```
AAV5     MSFVDHPPDWLEE-VGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNGLD  59
AAV2     MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLD  60
AAV9     MAADGYLPDWLEDNLSEGIREWWALKPGAPQPKANQQHQDNARGLVLPGYKYLGPGNGLD  60
AAV8     MAADGYLPDWLEDNLSEGIREWWALKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD  60
AAVrh74  MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDNGRGLVLPGYKYLGPFNGLD  60

AAV5     RGEPVNRADEVAREHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLGKAVFQ  119
AAV2     KGEPVNEADAAALEHDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ  120
AAV9     KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ  120
AAV8     KGEPVNAADAAALEHDKAYDQQLQAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ  120
AAVrh74  KGEPVNAADAAALEHDKAYDQQLQAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ  120

AAV5     AKKRVLEPFGLVEEGAKTAPTGKRIDDHFPKRKKARTEEDSK----PS-------TSSDA  168
AAV2     AKKRVLEPLGLVEEPVKTAPGKKRPVEHSPV-EPDSSSGTGKAGQQPARKRLNFGQTGDA  179
AAV9     AKKRLLEPLGLVEEAAKTAPGKKRPVEQSPQ-EPDSSAGIGKSGAQPAKKRLNFGQTGDT  179
AAV8     AKKRVLEPLGLVEEGAKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPARKRLNFGQTGDS  180
AAVrh74  AKKRVLEPLGLVESPVKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPAKKRLNFGQTGDS  180

AAV5     EAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDR  228
AAV2     DS-VPDPQPLGQPPAAPSGLGTNTMATGSGAPMADNNEGADGVGNSSGNWHCDSTWMGDR  238
AAV9     ES-VPDPQPIGEPPAAPSGVGSLTMASGGGAPVADNNEGADGVGSSSGNWHCDSQWLGDR  238
AAV8     ES-VPDPQPLGEPPAAPSGVGPNTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR  239
AAVrh74  ES-VPDPQPIGEPPAGPSGLGSGTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR  239

AAV5     VVTKSTRTWVLPSYNNHQYREIKSGSVDG-SNANAYFGYSTPWGYFDFNRFHSHWSPRDW  287
AAV2     VITTSTRTWALPTYNNHLYKQISS--QSGASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW  296
AAV9     VITTSTRTWALPTYNNHLYKQISNSTSGGSSNDNAYFGYSTPWGYFDFNRFHCHFSPRDW  298
AAV8     VITTSTRTWALPTYNNHLYKQISNGTSGGATNDNTYFGYSTPWGYFDFNRFHCHFSPRDW  299
AAVrh74  VITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDW  299

AAV5     QRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGN  347
AAV2     QRLINNNWGFRPKRLNFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS  356
AAV9     QRLINNNWGFRPKRLNFKLFNIQVKEVTDNNGVKTIANNLTSTVQVFTDSDYQLPYVLGS  358
AAV8     QRLINNNWGFRPKRLSFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS  359
AAVrh74  QRLINNNWGFRPKRLNFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS  359
```

FIG. 1A

```
AAV5      GTEGCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYN  407
AAV2      AHQGCLPPFPADVFMVPQYGYLTLNNG--SQAVGRSSFYCLEYFPSQMLRTGNNFTFSYT  414
AAV9      AHEGCLPPFPADVFMIPQYGYLTLNDG--SQAVGRSSFYCLEYFPSQMLRTGNNFQFSYE  416
AAV8      AHQGCLPPFPADVFMIPQYGYLTLNNG--SQAVGRSSFYCLEYFPSQMLRTGNNFQFTYT  417
AAVrh74   AHQGCLPPFPADVFMIPQYGYLTLNNG--SQAVGRSSFYCLEYFPSQMLRTGNNFEFSYN  417

AAV5      FEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGGVQ------FNKNLAGRYANTY  461
AAV2      FEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTNTPSGTTTQSRLQFSQAGASDIRDQS  474
AAV9      FENVPFHSSYAHSQSLDRLMNPLIDQYLYYLSKTIN-GSGQNQQTLKFSVAGPSNMAVQG  475
AAV8      FEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQTTGGTANTQTLGFSQGGPNTMANQA  477
AAVrh74   FEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQSTGGTAGTQQLLFSQAGPNNMSAQA  477

AAV5      KNWFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSNTY  521
AAV2      RNWLPGPCYRQQRVSKTSADNNNSEYSWTGATKYHLNGRDSLVNPGPAMASHKDDEEKFF  534
AAV9      RNYIPGPSYRQQRVSTTVTQNNNSEFAWPGASSWALNGRNSLMNPGPAMASHKEGEDRFF  535
AAV8      KNWLPGPCYRQQRVSTTTGQNNNSNFAWTAGTKYHLNGRNSLANPGIAMATHKDDEERFF  537
AAVrh74   KNWLPGPCYRQQRVSTTLSQNNNSNFAWTGATKYHLNGRDSLVNPGVAMATHKDDEERFF  537

AAV5      ALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSSTTAPA  581
AAV2      PQSGVLIFGKQGSEKTN---VDIEKVMITDEEEIRTTNPVATEQYGSVSTNLQRGNRQAA  591
AAV9      RLSGSLIFGKQGTGRDN---VDADKVMITNEEEIKTTNPVATESYGQVATNHQSAQAQAQ  592
AAV8      PSNGLLIFGKQNAARDN---ADYSDVMLTSEEEIKTTNPVATEEYGIVADNLQQQNTAPQ  594
AAVrh74   PSSGVLMFGKQGAGKDN---VDYSSVMLTSEEEIKTTNPVATEQYGVVADNLQQQNAAPI  594
```

