

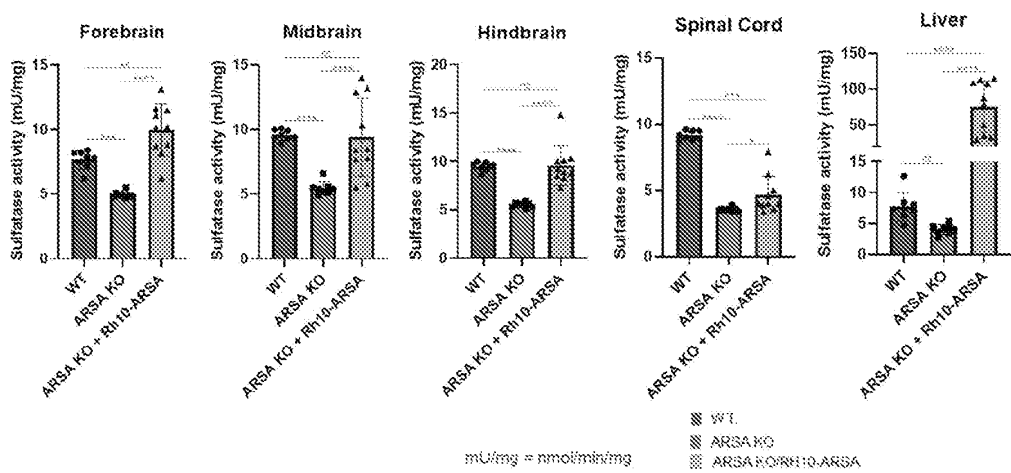


FIG. 2

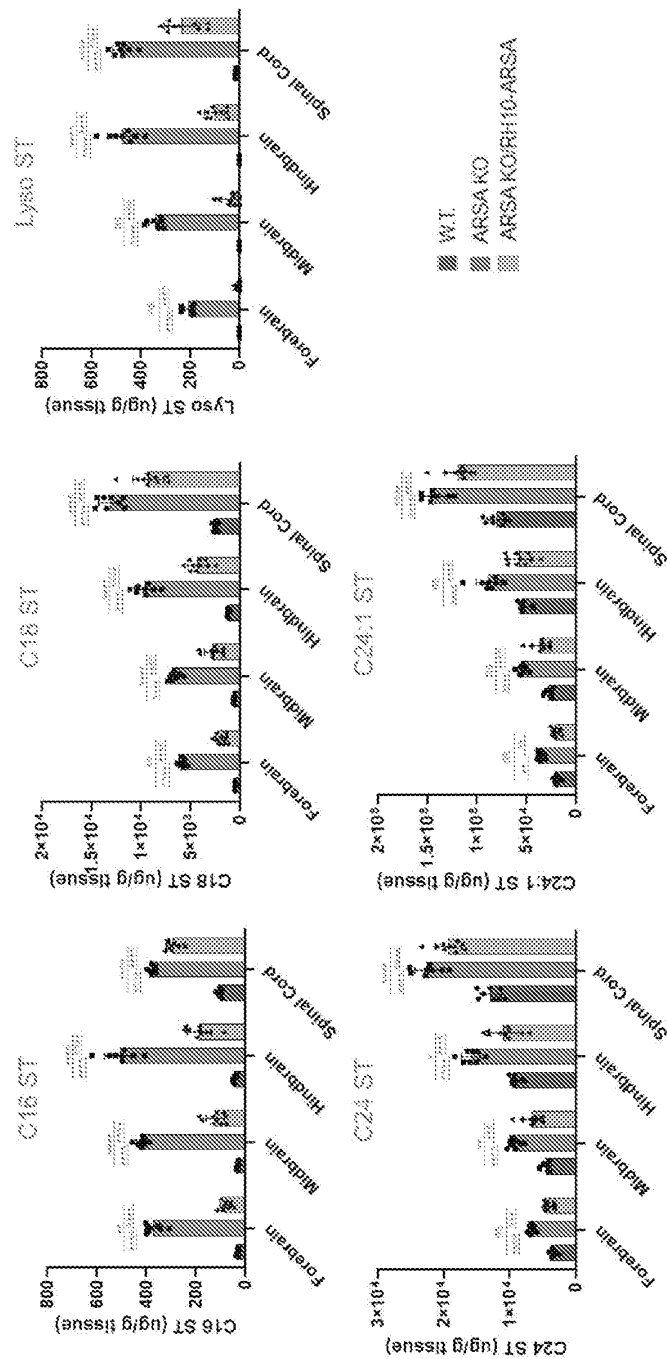


FIG. 3

FIG. 4

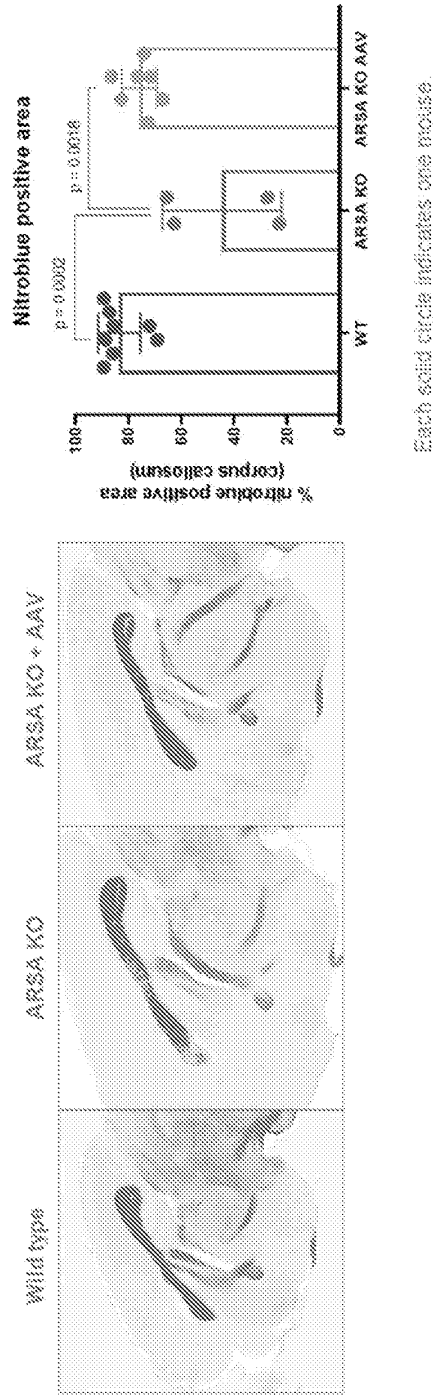


FIG. 5

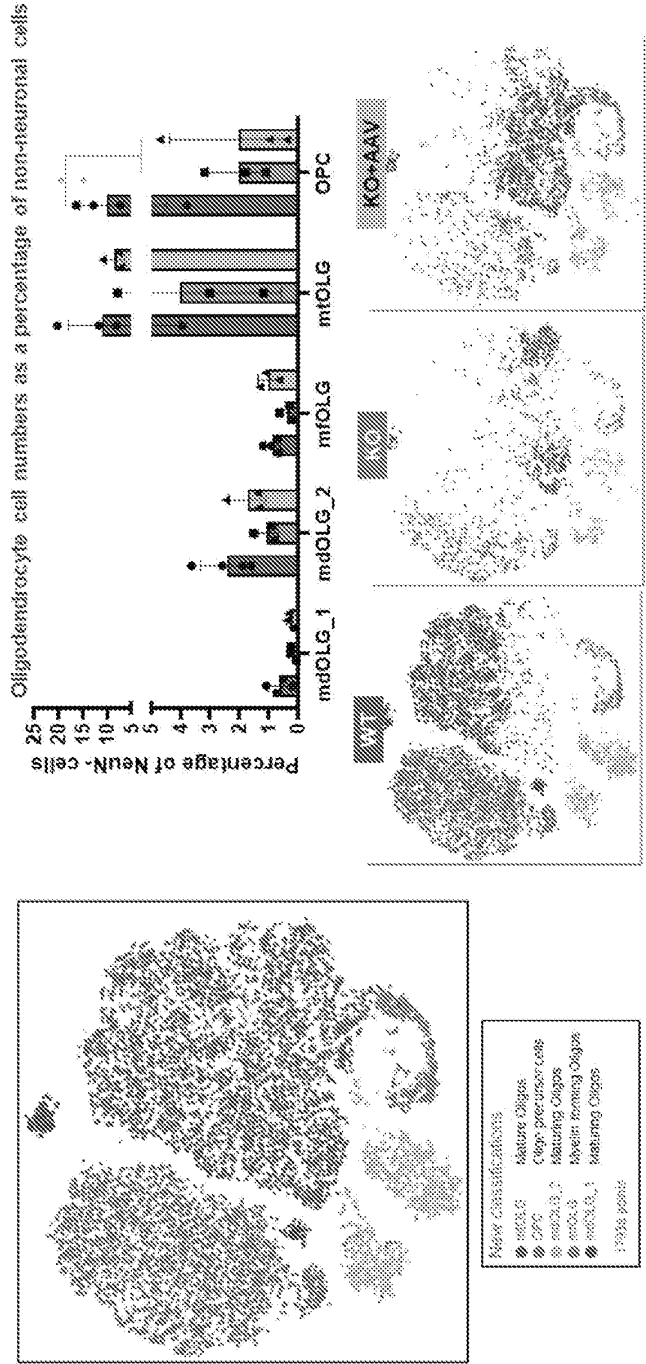


FIG. 6A

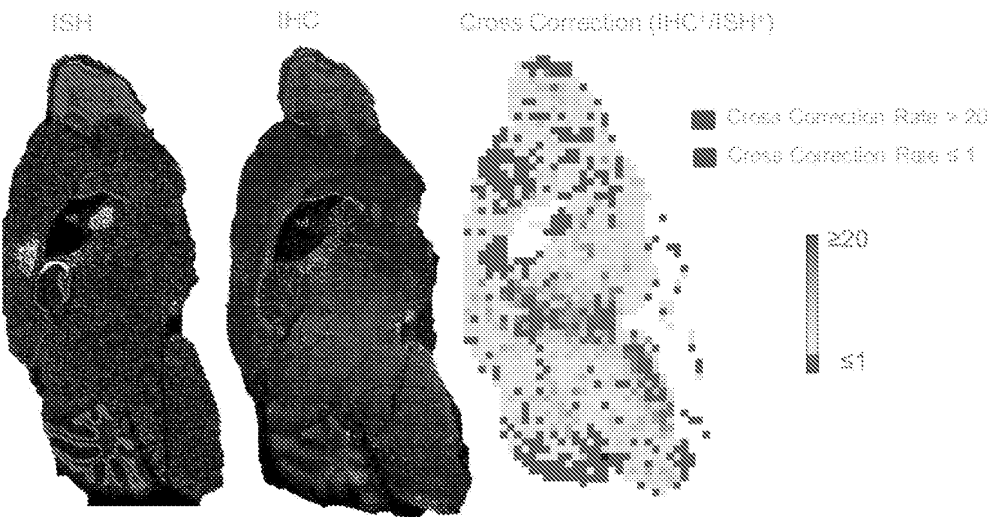


FIG. 6B

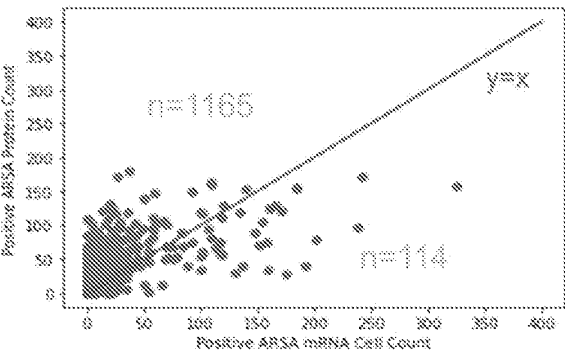


FIG. 7A

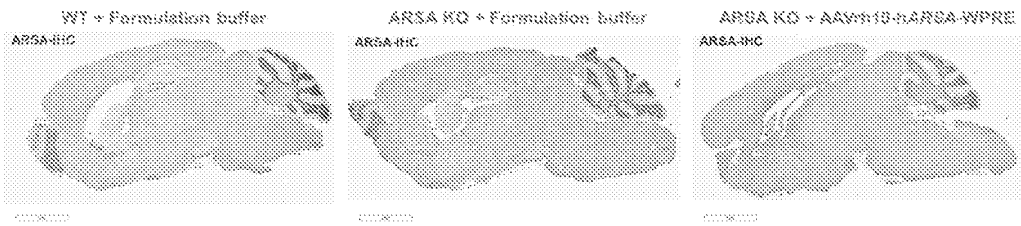


FIG. 7B

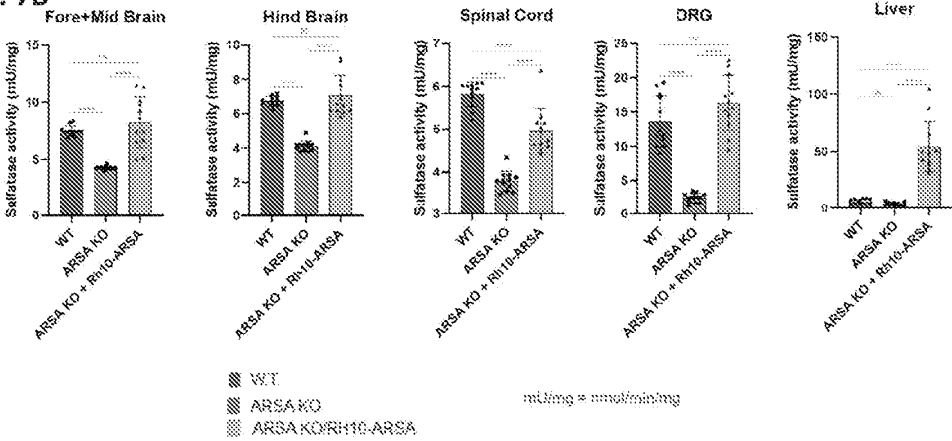


FIG. 8A

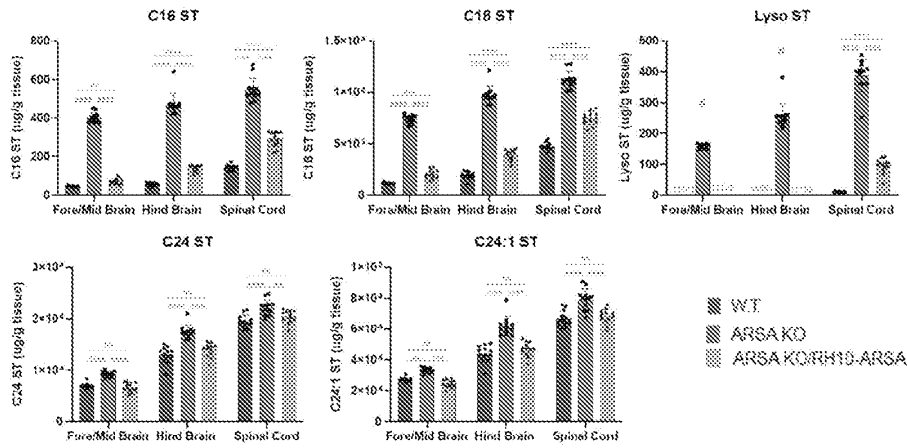


