FISSEQ established culture models for brain cell types

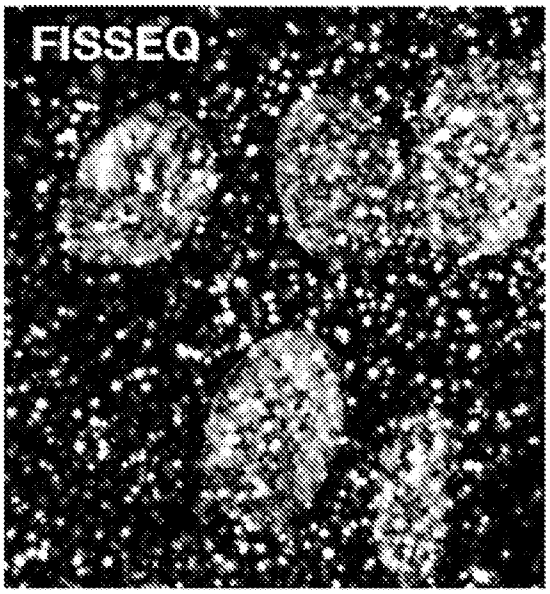


FIG. 1A

Segment sub-cellular compartments

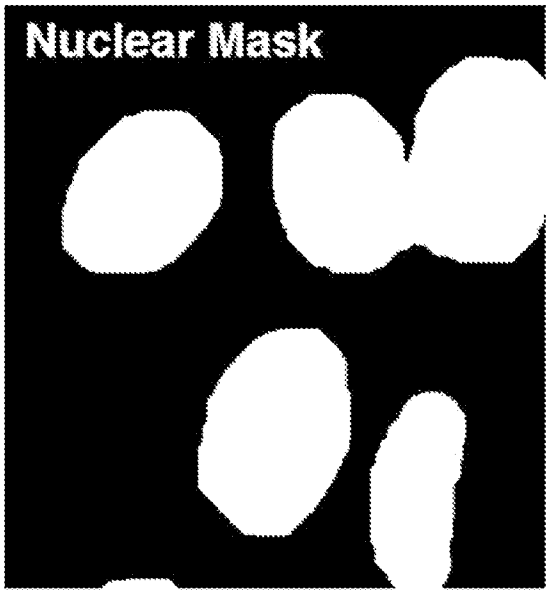


FIG. 1B

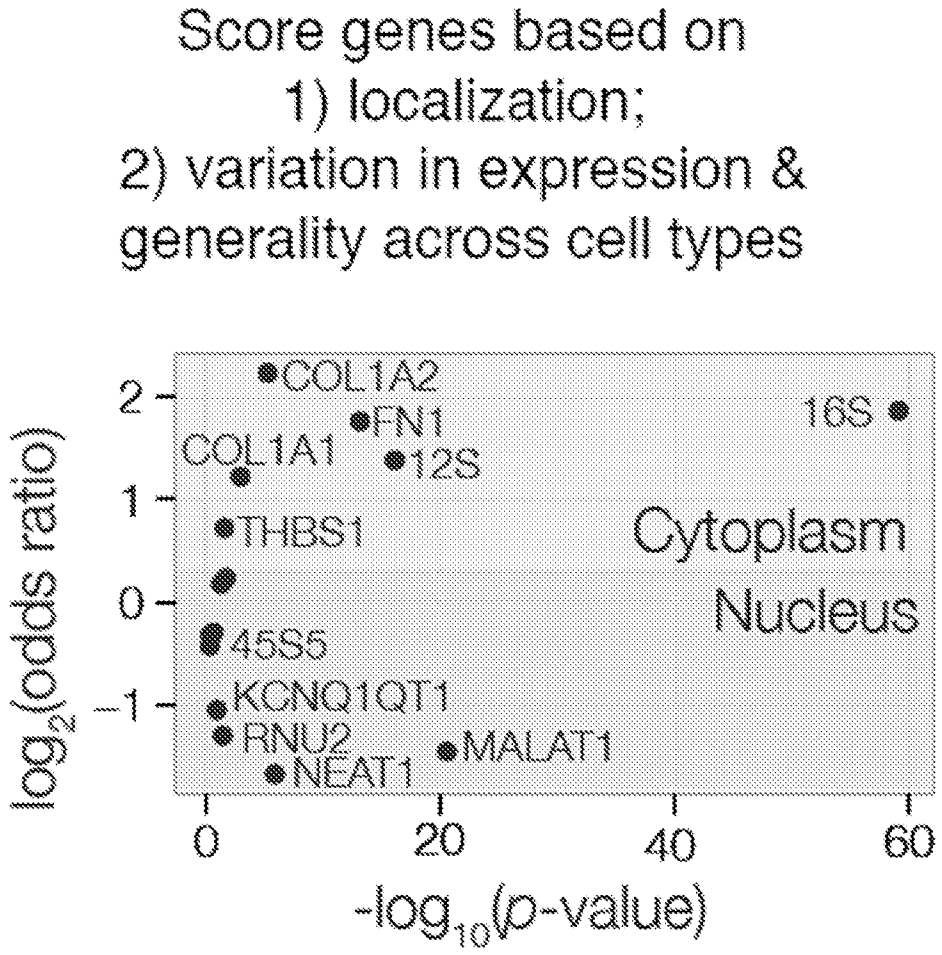

Score genes based on
1) localization;
2) variation in expression &
generality across cell types
COL1A2
FN1
COL1A1
12S
16S
THBS1
Cytoplasm
Nucleus
45S5
KCNQ1OT1
RNU2
NEAT1
MALAT1
2
1
0
−1
0
20
40
60
log2(odds ratio)
-log10(p-value)