FIG. 1B

```
AAV5      TGTYNLQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPMMLIKNT  641
AAV2      TADVNTQGVLPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHPPPQILIKNT  651
AAV9      TGWVQNQGILPGMVWQDRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGMKHPPPQILIKNT  652
AAV8      IGTVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKHPPPQILIKNT  654
AAVrh74   VGAVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKHPPPQILIKNT  654

AAV5      PVPGNI-TSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVD  700
AAV2      PVPANPSTTFSAAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNYNKSVNVD  711
AAV9      PVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNYYKSNNVE  712
AAV8      PVPADPPTTFNQSKLNSFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNYYKSTSVD  714
AAVrh74   PVPADPPTTFNQAKLASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNYYKSTNVD  714

AAV5      FAPDSTGEYRTTRPIGTRYLTRPL                                       724
AAV2      FTVDTNGVYSEPRPIGTRYLTRNL                                       735
AAV9      FAVNTEGVYSEPRPIGTRYLTRNL                                       736
AAV8      FAVNTEGVYSEPRPIGTRYLTRNL                                       738
AAVrh74   FAVNTEGTYSEPRPIGTRYLTRNL                                       738
```

FIG. 1C

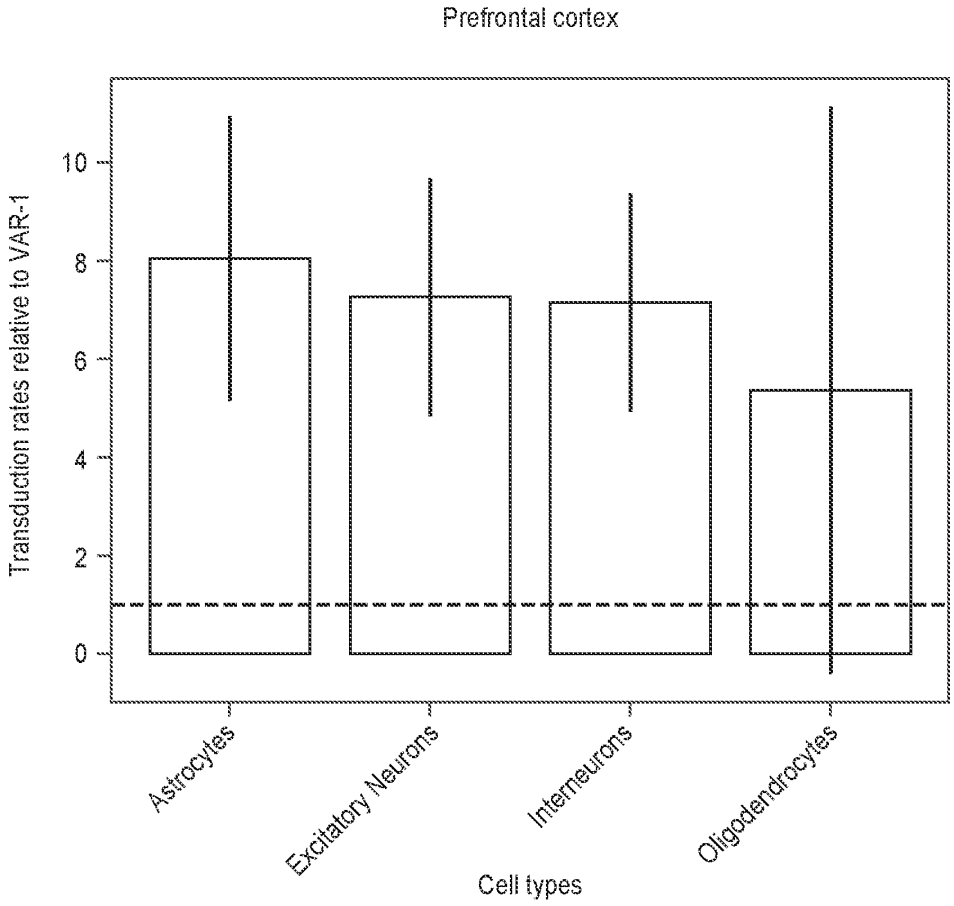

Prefrontal cortex
Transduction rates relative to VAR-1
0
2
4
6
8
10
Astrocytes
Excitatory Neurons
Interneurons
Oligodendrocytes
Cell types

FIG. 2

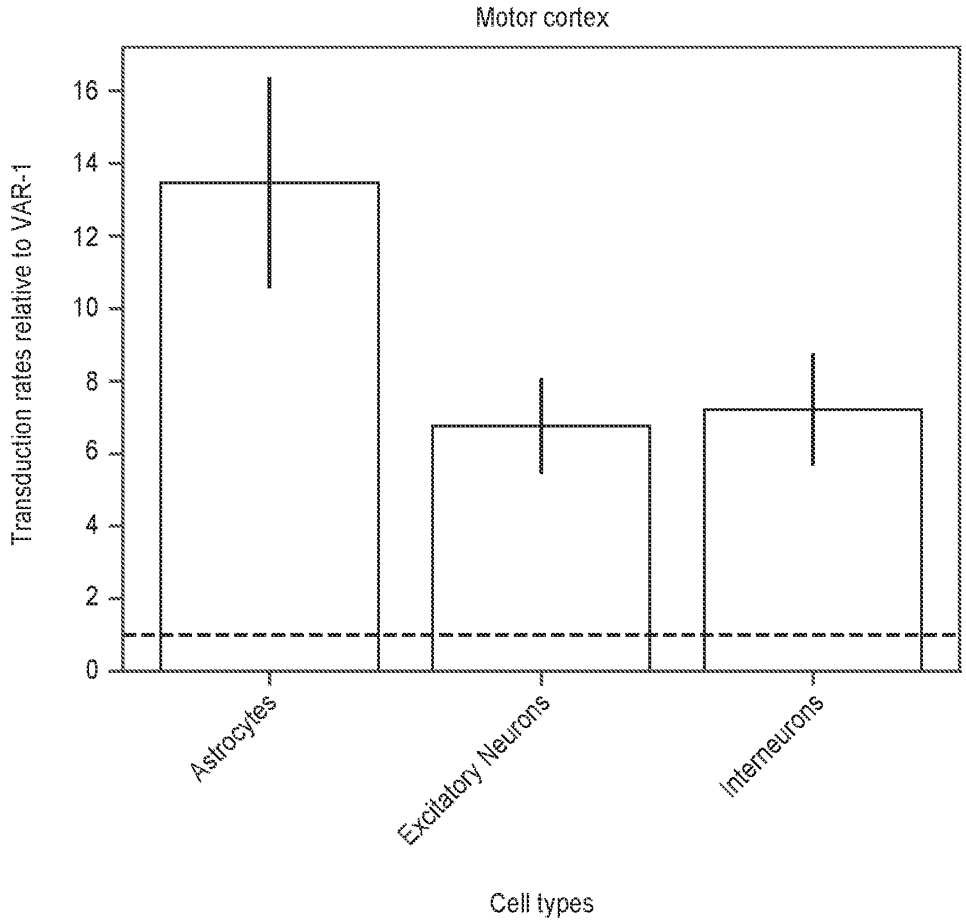

Motor cortex
Transduction rates relative to VAR-1
16
14
12
10
8
6
4
2
0
Astrocytes
Excitatory Neurons
Interneurons
Cell types

