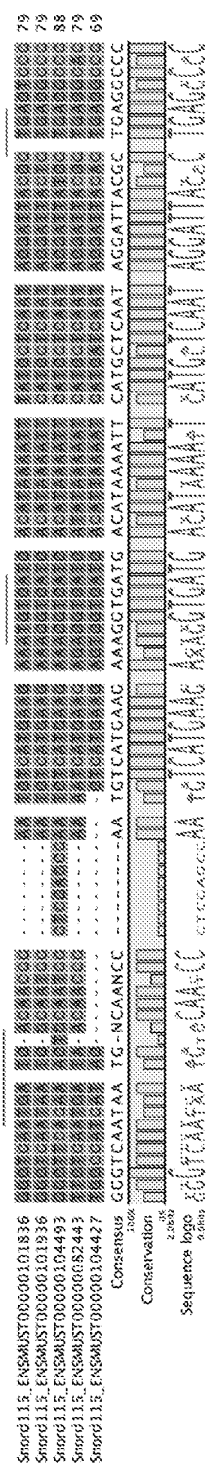

C Box
C' Box
D Box
Snord115_ENSMUST00000101836
Snord115_ENSMUST00000101936
Snord115_ENSMUST00000104493
Snord115_ENSMUST00000082443
Snord115_ENSMUST00000104427
Consensus
Conservation
Sequence logo
79
79
88
79
69