FIG. 8B

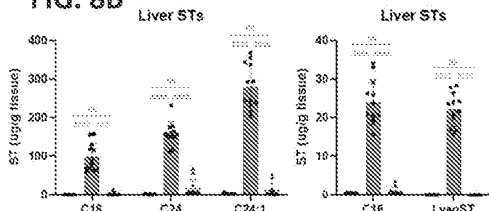


FIG. 8C

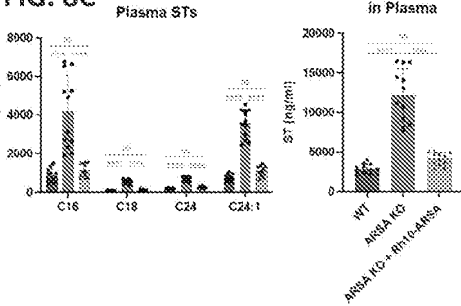


FIG. 8D

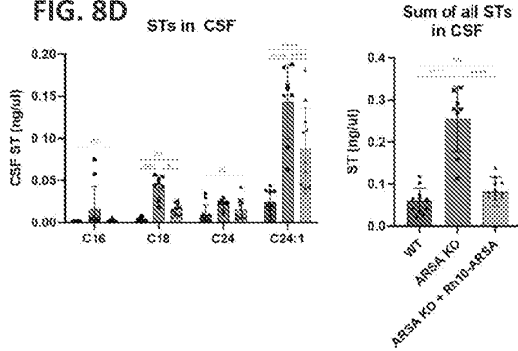


FIG. 9A

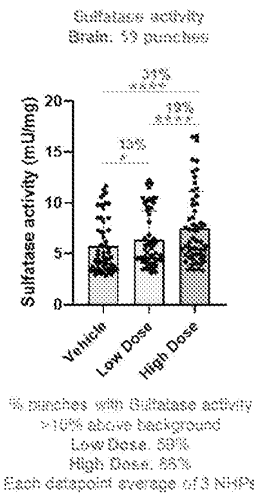


FIG. 9B

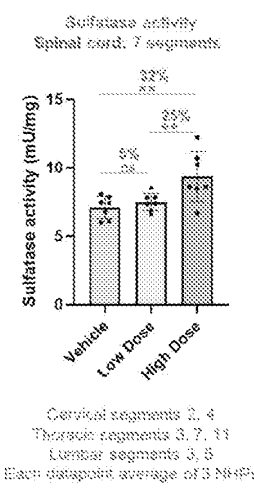


FIG. 9C

80001: AAVrh16-CBA-ARISA-FLAG-WPRE, High dose: 2.75e13 VG

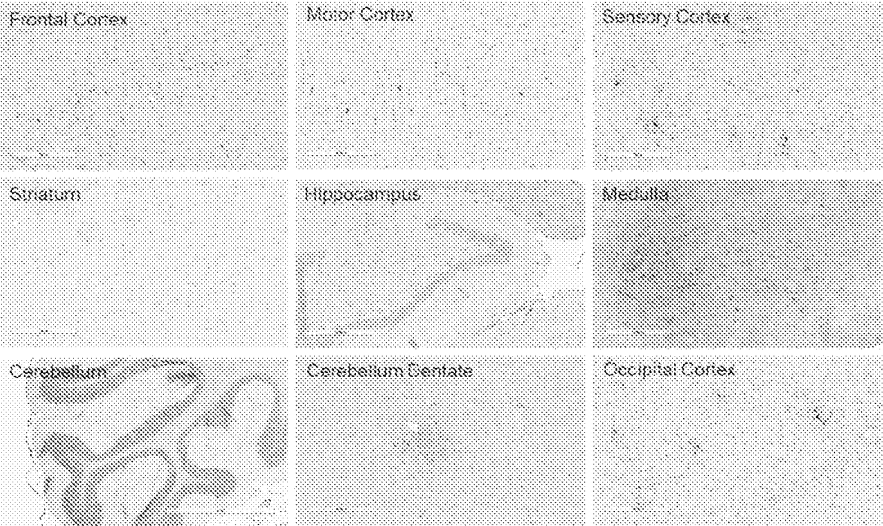
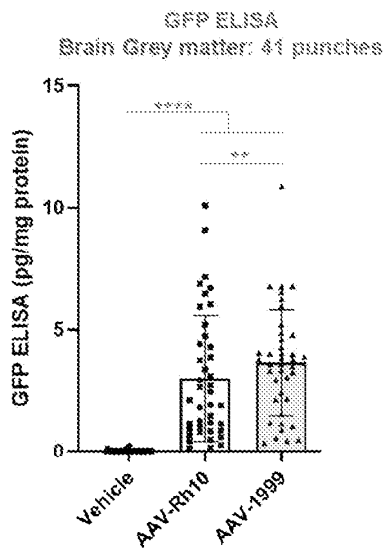
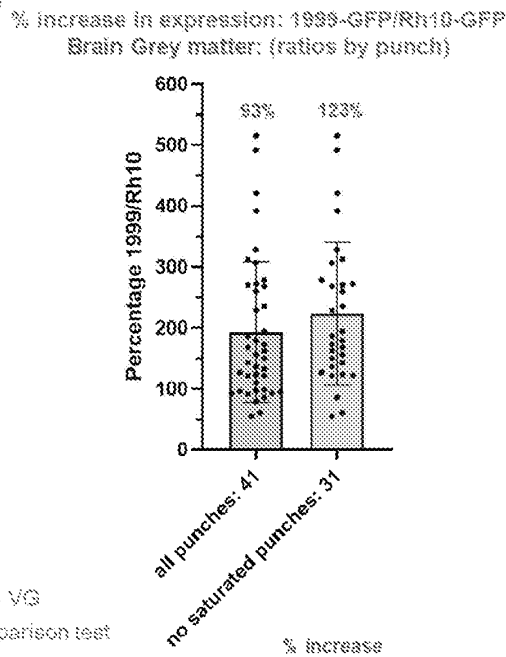