FIG. 3

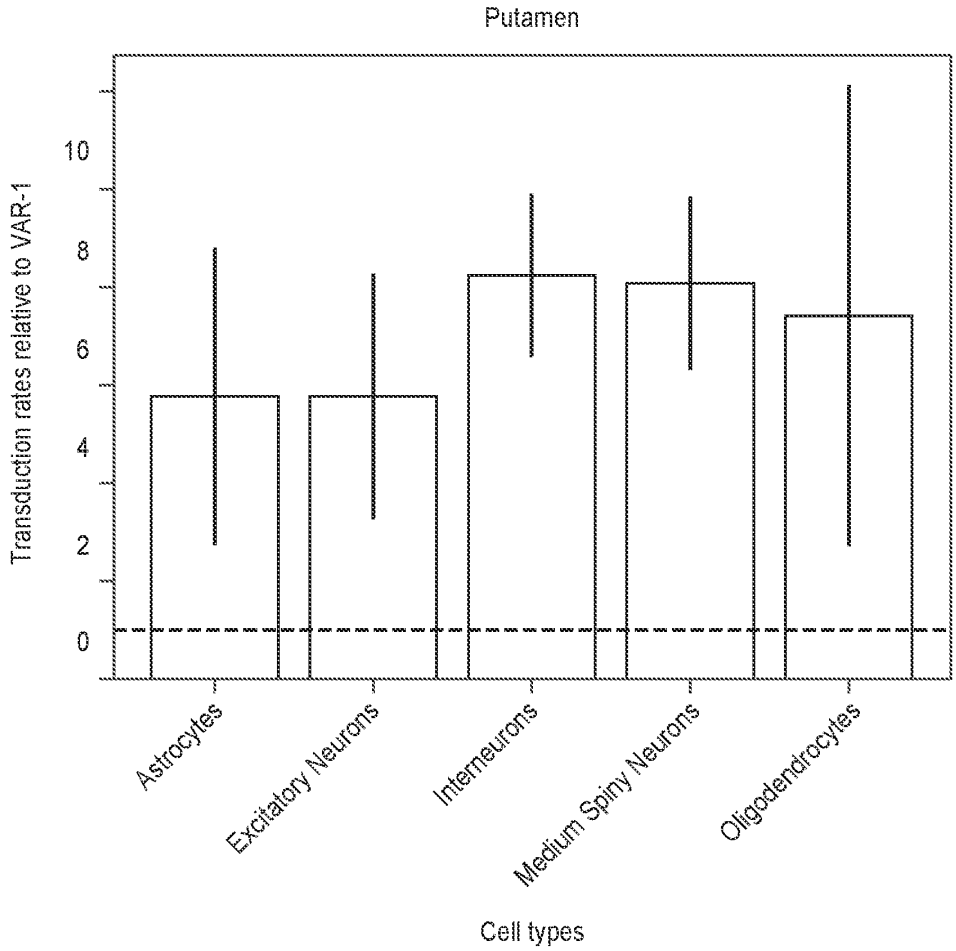

Putamen
Transduction rates relative to VAR-1
0
2
4
6
8
10
Astrocytes
Excitatory Neurons
Interneurons
Medium Spiny Neurons
Oligodendrocytes
Cell types