FIG. 6D

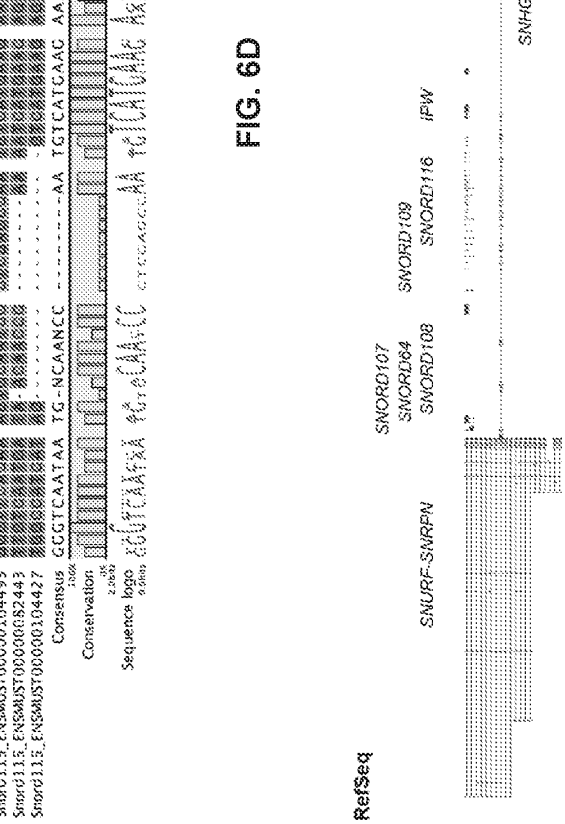

RefSeq
SNURF-SNRPN
SNORD107
SNORD64
SNORD108
SNORD109
SNORD116
iFW
SNORD115
SNORD109B
UBE3A
SNHG14
UBE3A-AS

FIG. 7A

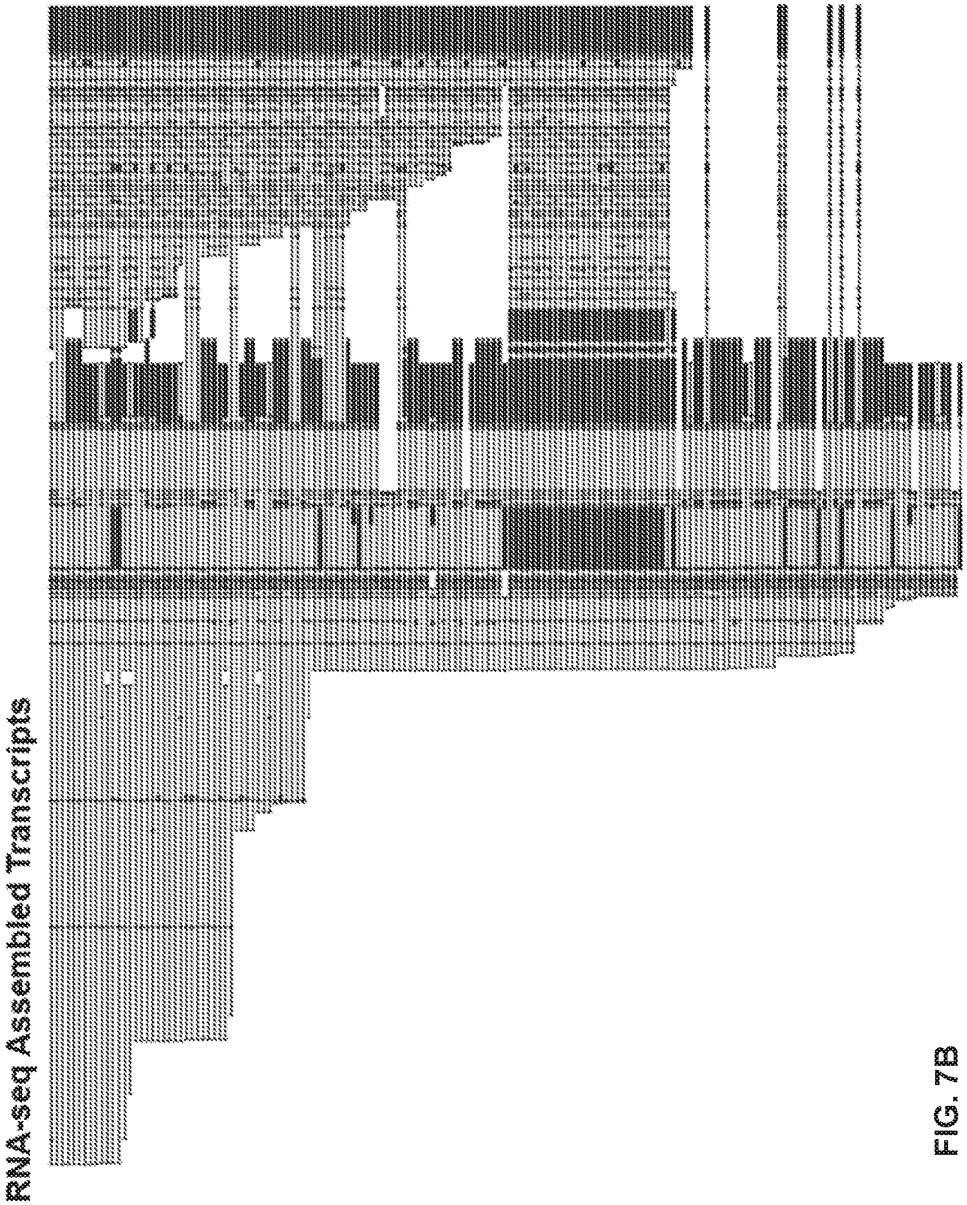


FIG. 7B

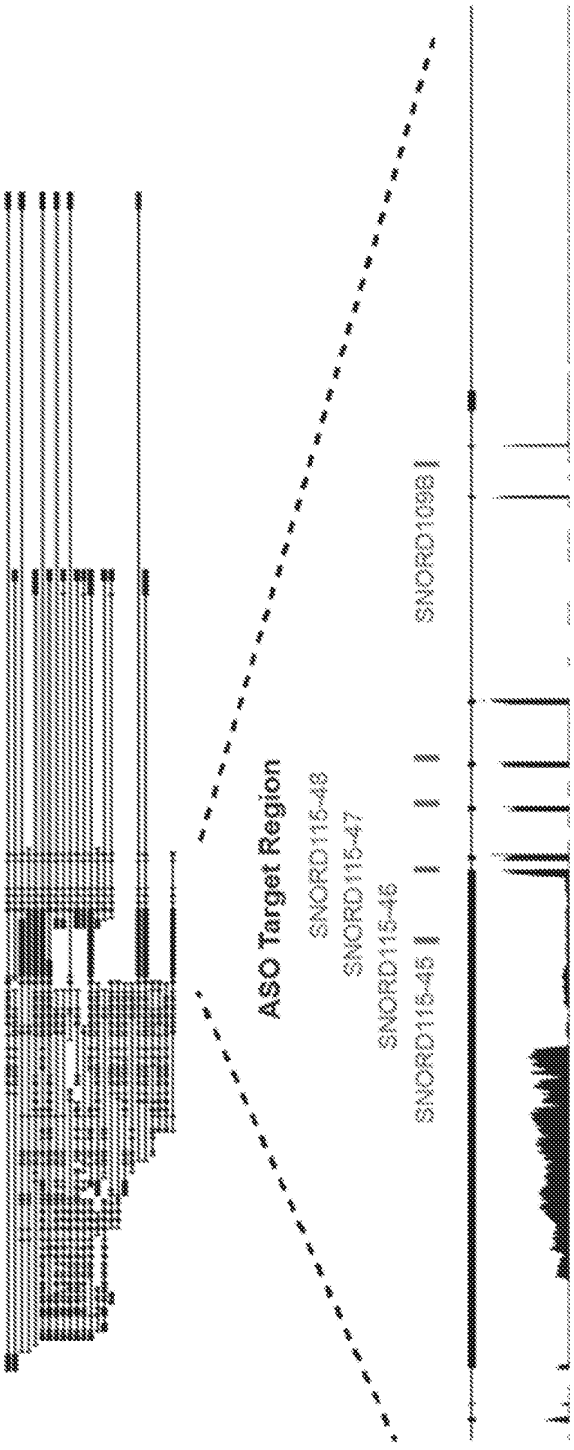