FIG. 10A



AAV (rh10/1999/Myo)-GFP-bGH: 2.75e13 VG
Two-way ANOVA with Tukey multiple comparison test
Each datapoint average of 3 NHPs

FIG. 10B



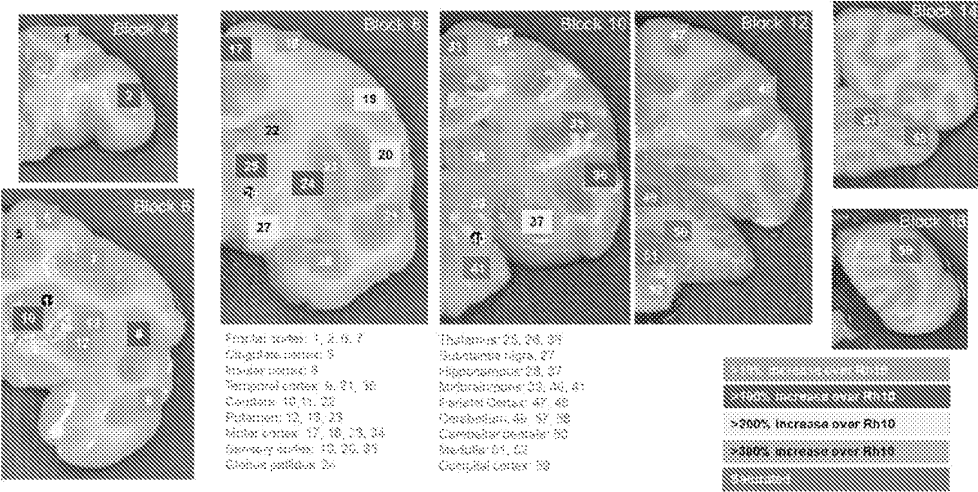


FIG. 11

12/42

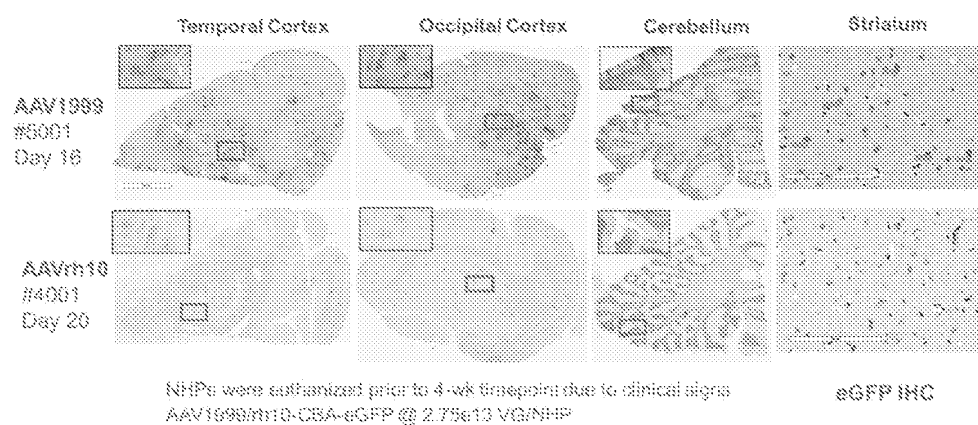
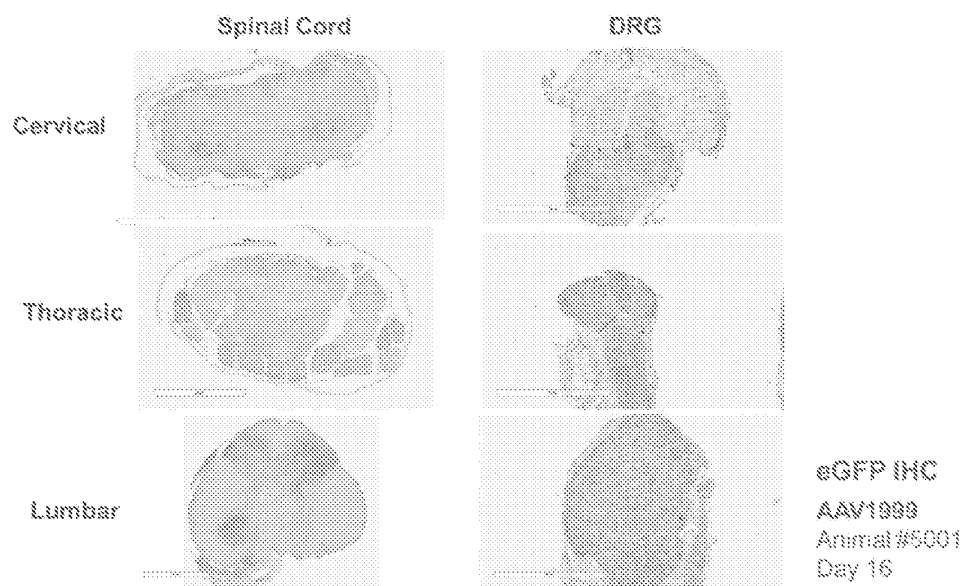


FIG. 12

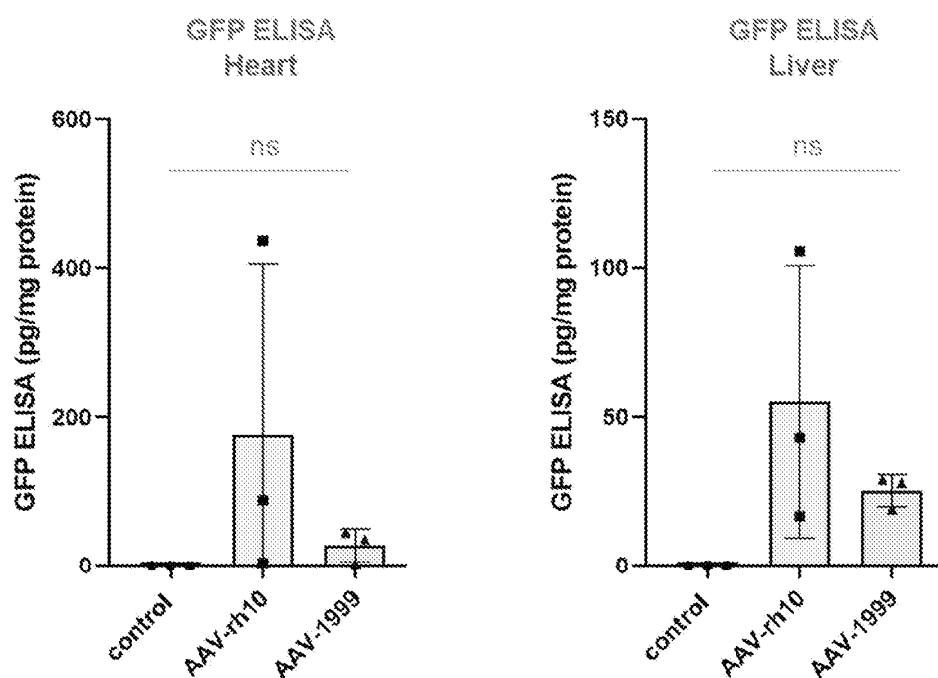
13/42



NHPs were euthanized prior to 4-wk timepoint due to clinical signs
AAV1999/m10-CBA-eGFP @ 2.75×10^{13} VG/NHP

FIG. 13

14/42

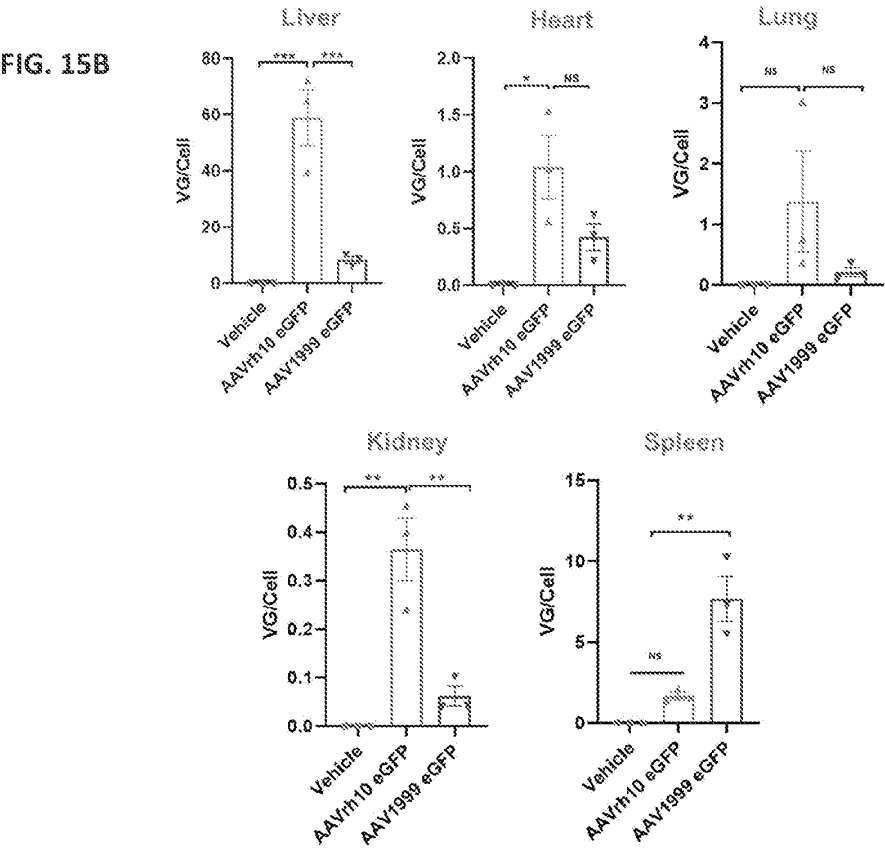
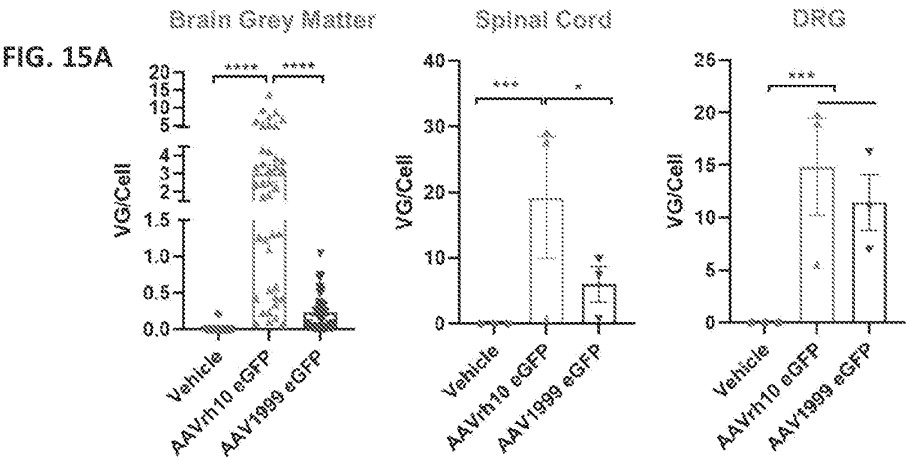