FIG. 1C

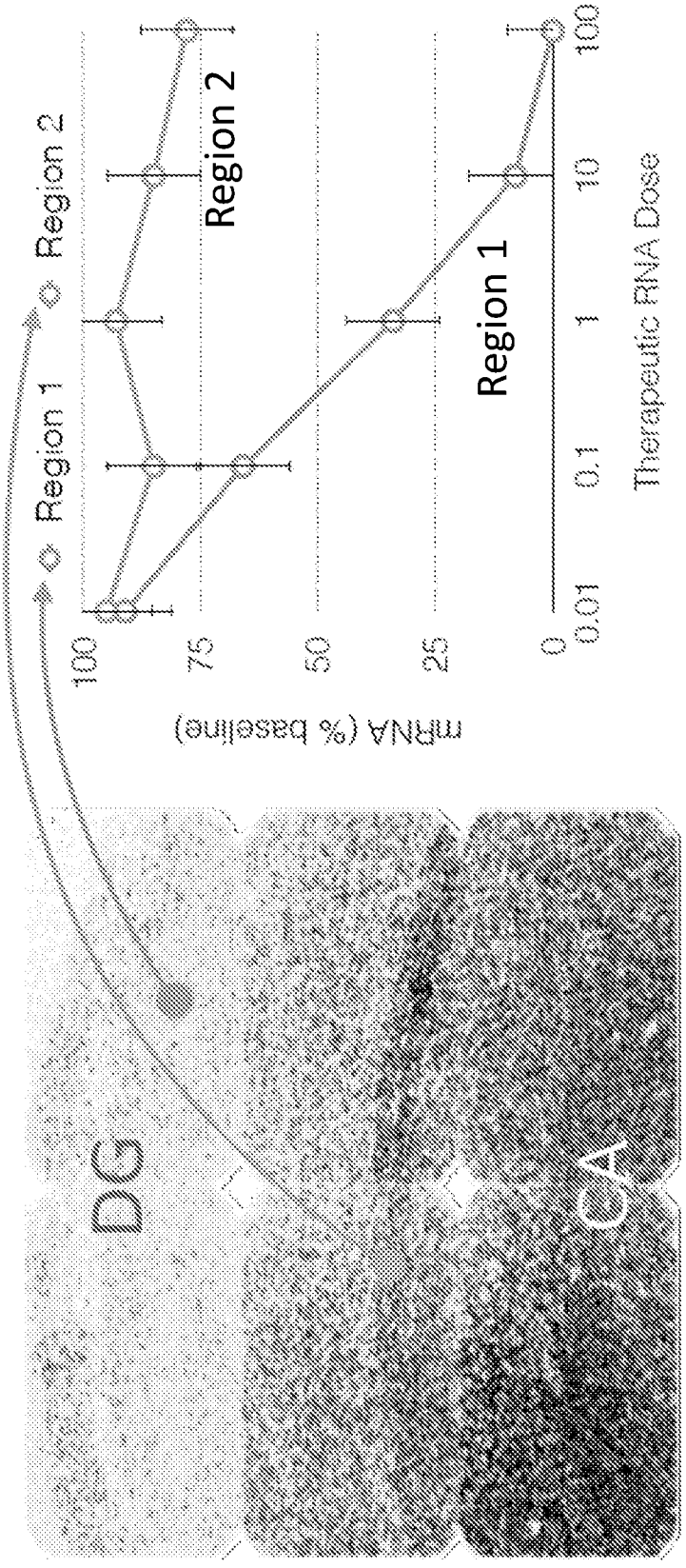

Region 2
Region 1
DG
CA1
CA3
mRNA (% baseline)
100
75
50
25
0
Region 2
Region 1
0.01
0.1
1
10
100
Therapeutic RNA Dose