ASO Target Region
SNORD116-48
SNORD116-47
SNORD116-46
SNORD116-45
SNORD109B

FIG. 7C

FIG. 7D

FIG. 7E

FIG. 7F

FIG. 7G

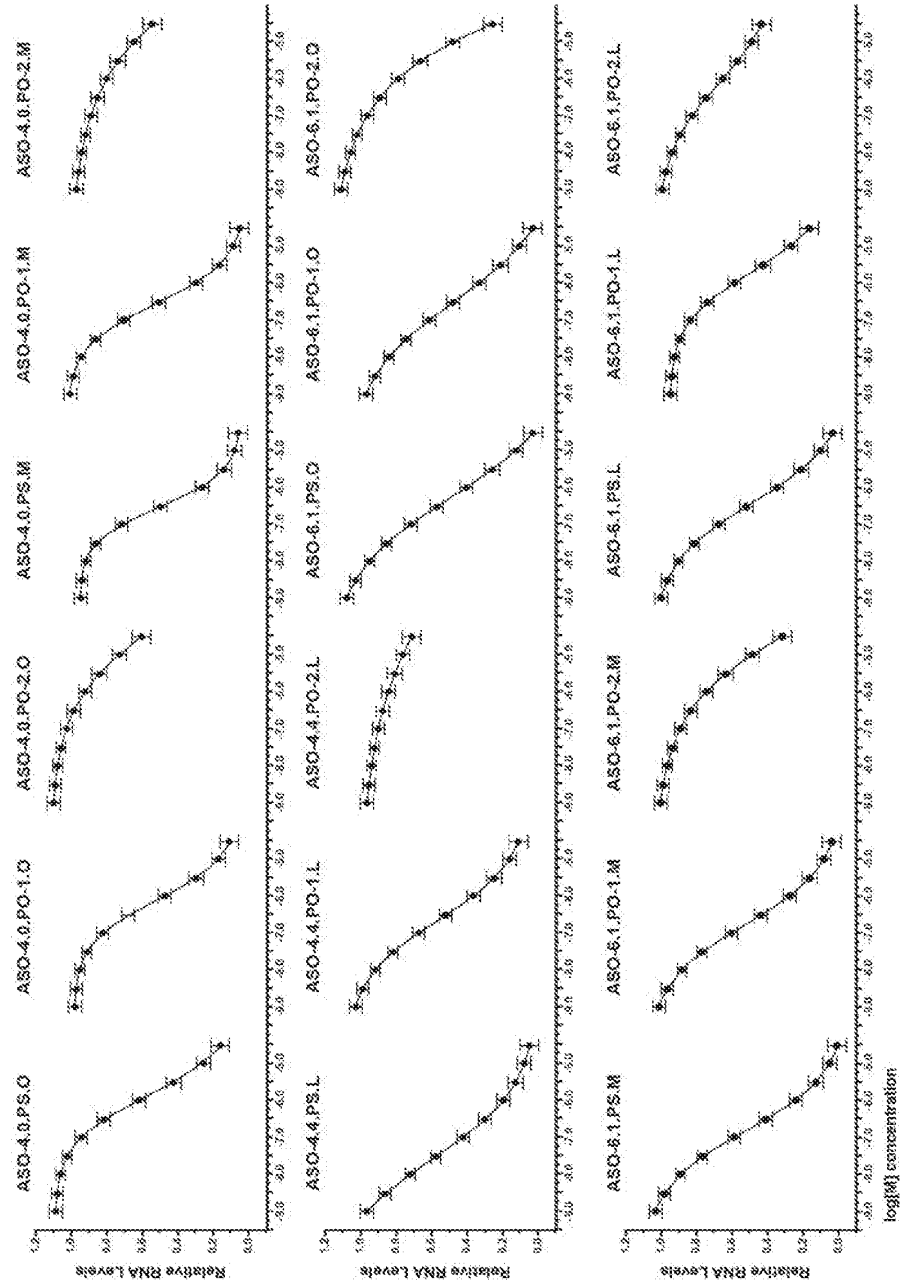

ASO-4.0.PS.O
ASO-4.0.PO-1.O
ASO-4.0.PO-2.O
ASO-4.0.PS.M
ASO-4.0.PO-1.M
ASO-4.0.PO-2.M
ASO-4.4.PS.L
ASO-4.4.PO-1.L
ASO-4.4.PO-2.L
ASO-6.1.PS.O
ASO-6.1.PO-1.O
ASO-6.1.PO-2.O
ASO-6.1.PS.M
ASO-6.1.PO-1.M
ASO-6.1.PO-2.M
ASO-6.1.PS.L
ASO-6.1.PO-1.L
ASO-6.1.PO-2.L
Relative RNA Levels
log[M] concentration