AAV (rh10/1999/Myo)-GFP-bGH: 2.75e13 VG

One-way ANOVA with Tukey multiple comparison test

Each datapoint average of 3 NHPs

FIG. 14



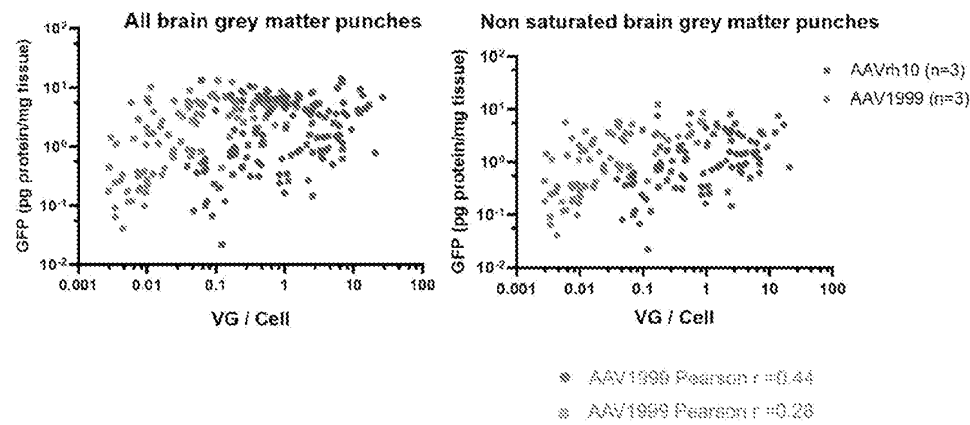


FIG. 16

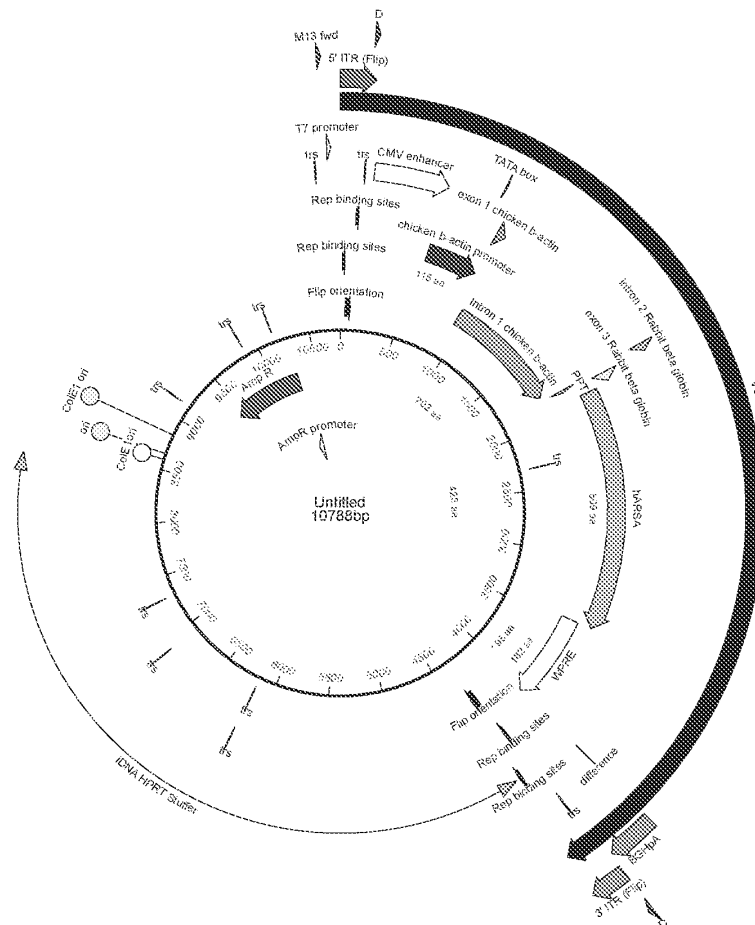


FIG. 17

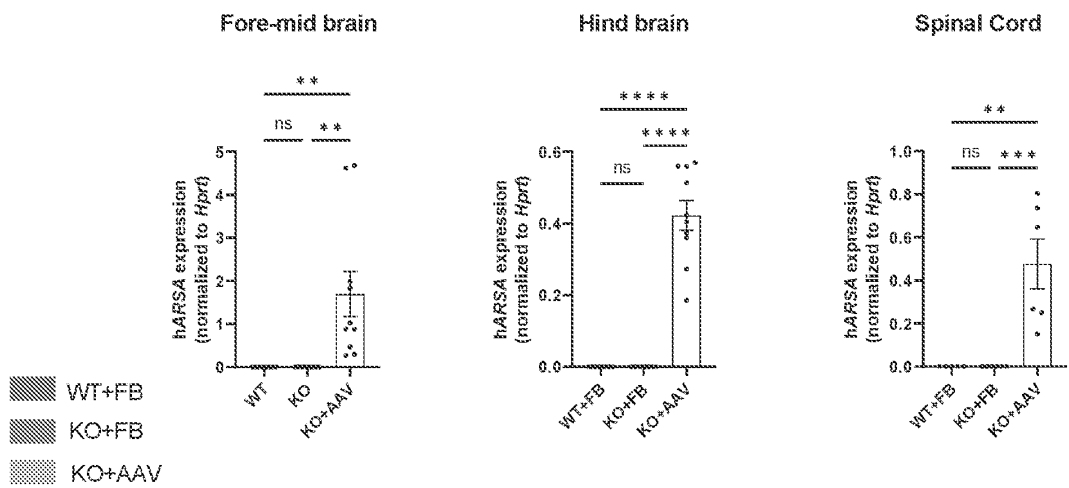


FIG. 18

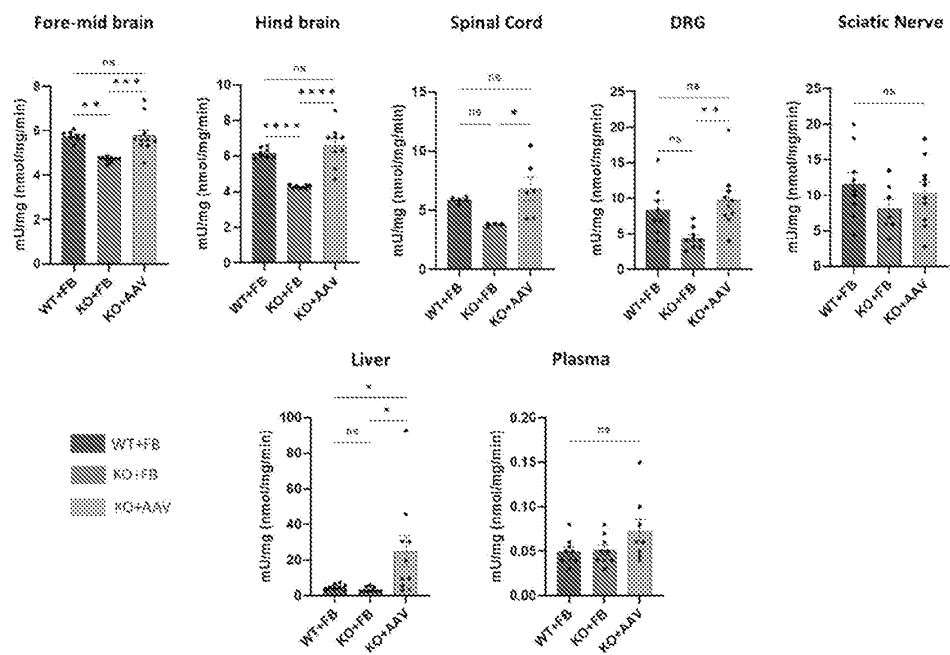


FIG. 19

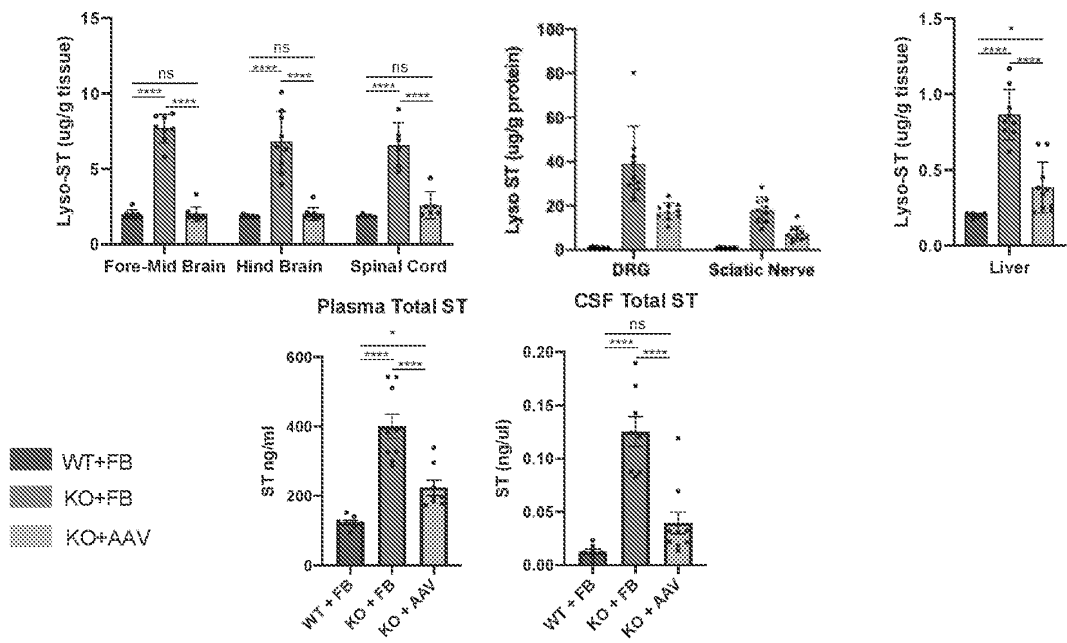


FIG. 20

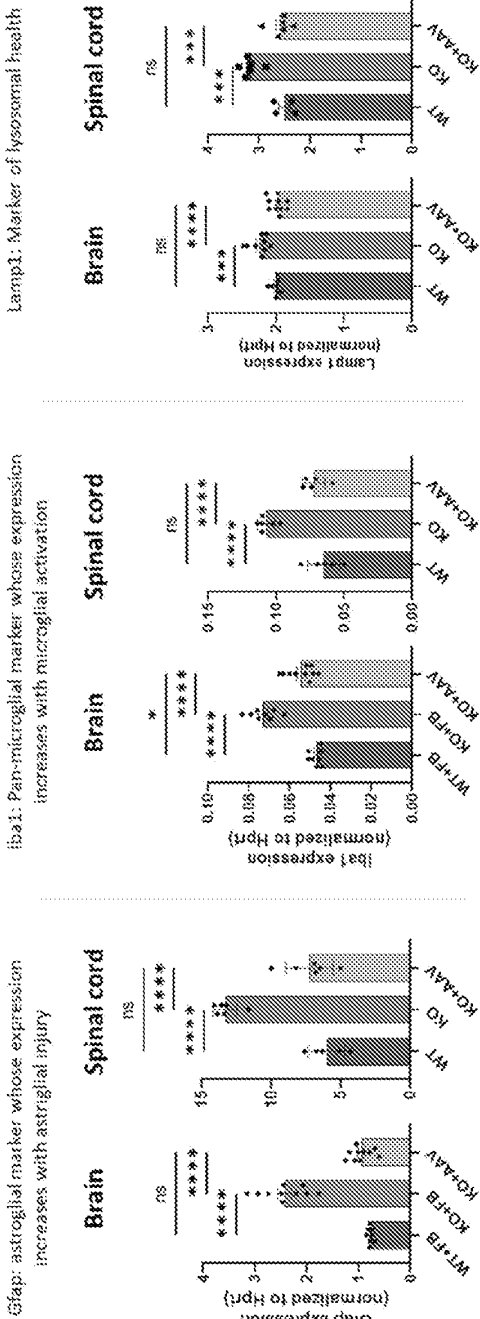


FIG. 21

22/42

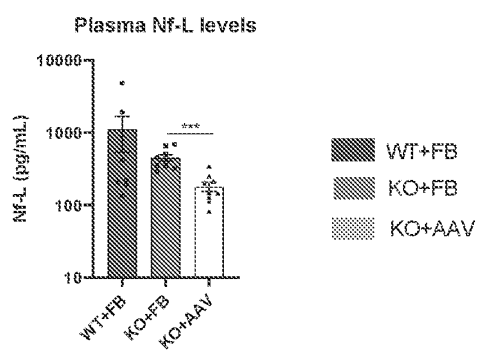


FIG. 22

FIG. 23

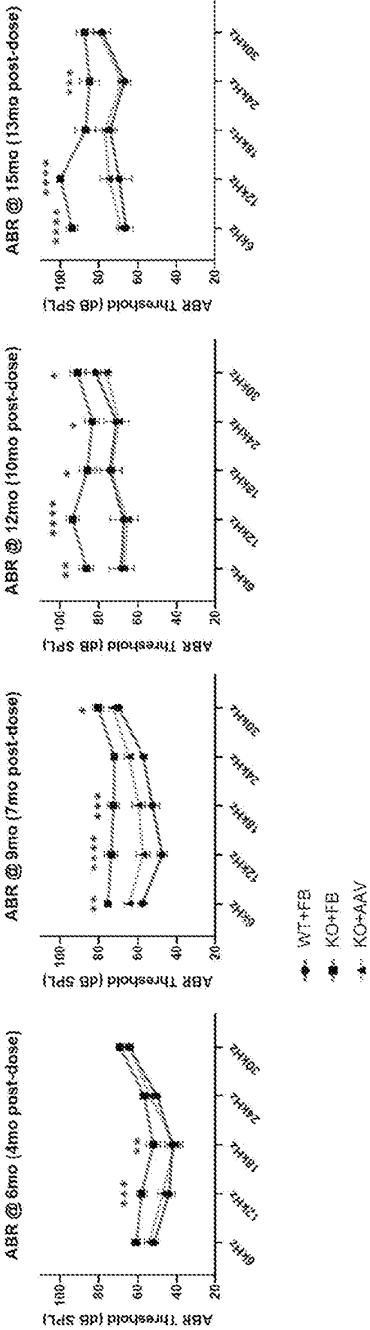