FIG. 2A

FIG. 2B

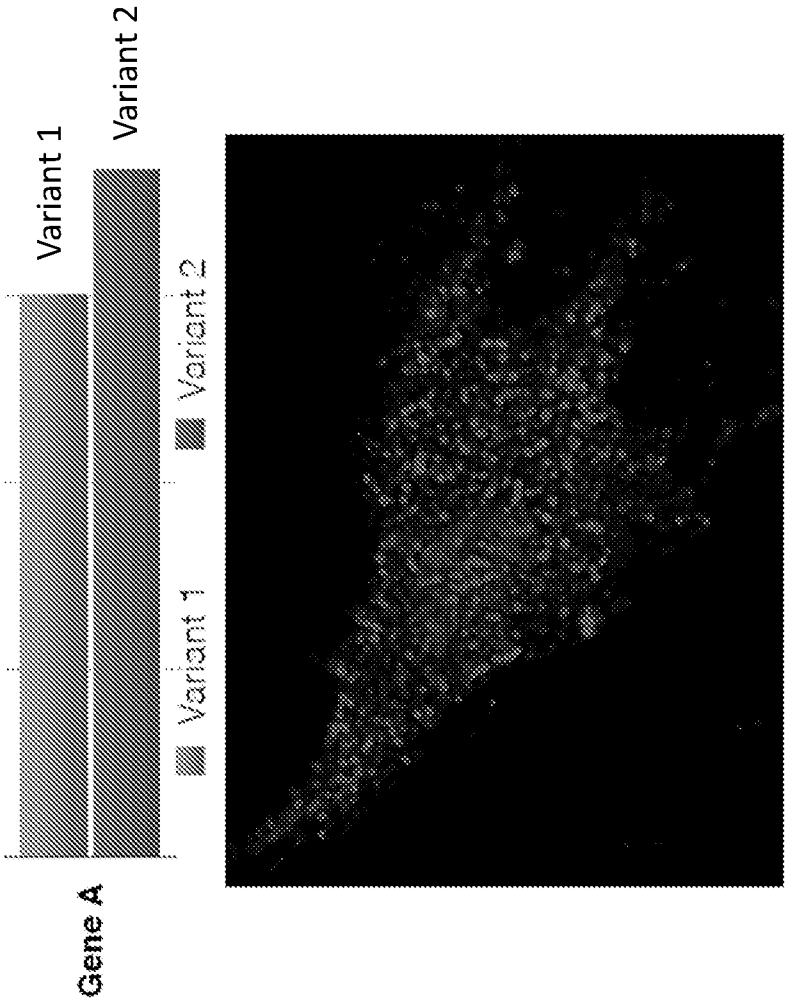

Variant 1
Variant 2
Variant 1
Variant 2
Gene A

FIG. 3B

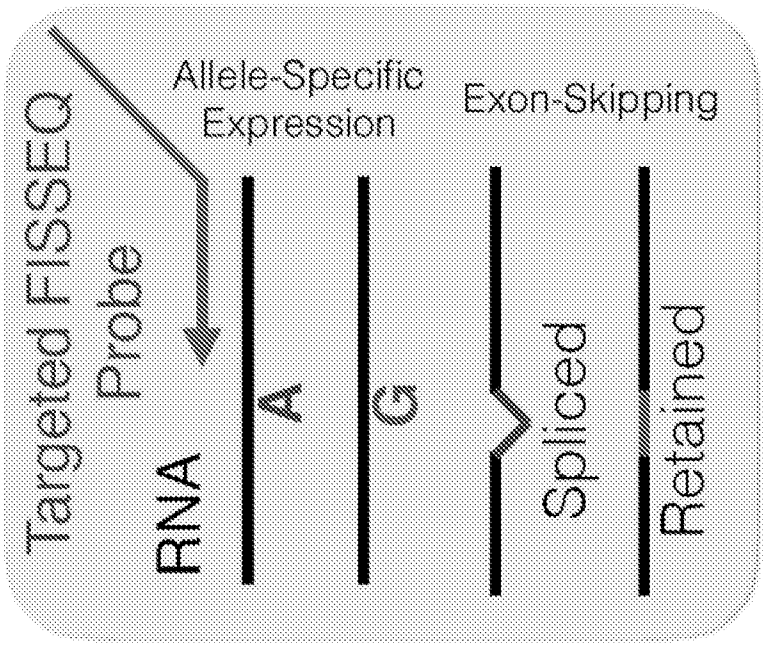

Targeted FISSEQ Probe
RNA
Allele-Specific Expression
A
G
Exon-Skipping
Spliced
Retained