FIG. 8A

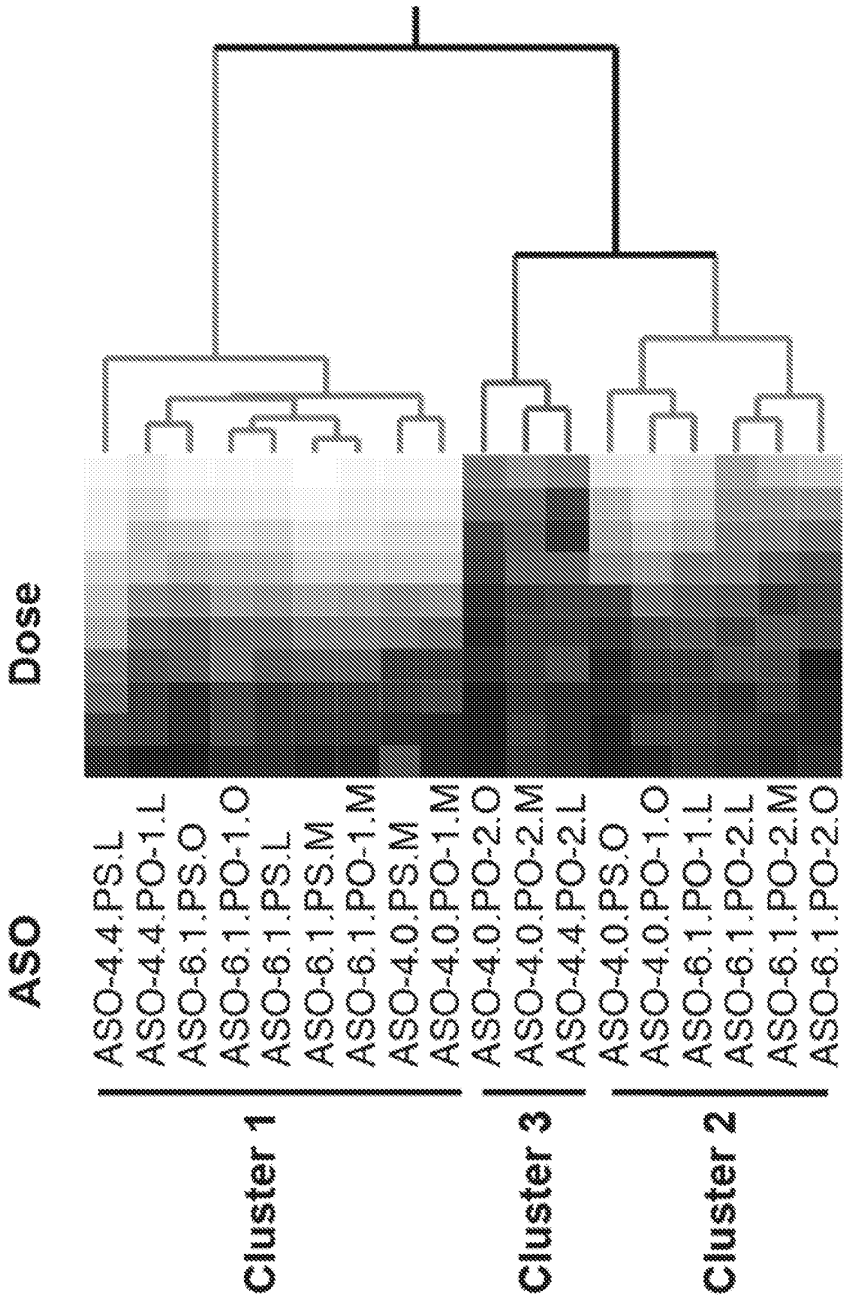

Dose
ASO
ASO-4.4.PS.L
ASO-4.4.PO-1.L
ASO-6.1.PS.O
ASO-6.1.PO-1.O
ASO-6.1.PS.L
ASO-6.1.PS.M
ASO-6.1.PO-1.M
ASO-4.0.PS.M
ASO-4.0.PO-1.M
ASO-4.0.PO-2.O
ASO-4.0.PO-2.M
ASO-4.4.PO-2.L
ASO-4.0.PS.O
ASO-4.0.PO-1.O
ASO-6.1.PO-1.L
ASO-6.1.PO-2.L
ASO-6.1.PO-2.M
ASO-6.1.PO-2.O
Cluster 1
Cluster 3
Cluster 2

FIG. 8B

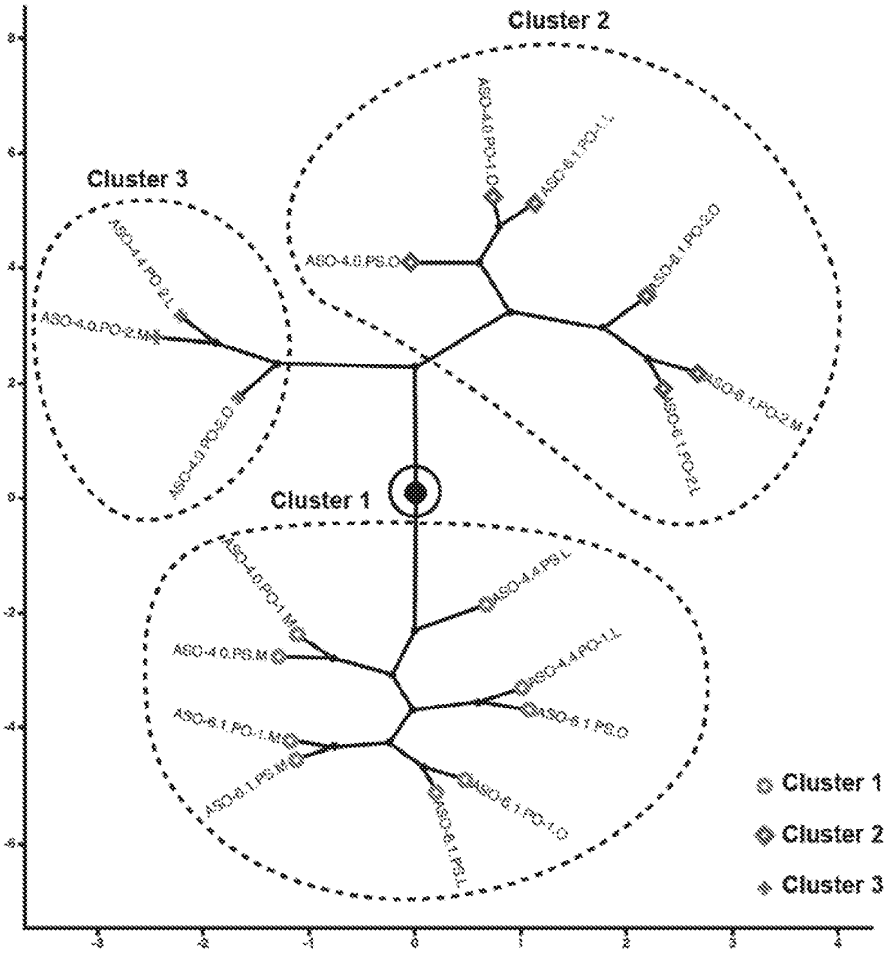

Cluster 2
Cluster 3
Cluster 1
ASO-4.0.PO-1.O
ASO-6.1.PO-1.L
ASO-4.0.PS.O
ASO-6.1.PO-2.O
ASO-6.1.PO-2.M
ASO-6.1.PO-2.L
ASO-4.4.PO.L
ASO-4.0.PO-2.M
ASO-4.0.PO-2.O
ASO-4.0.PO-1.M
ASO-4.4.PS.L
ASO-4.0.PS.M
ASO-4.4.PO-1.L
ASO-6.1.PS.O
ASO-6.1.PO-1.M
ASO-6.1.PS.M
ASO-6.1.PO-1.O
ASO-6.1.PS.L
Cluster 1
Cluster 2
Cluster 3