FIG. 4

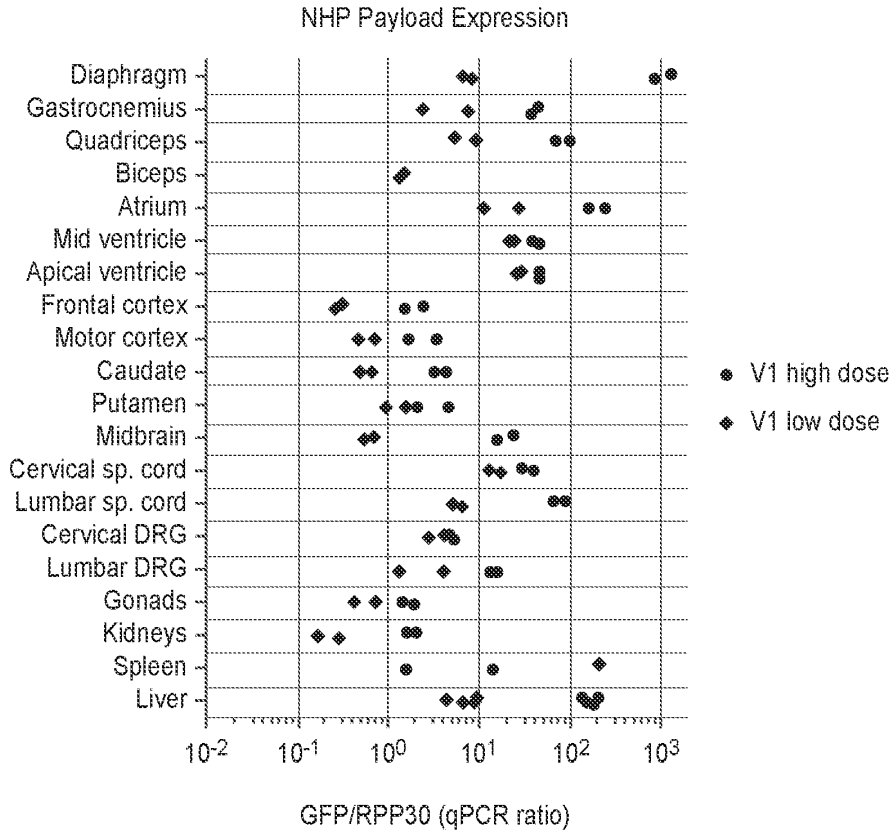

NHP Payload Expression
Diaphragm
Gastrocnemius
Quadriceps
Biceps
Atrium
Mid ventricle
Apical ventricle
Frontal cortex
Motor cortex
Caudate
Putamen
Midbrain
Cervical sp. cord
Lumbar sp. cord
Cervical DRG
Lumbar DRG
Gonads
Kidneys
Spleen
Liver
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}
GFP/RPP30 (qPCR ratio)
V1 high dose
V1 low dose

FIG. 5A

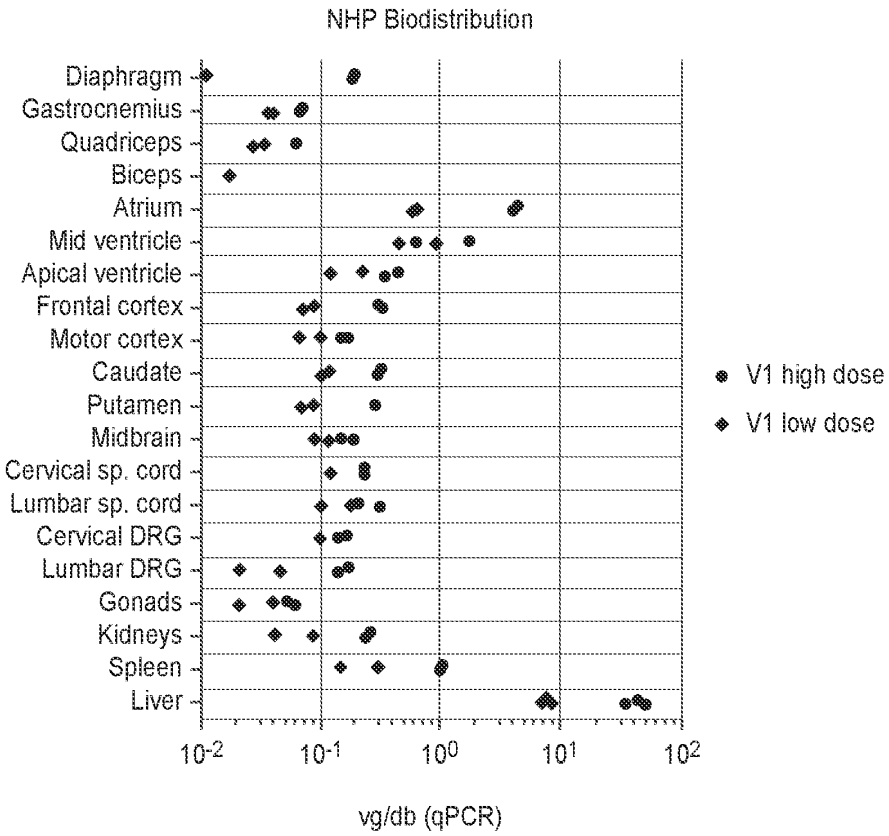

NHP Biodistribution
Diaphragm
Gastrocnemius
Quadriceps
Biceps
Atrium
Mid ventricle
Apical ventricle
Frontal cortex
Motor cortex
Caudate
Putamen
Midbrain
Cervical sp. cord
Lumbar sp. cord
Cervical DRG
Lumbar DRG
Gonads
Kidneys
Spleen
Liver
10-2
10-1
100
101
102
vg/db (qPCR)
V1 high dose
V1 low dose