FIG. 3A

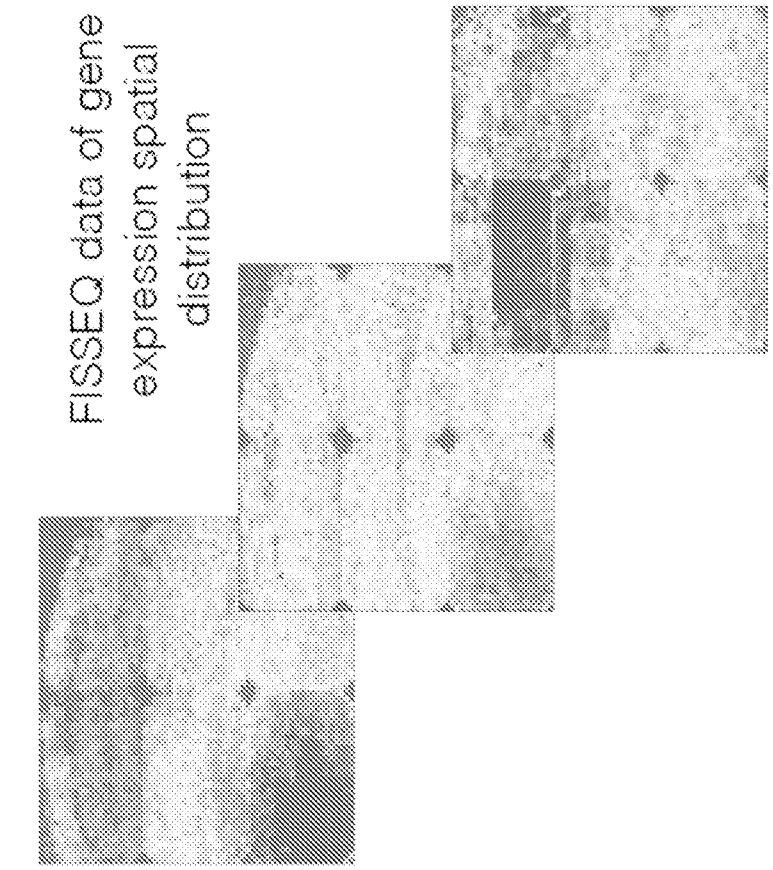

FISSEQ data of gene expression spatial distribution

FIG. 4B

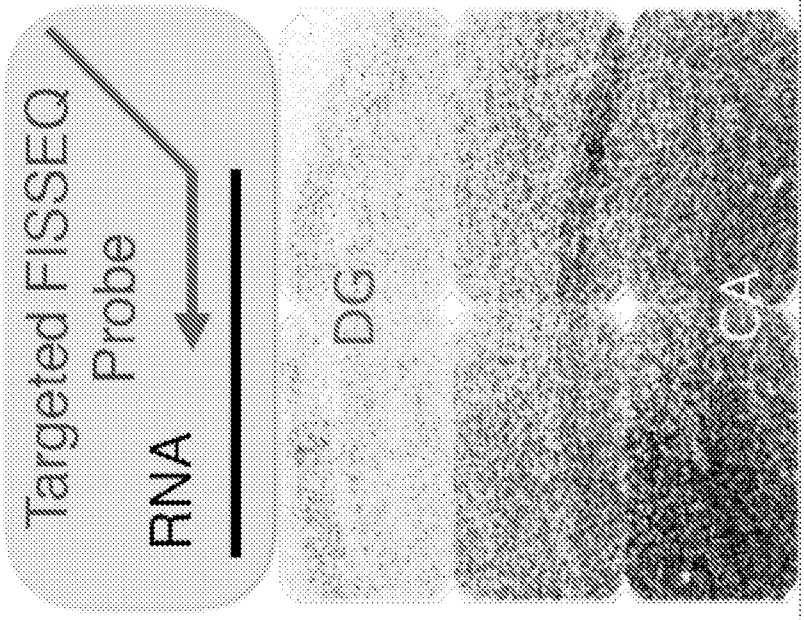

Targeted FISSEQ Probe
RNA
DG
CA

FIG. 4A

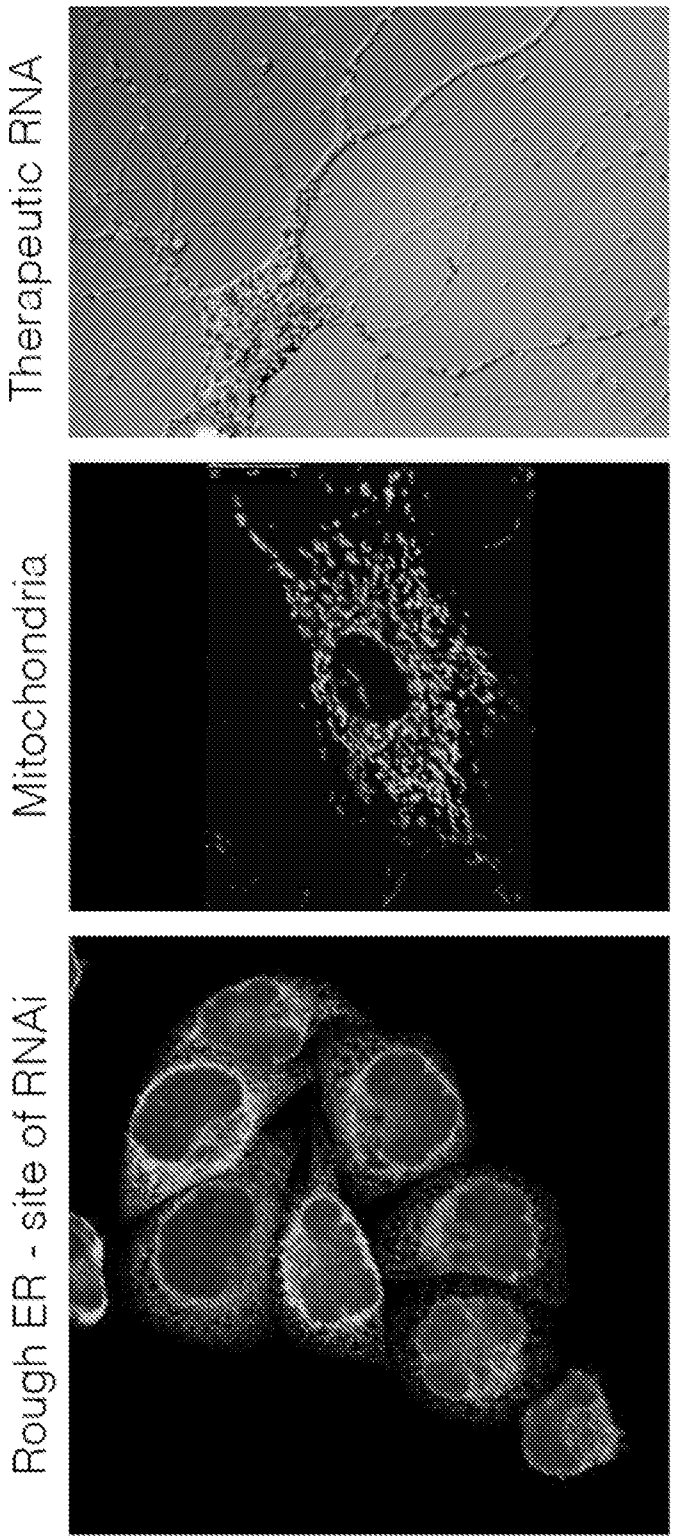


FIG. 5A *FIG. 5B* *FIG. 5C*



FIG. 6A



FIG. 6B

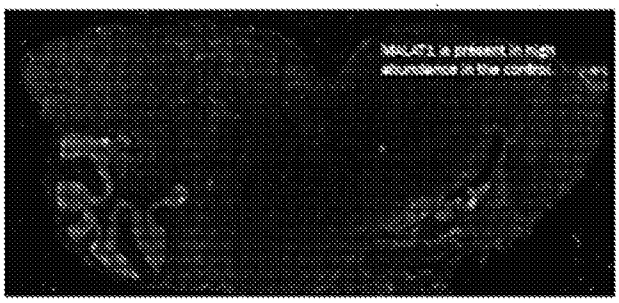