FIG. 8C

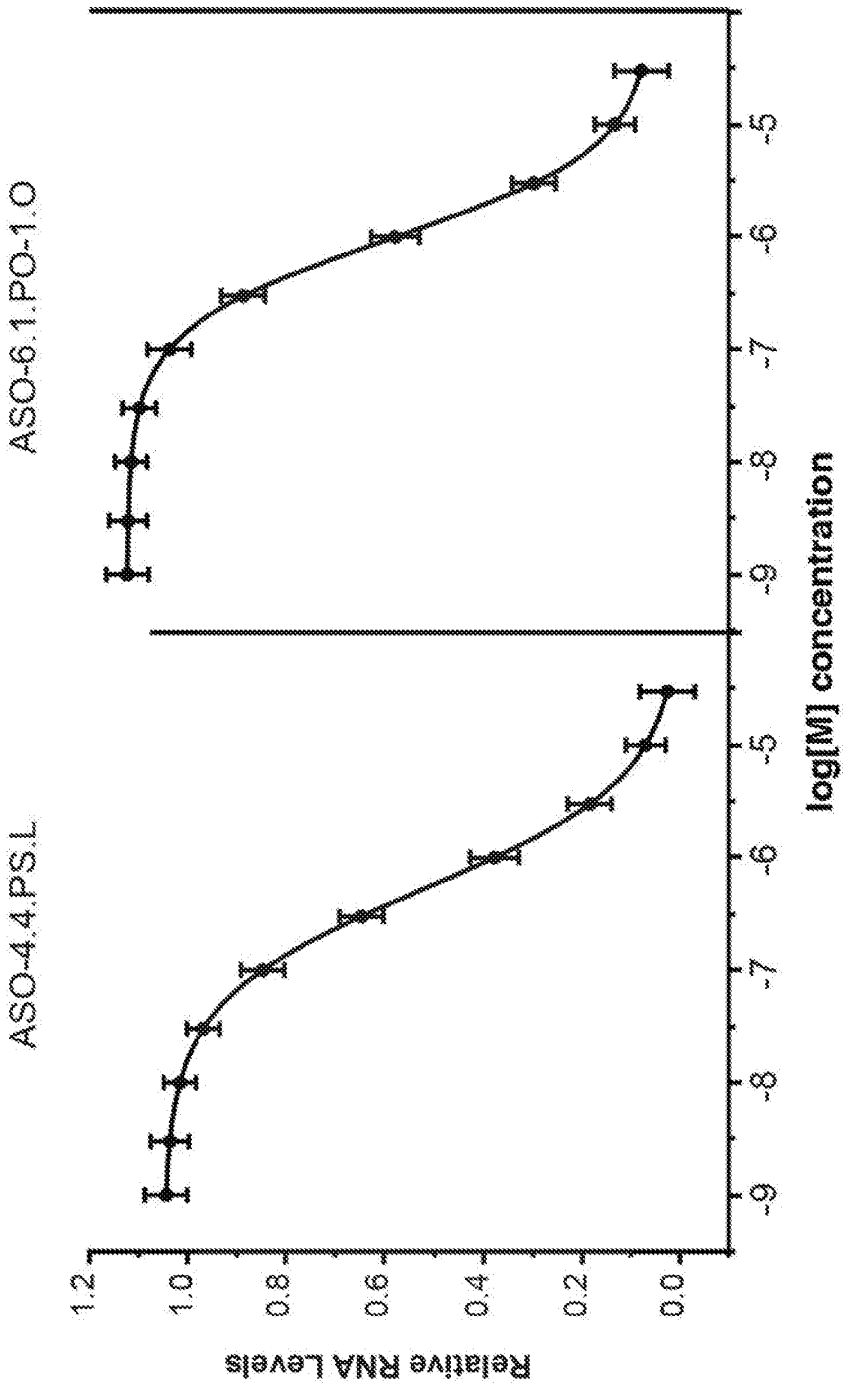

ASO-6.1.PO-1.O
ASO-4.4.PS.L
Relative RNA Levels
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-9
-8
-7
-6
-5
log[M] concentration