FIG. 5B

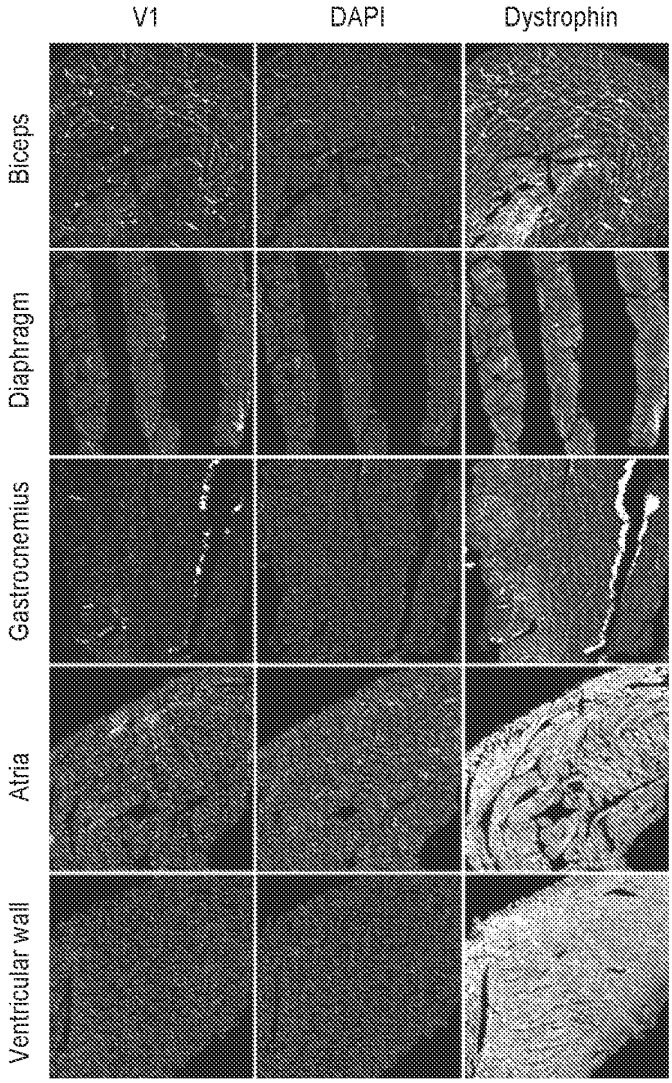

V1
DAPI
Dystrophin
Biceps
Diaphragm
Gastrocnemius
Atria
Ventricular wall

FIG. 6A

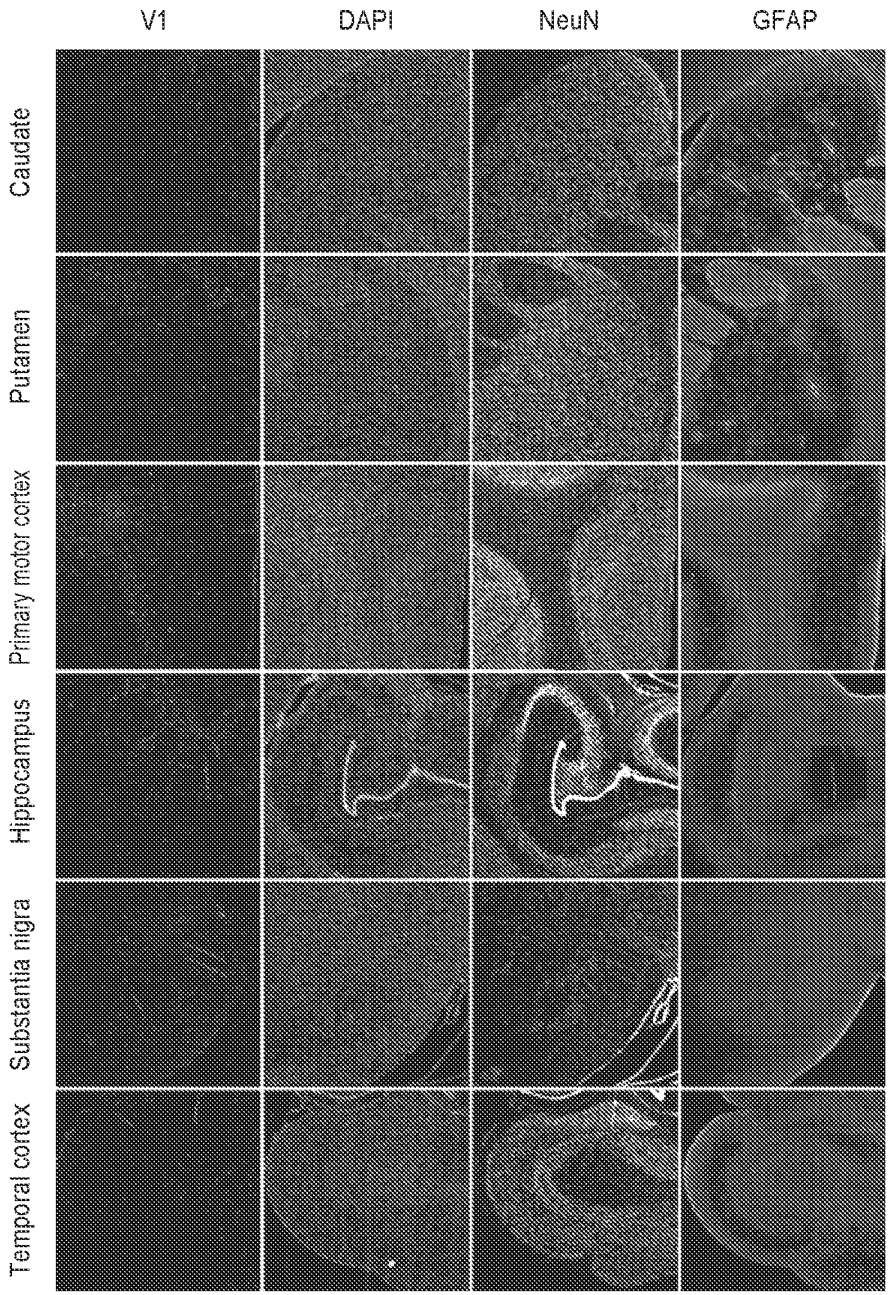

V1
DAPI
NeuN
GFAP
Caudate
Putamen
Primary motor cortex
Hippocampus
Substantia nigra
Temporal cortex

FIG. 6B

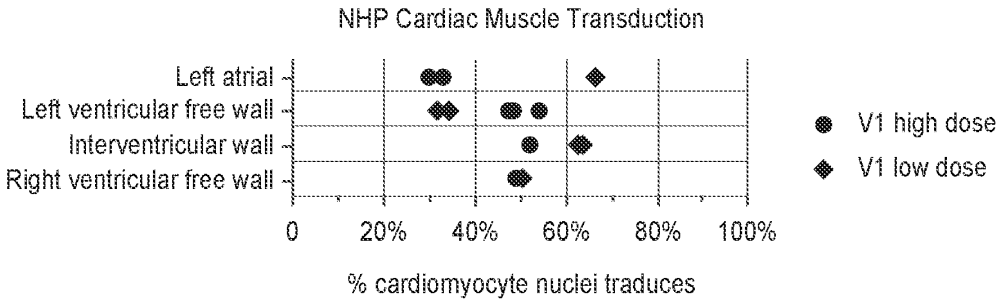

NHP Cardiac Muscle Transduction
Left atrial
Left ventricular free wall
Interventricular wall
Right ventricular free wall
0
20%
40%
60%
80%
100%