FIG. 24A

FIG. 24B

FIG. 24C

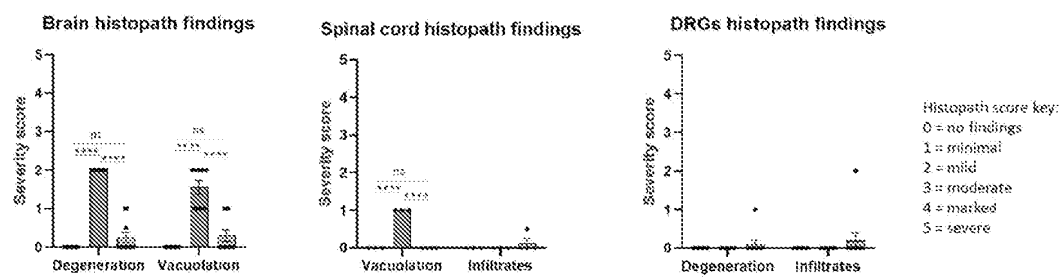


FIG. 25A

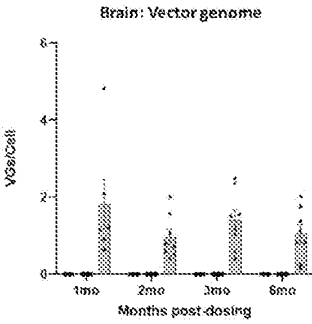


FIG. 25B

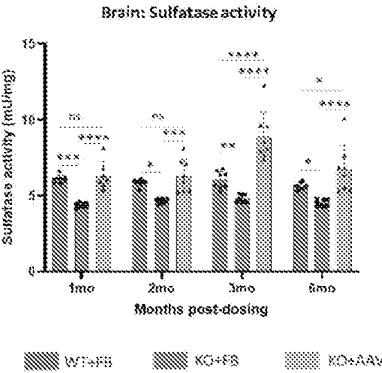


FIG. 25C

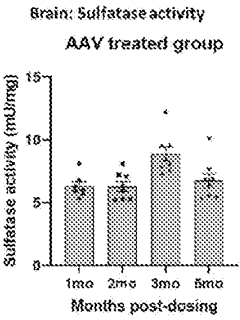


FIG. 26A

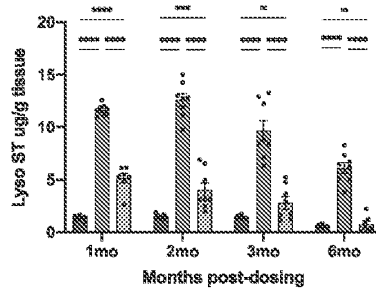


FIG. 26B

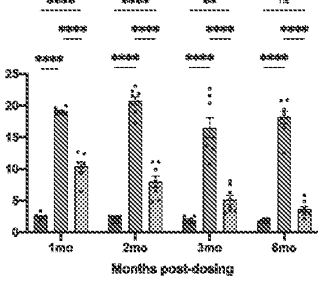


FIG. 26C

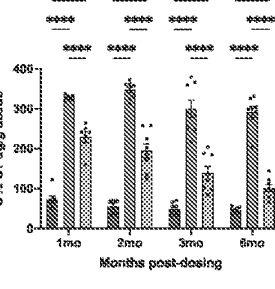


FIG. 26D

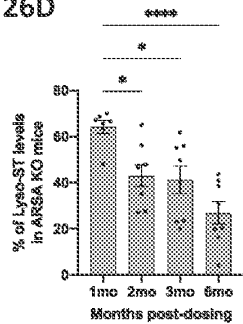


FIG. 26E

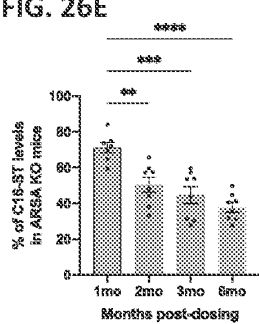
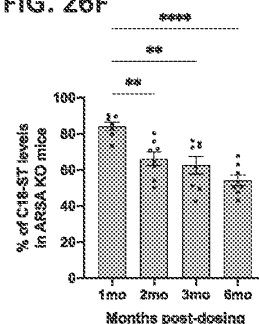