FIG. 6C

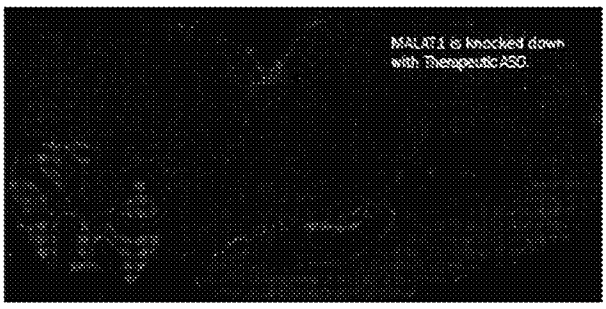


FIG. 6D

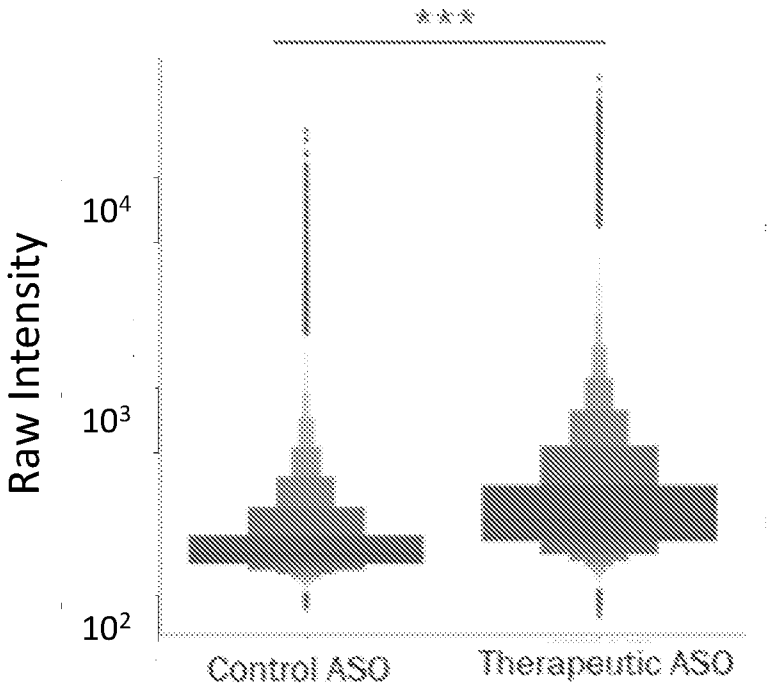

***
Raw Intensity
10⁴
10³
10²
Control ASO
Therapeutic ASO

FIG. 6E

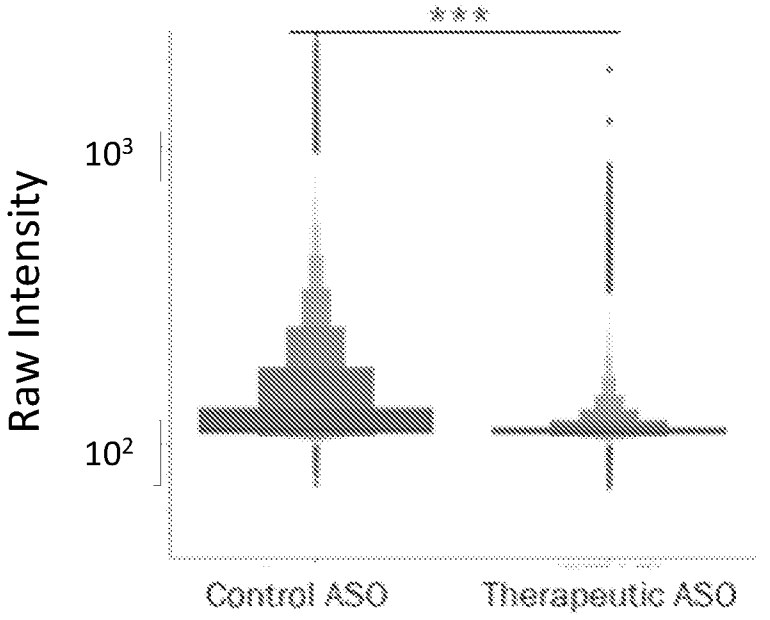

***
Raw Intensity
10³
10²
Control ASO
Therapeutic ASO

FIG. 6F

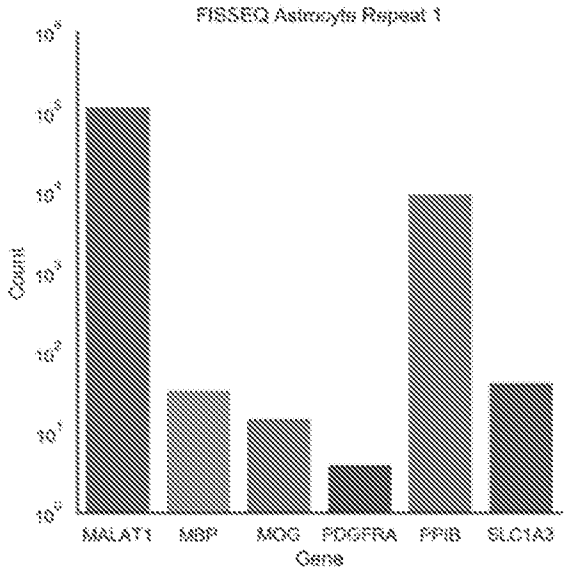