% cardiomyocyte nuclei traduces
V1 high dose
V1 low dose

FIG. 6C

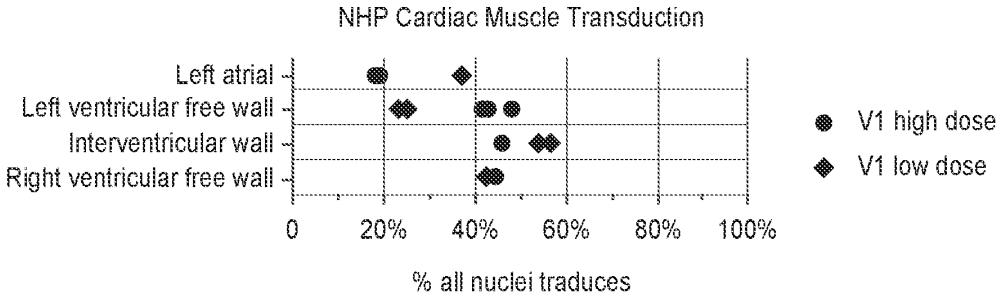

NHP Cardiac Muscle Transduction
Left atrial
Left ventricular free wall
Interventricular wall
Right ventricular free wall
0
20%
40%
60%
80%
100%
% all nuclei traduces
V1 high dose
V1 low dose

FIG. 6D

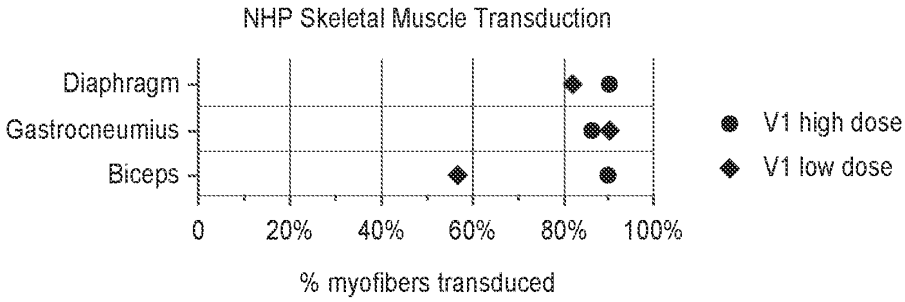

NHP Skeletal Muscle Transduction
Diaphragm
Gastrocneumius
Biceps
0
20%
40%
60%
80%
100%
% myofibers transduced
V1 high dose
V1 low dose