FIG. 26F



■ WT+FB ▨ KO+FB ▩ KO+AAV

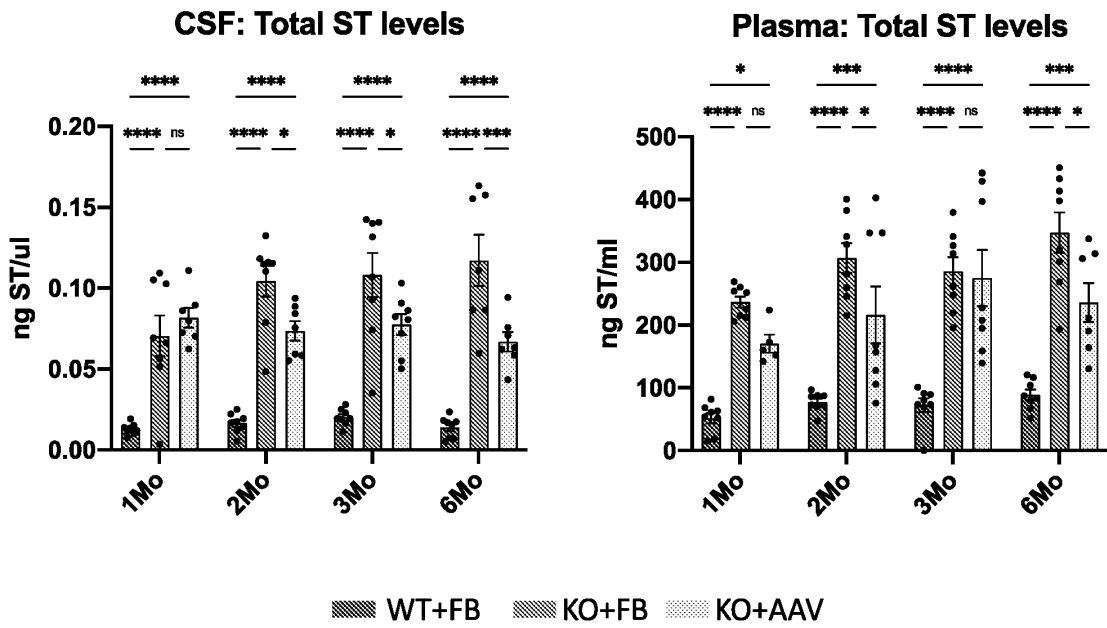


FIG. 27

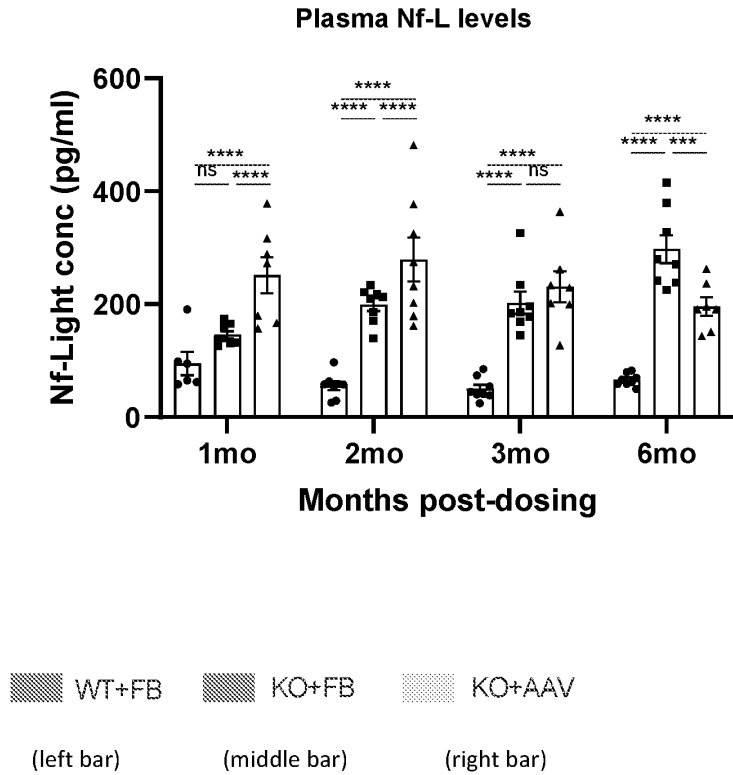


FIG. 28

FIG. 29A

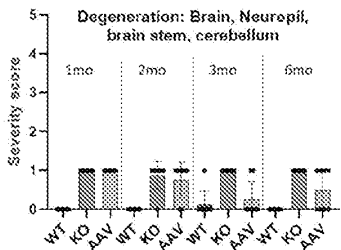


FIG. 29B

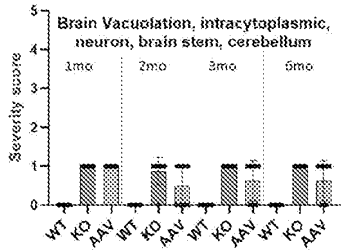


FIG. 29C

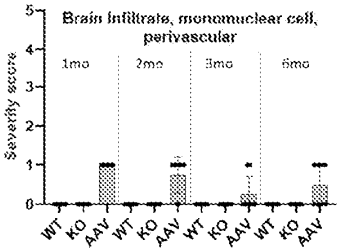
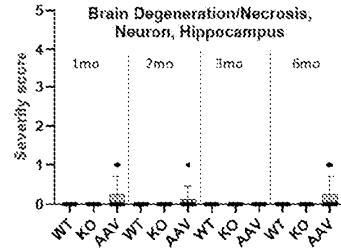


FIG. 29D



Histopath score key:
0 = no findings
1 = minimal
2 = mild
3 = moderate
4 = marked
5 = severe

FIG. 30A

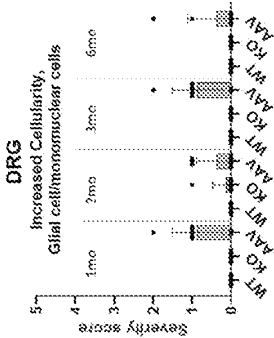


FIG. 30B

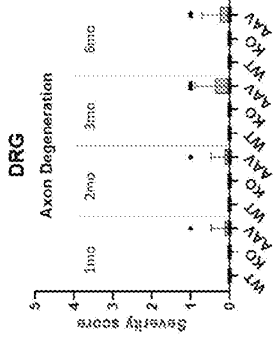


FIG. 30C

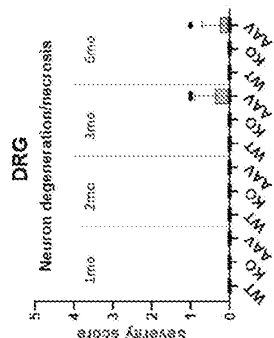


FIG. 30D

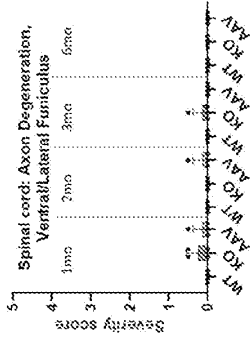
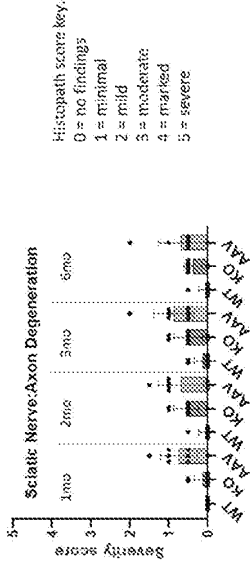


FIG. 30E



Histopath score key:
0 = no findings
1 = minimal
2 = mild
3 = moderate
4 = marked
5 = severe