FIG. 9

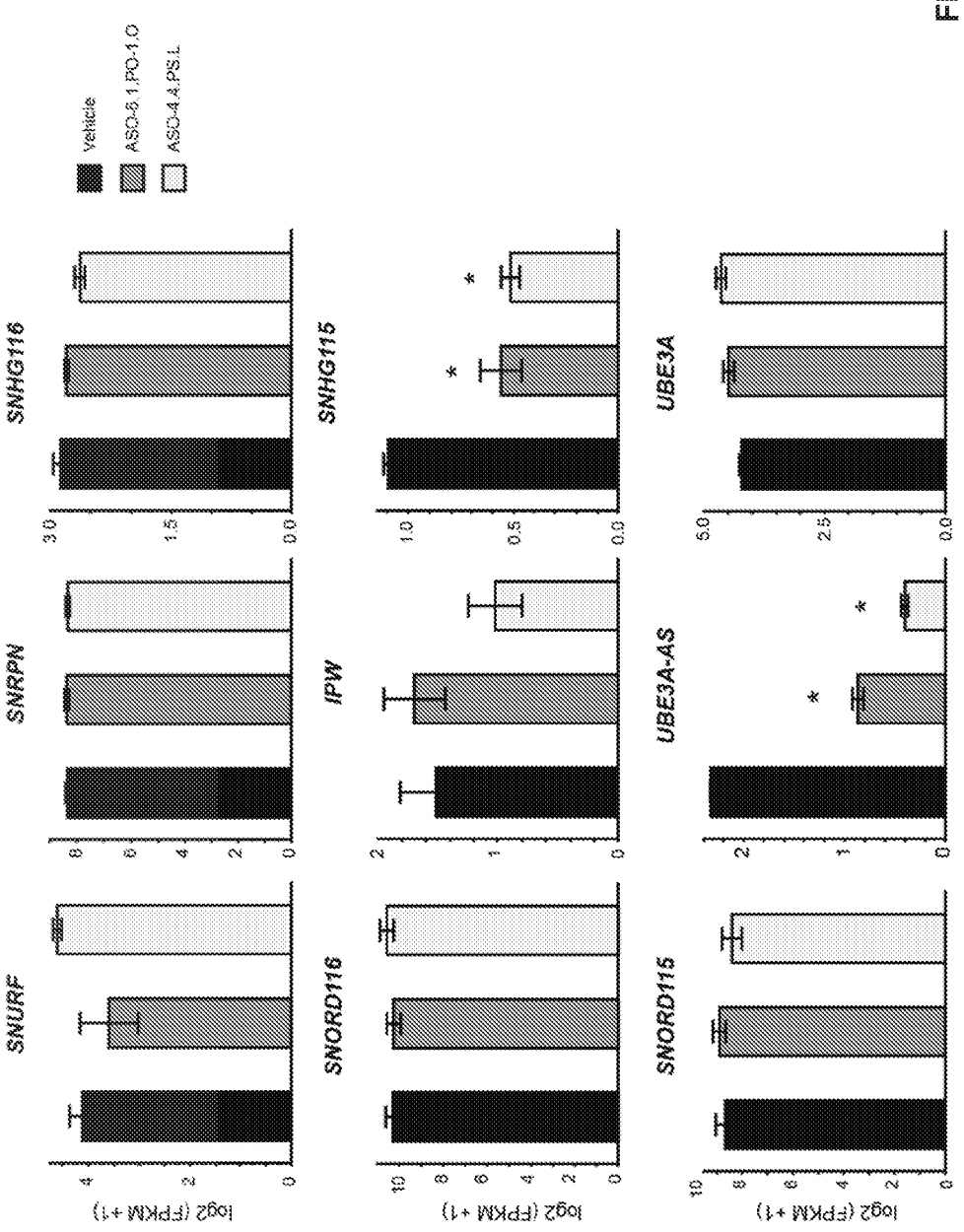

Vehicle
ASO-6.1.PO-1.O
ASO-4.4.PS.L
SNURF
SNRPN
SNHG116
SNORD116
IPW
SNHG115
SNORD115
UBE3A-AS
UBE3A
log2 (FPKM +1)