FIG. 6E

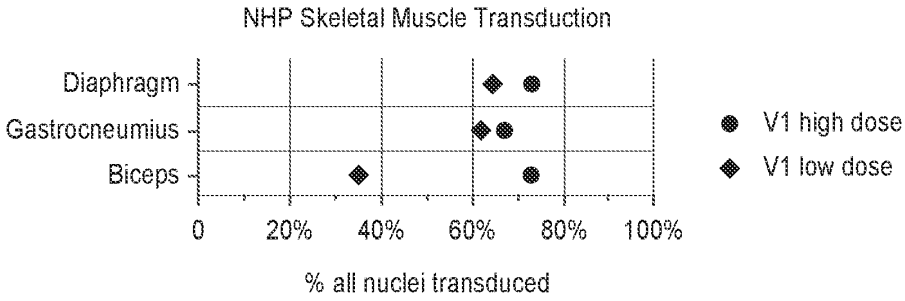

NHP Skeletal Muscle Transduction
Diaphragm
Gastrocneumius
Biceps
0
20%
40%
60%
80%
100%
% all nuclei transduced
V1 high dose
V1 low dose

FIG. 6F

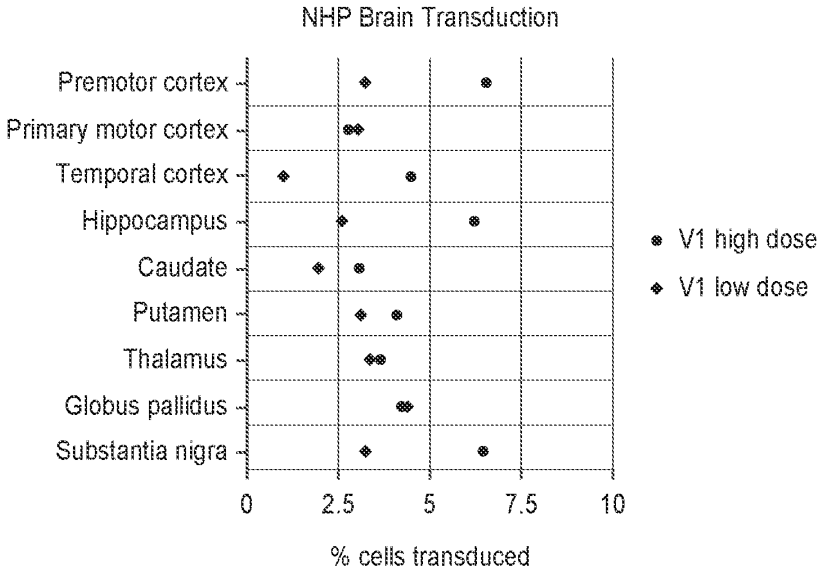

NHP Brain Transduction
Premotor cortex
Primary motor cortex
Temporal cortex
Hippocampus
Caudate
Putamen
Thalamus
Globus pallidus
Substantia nigra
0
2.5
5
7.5
10
% cells transduced
V1 high dose
V1 low dose

FIG. 6G

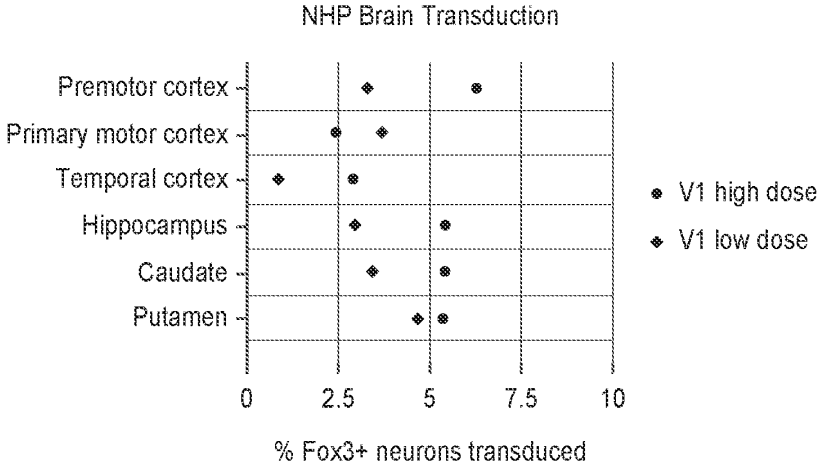

NHP Brain Transduction
Premotor cortex
Primary motor cortex
Temporal cortex
Hippocampus
Caudate
Putamen
0
2.5
5
7.5
10
% Fox3+ neurons transduced
V1 high dose
V1 low dose

FIG. 6H