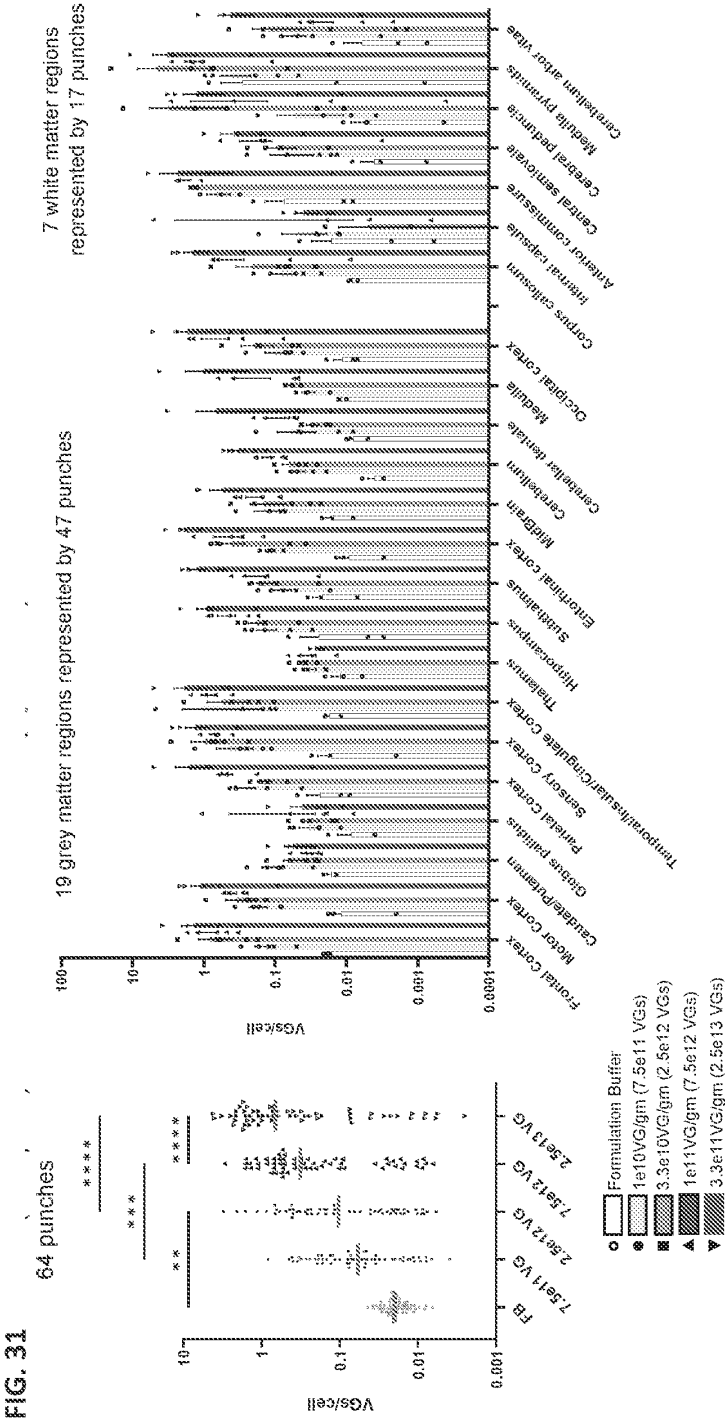


FIG. 32

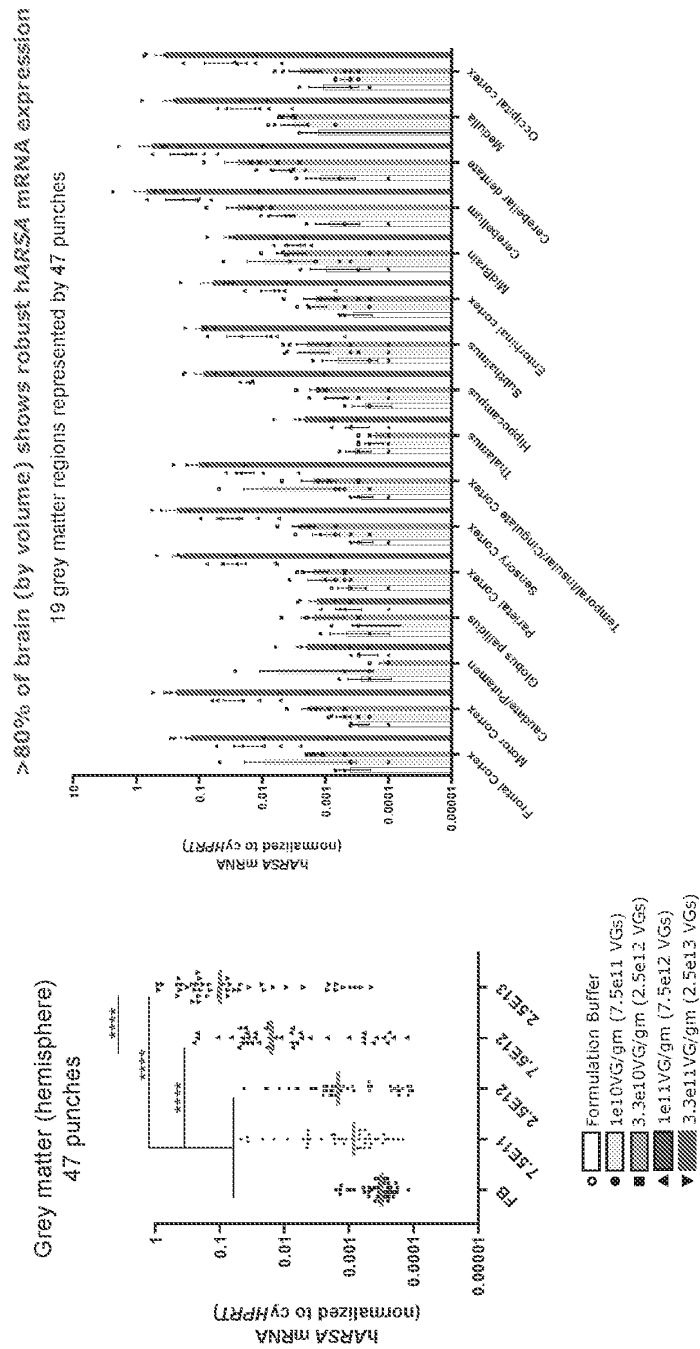


FIG. 34A

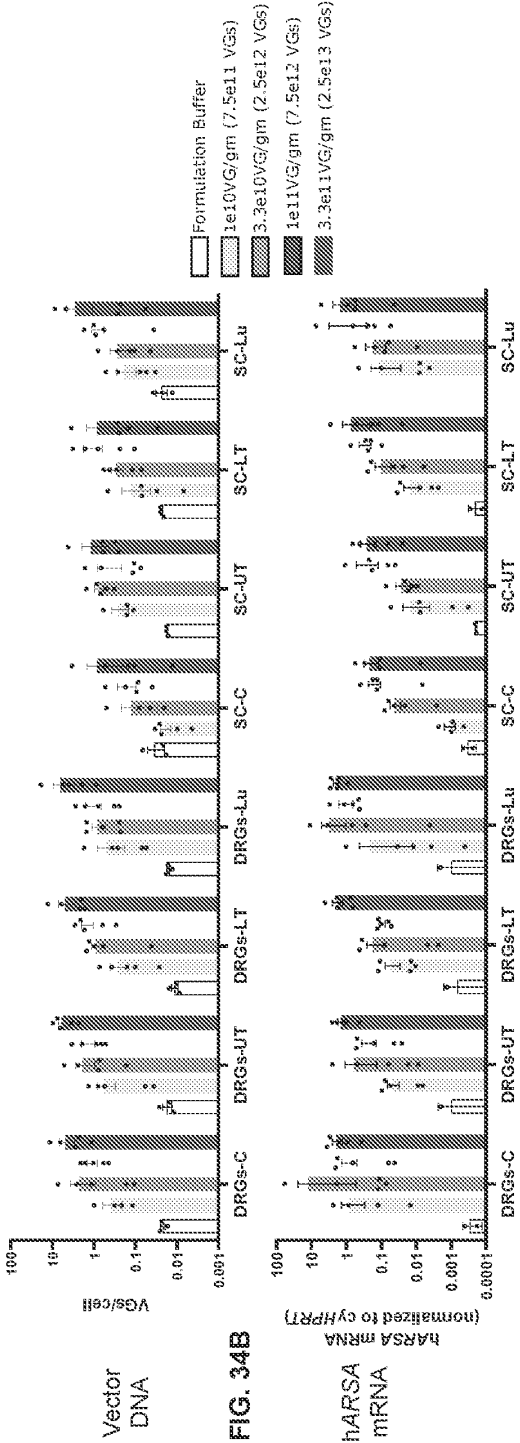
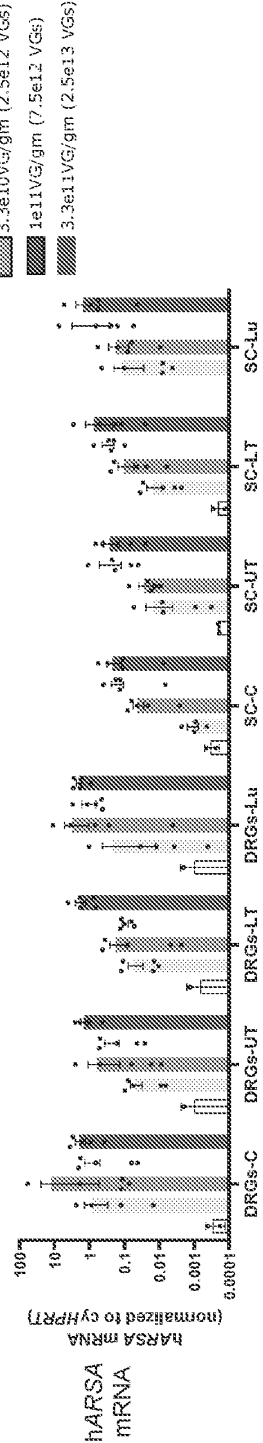


FIG. 34B



C: cervical; UT: upper thoracic; LT: lower thoracic; Lu: Lumbar; SC: spinal cord

FIG. 35

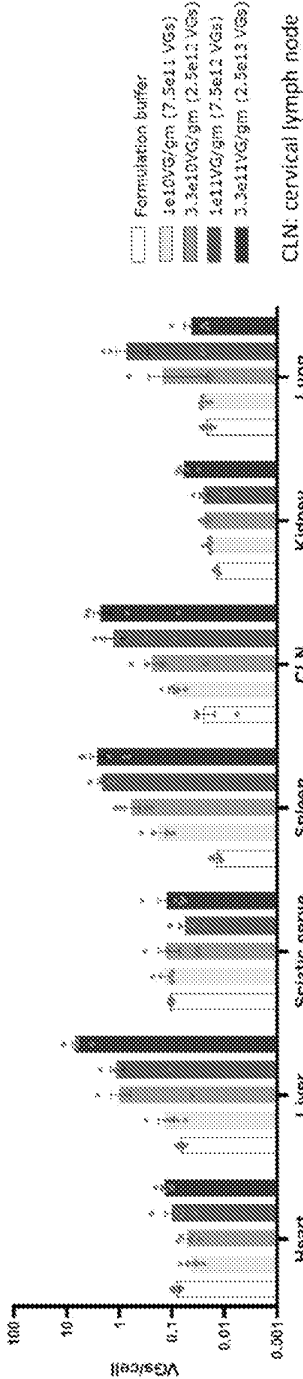
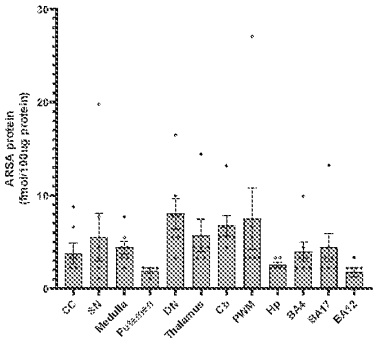


FIG. 37A

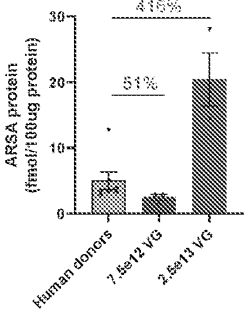
Human brain from 7 healthy 3-8yr old donors have an average of 4.9 fmol ARSA protein per 100ug total protein



BA, Broadman area; CC, corpus callosum; Cb, cerebellum; DN, dentate nucleus; Hp, hippocampus; PWM, periventricular white matter; SN, substantia nigra

FIG. 37B

hARSA protein in NHP brain equals 51% (1e11VG/gm) and 416% (3.3e11VG/gm) of ARSA protein levels in brain of 7 healthy 3-8yr old donors



◆ hARSA: 12 brain regions from 7 human healthy donors (3-8 yrs old)
▲ hARSA: 1e11VG/gm (7.5e12 VGs); n=3 NHPs; ICM ROA
▼ hARSA: 3.3e11VG/gm (2.5e13 VGs); n=3 NHPs; ICM ROA

FIG. 38

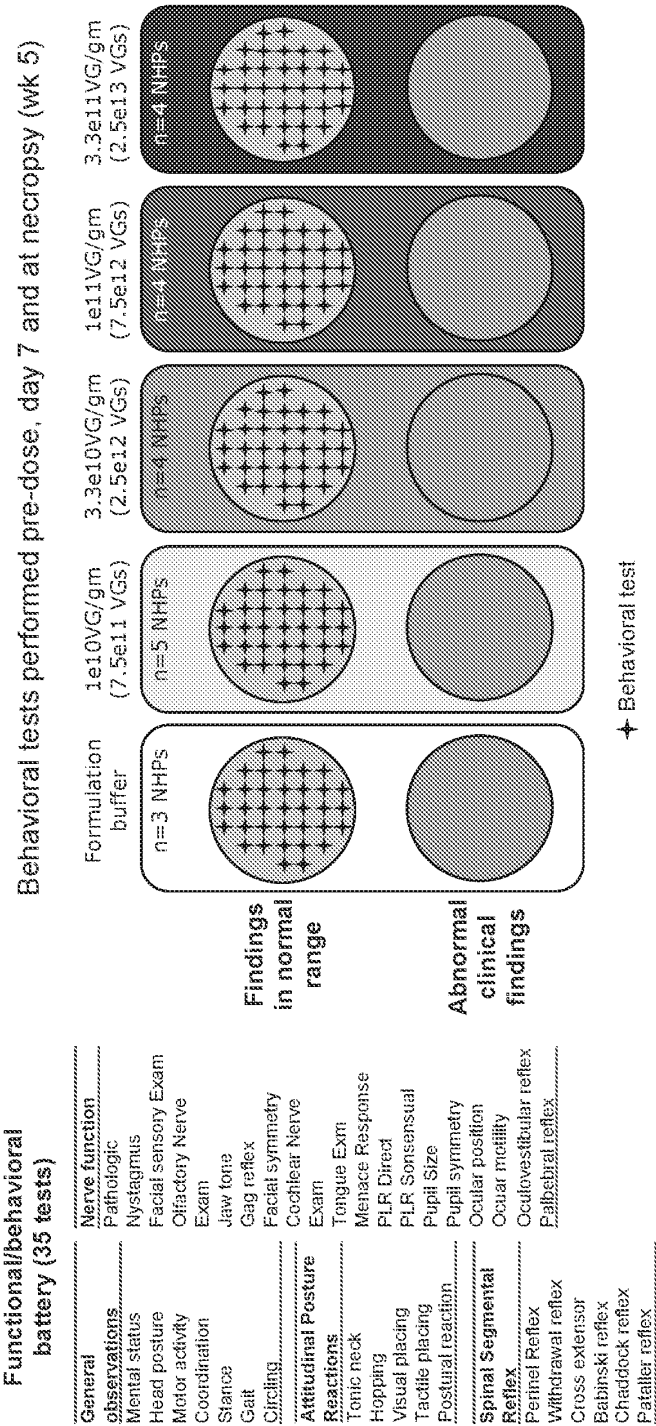
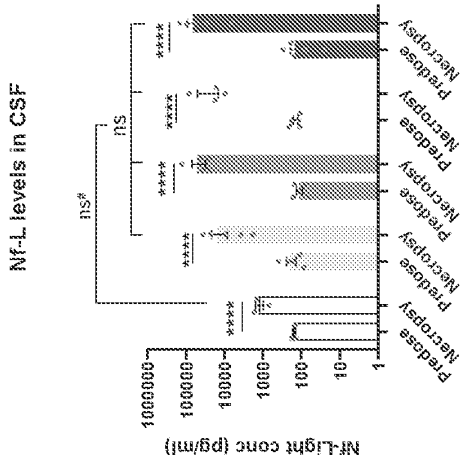
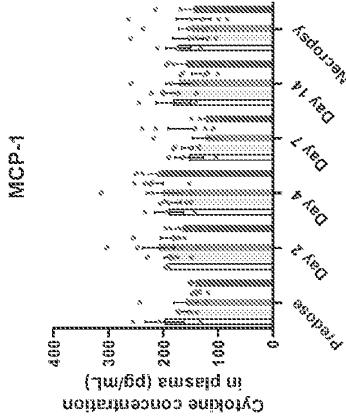