FIG. 7A

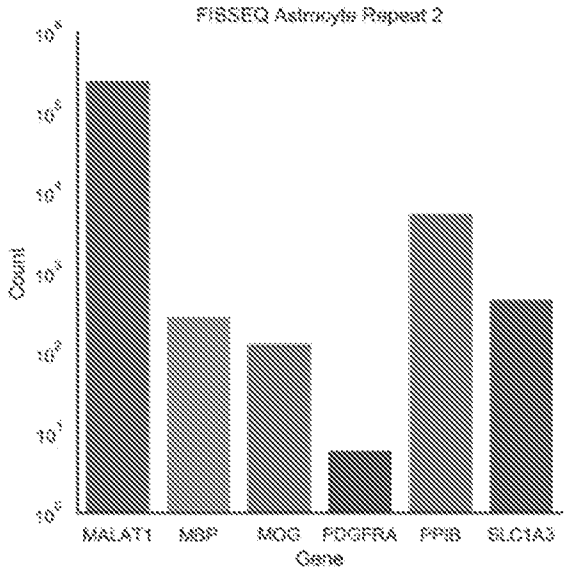


FIG. 7B

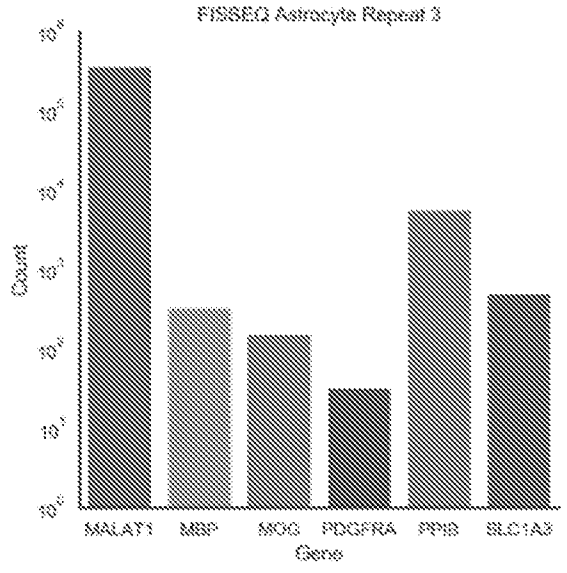


FIG. 7C

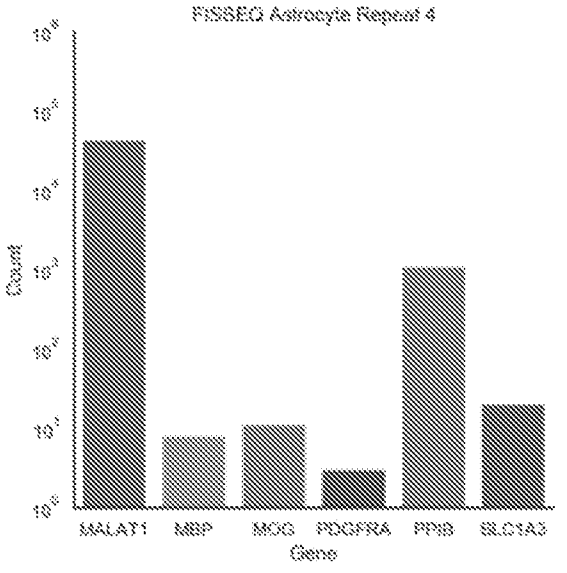


FIG. 7D

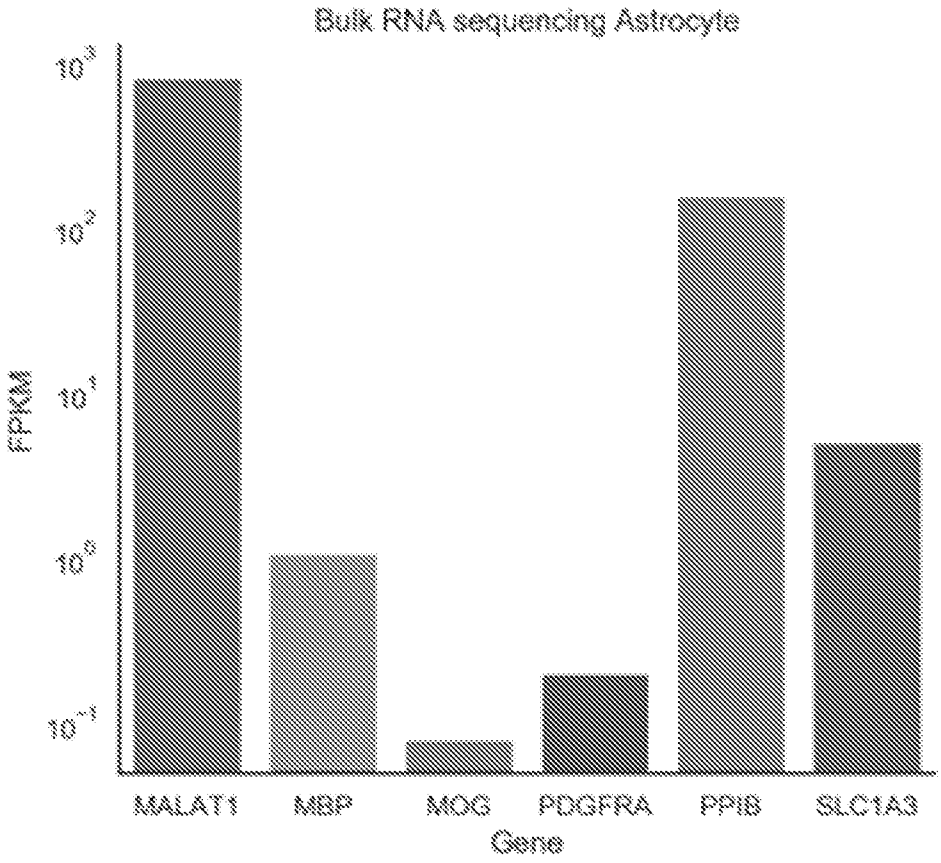

Bulk RNA sequencing Astrocyte
FPKM
10^{3}
10^{2}
10^{1}
10^{0}
10^{-1}
MALAT1
MBP
MOG
PDGFRA
PPIB
SLC1A3
Gene