FIG. 10

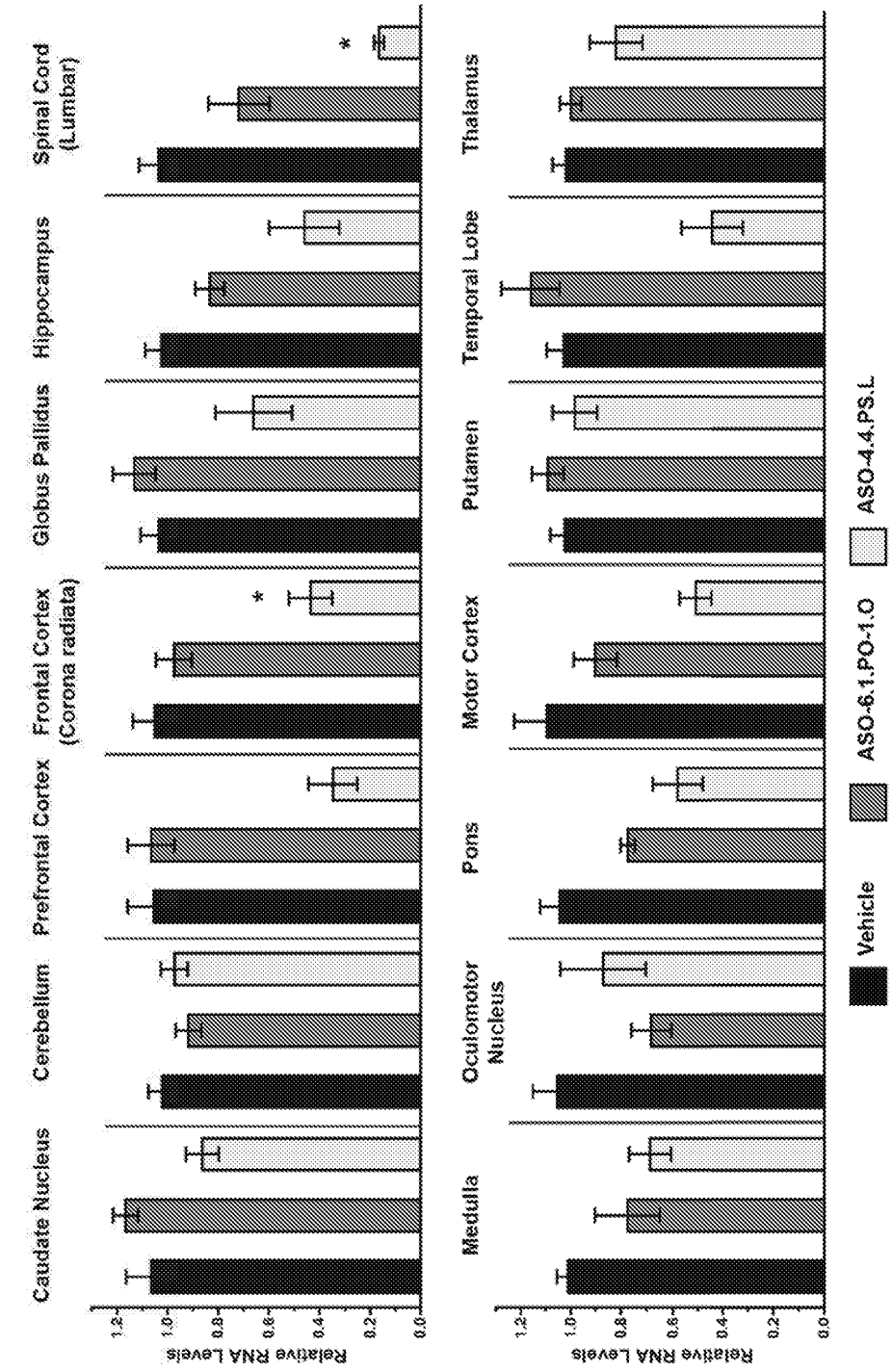

Caudate Nucleus
Cerebellum
Prefrontal Cortex
Frontal Cortex (Corona radiata)
Globus Pallidus
Hippocampus
Spinal Cord (Lumbar)
Medulla
Oculomotor Nucleus
Pons
Motor Cortex
Putamen
Temporal Lobe
Thalamus
Relative RNA Levels
1.2
1.0
0.8
0.6
0.4
0.2
0.0
*
*
Vehicle
ASO-6.1.PO-1.0
ASO-4.4.PS.L

FIG. 11