FIG. 39A



6 weeks between pre-dose and necropsy

FIG. 39B



Proinflammatory cytokines: IL-6, IL-8, IFN- γ , IL-1 β , IL-1ra, MCP-1, MIP-1 β , G-CSF, GM-CSF, IL-18 and TNF- α
T cell activation cytokines: IL-2, IL-4

FIG. 39C

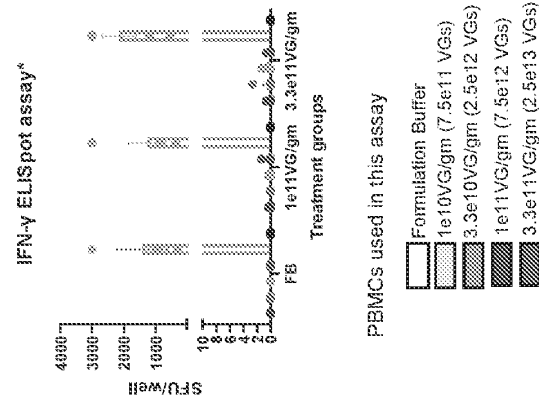


FIG. 40

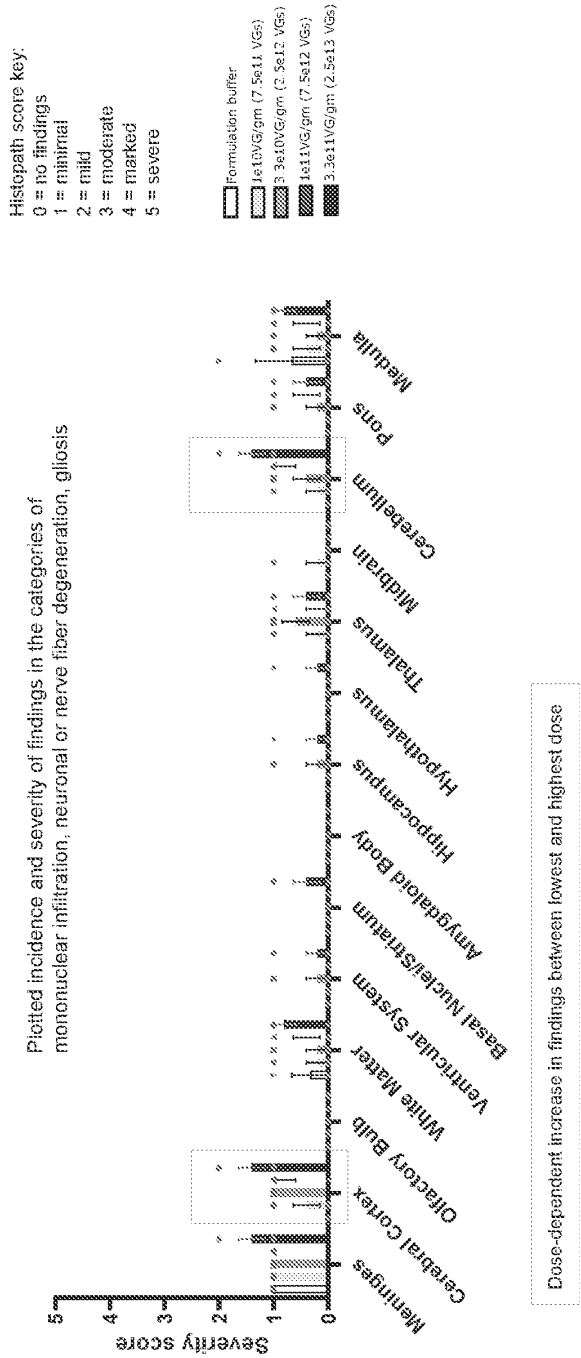


FIG. 41A

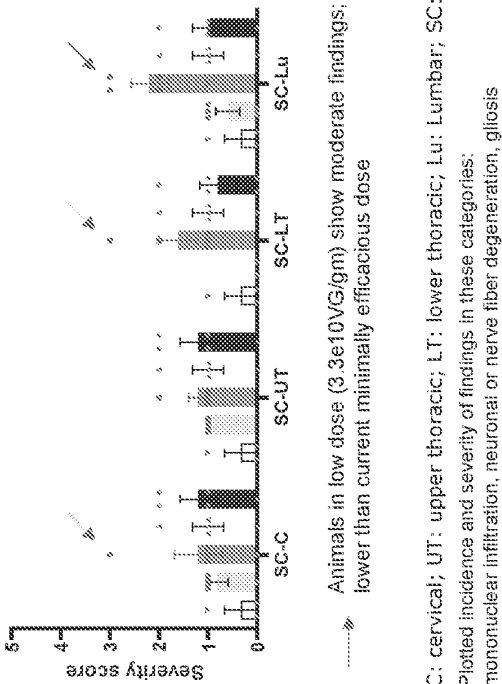
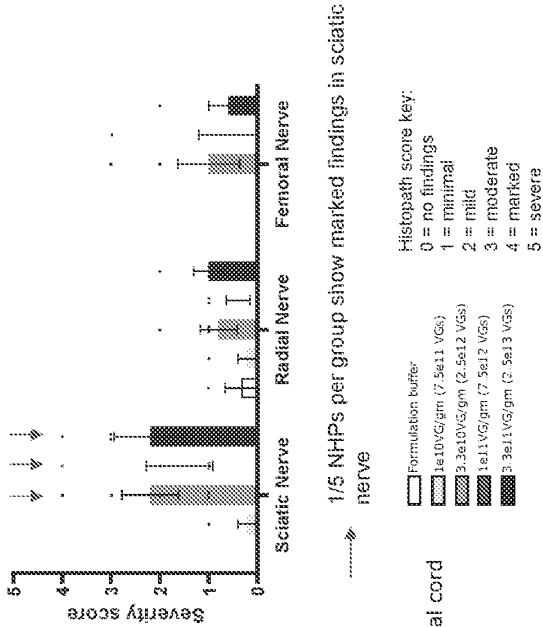


FIG. 41B



C: cervical; UT: upper thoracic; LT: lower thoracic; Lu: Lumbar; SC: spinal cord

Plotted incidence and severity of findings in these categories:
mononuclear infiltration, neuronal or nerve fiber degeneration, gliosis

Histopath score key:
0 = no findings
1 = minimal
2 = mild
3 = moderate
4 = marked
5 = severe

FIG. 42A

DRG:degeneration/necrosis
(avg score across 8 segments)

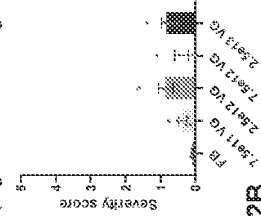
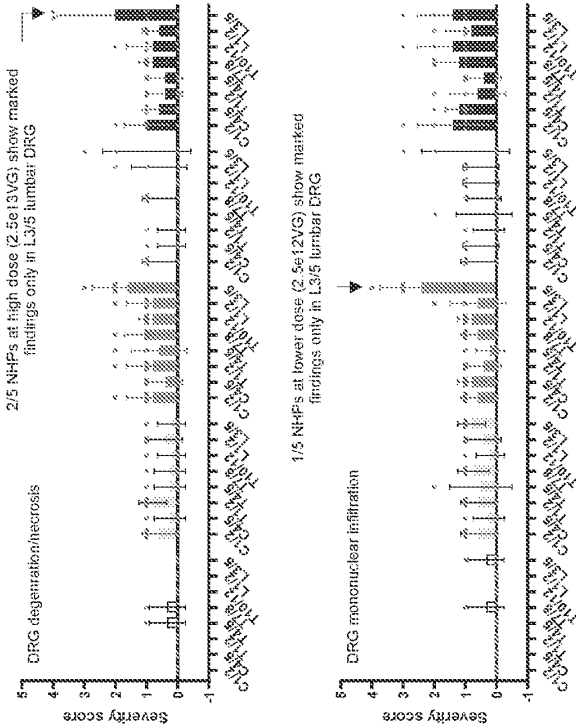
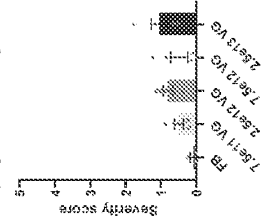
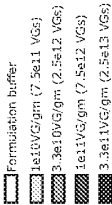


FIG. 42B

DRG: Mononuclear infiltration
(avg across 8 segments)



C: cervical; T: thoracic;
L: Lumbar



Histopath score key:

- 0 = no findings
- 1 = minimal
- 2 = mild
- 3 = moderate
- 4 = marked
- 5 = severe