FIG. 7E

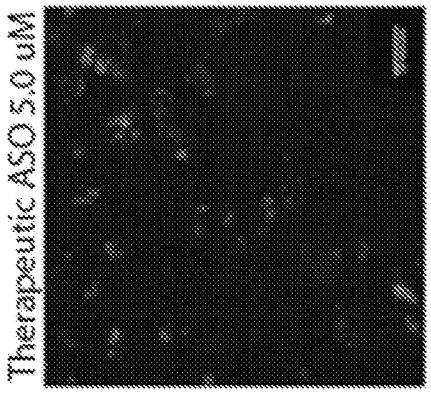


FIG. 8D

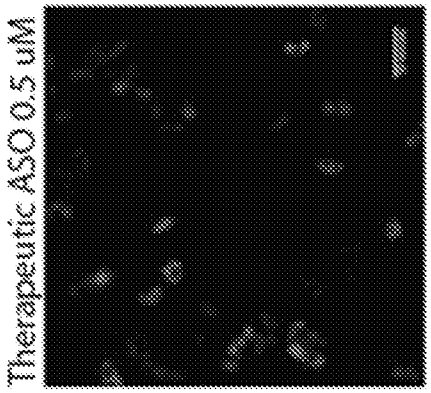


FIG. 8C

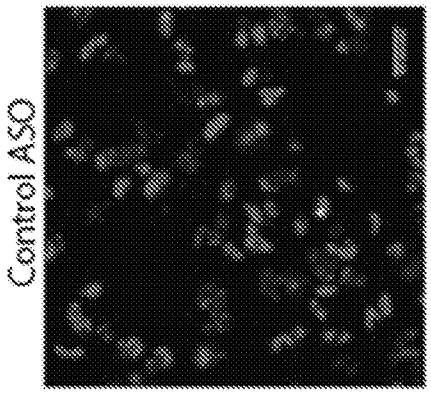


FIG. 8B

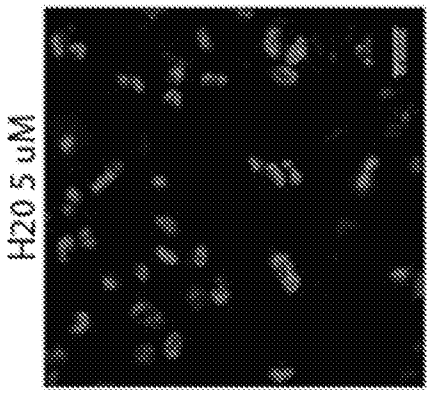


FIG. 8A

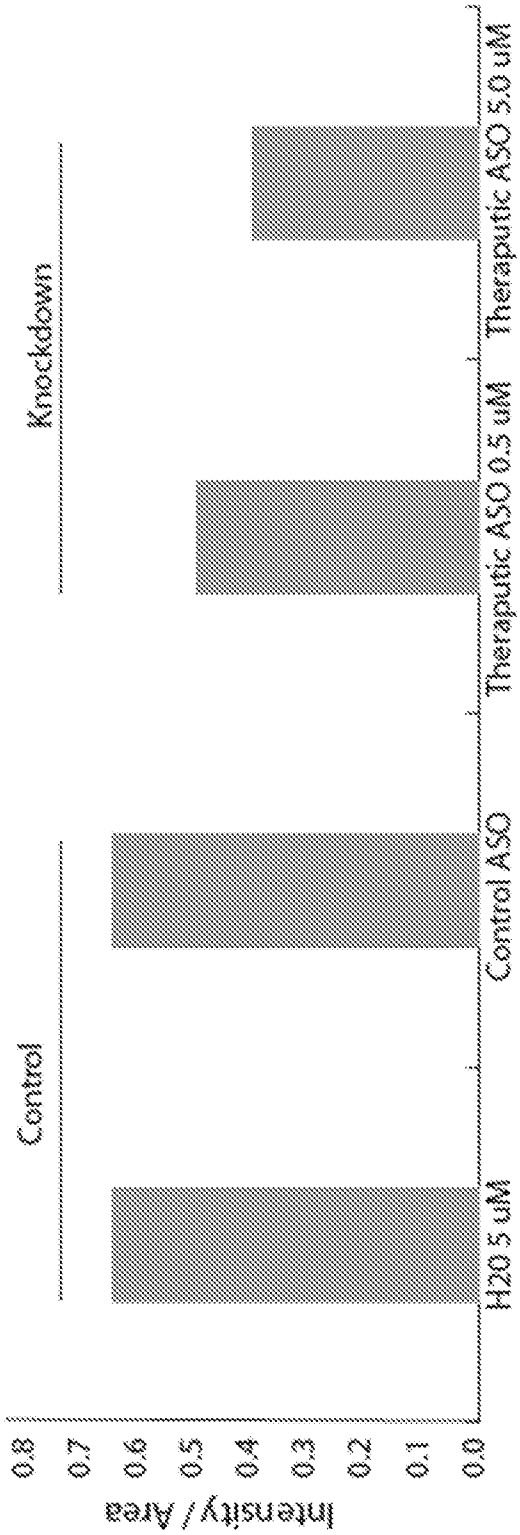

Intensity / Area
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
Control
Knockdown
H20 5 uM
Control ASO
Theraputic ASO 0.5 uM
Theraputic ASO 5.0 uM

FIG. 8E

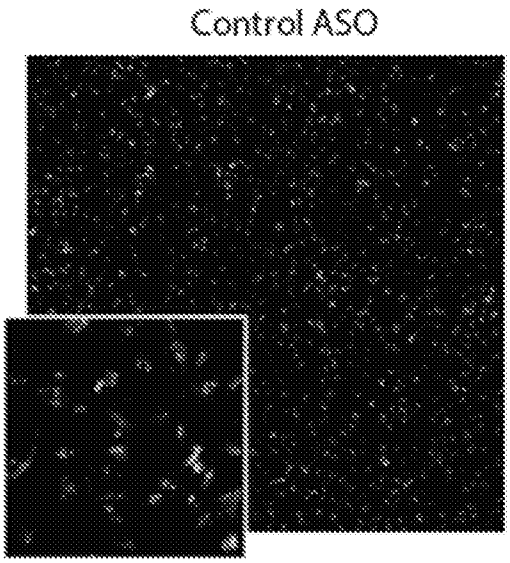


FIG. 9A

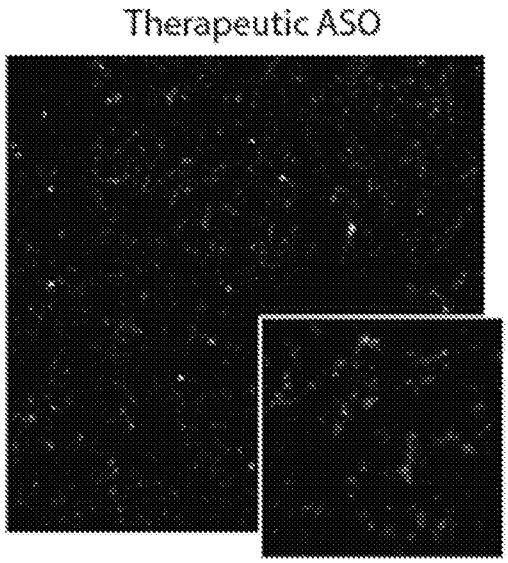


FIG. 9B

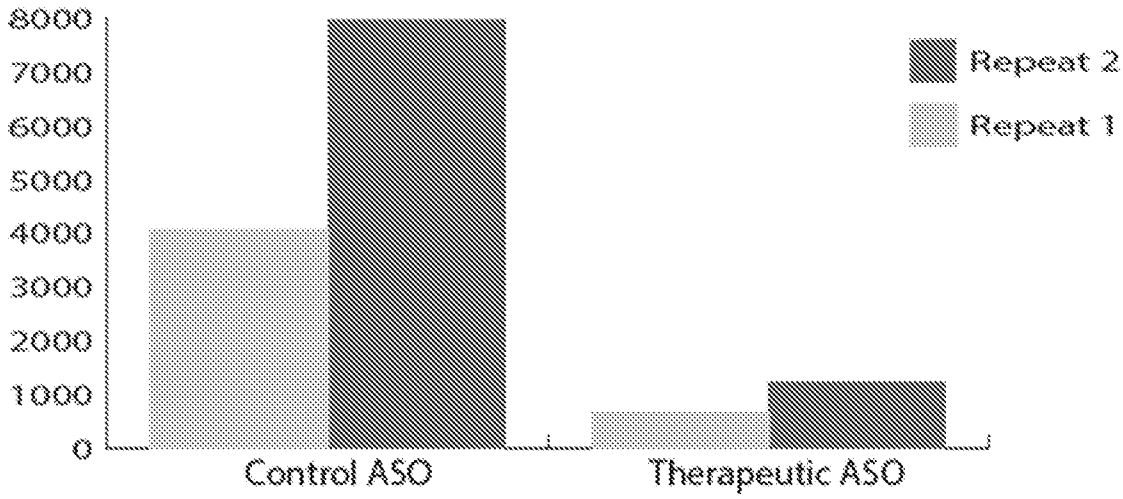


FIG. 9C

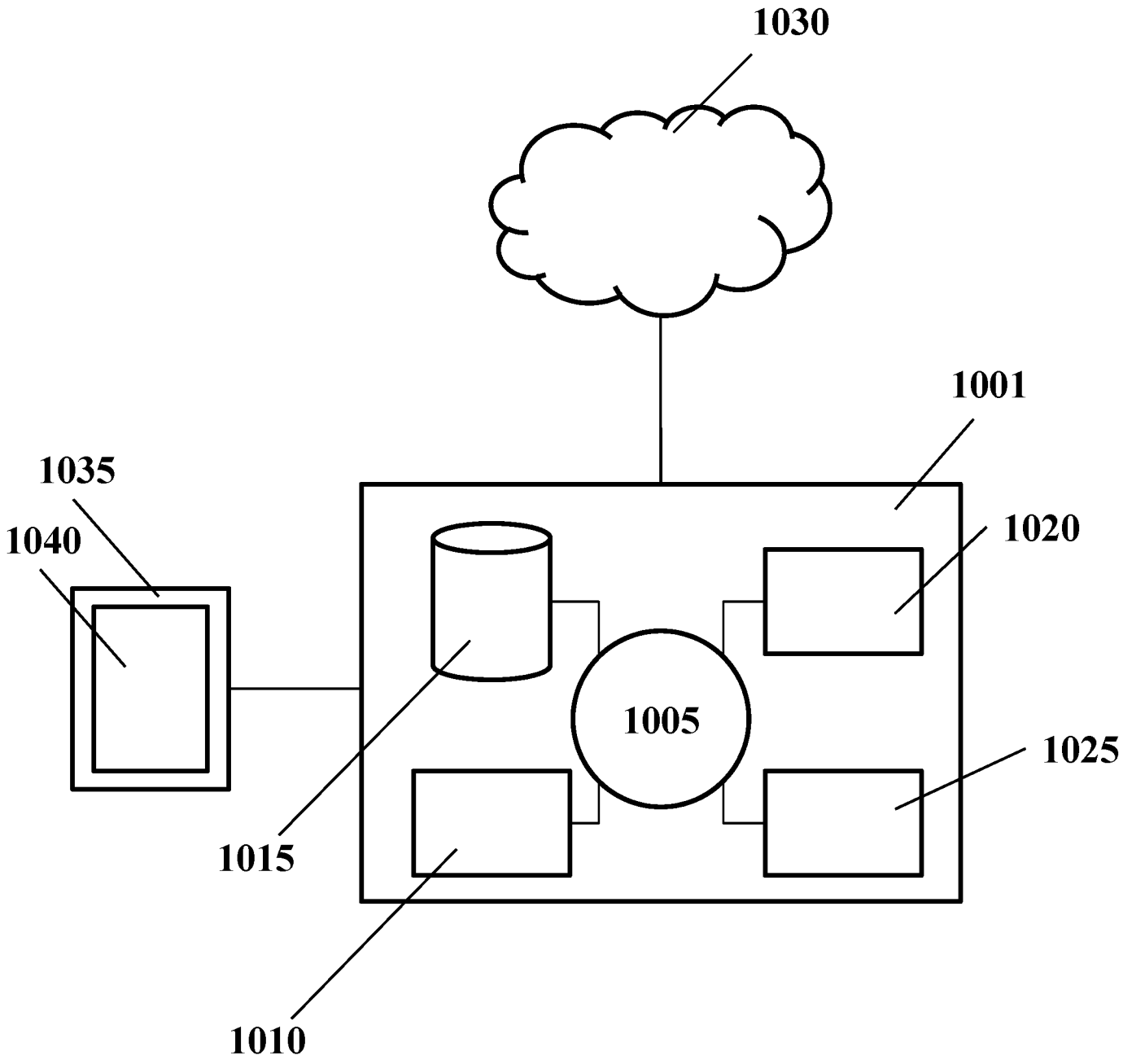


FIG. 10