

FIG. 1

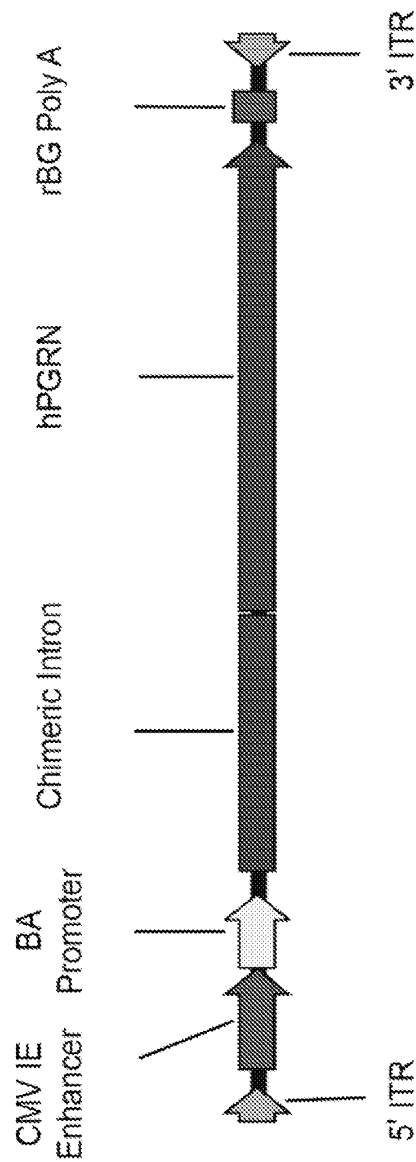


FIG. 2

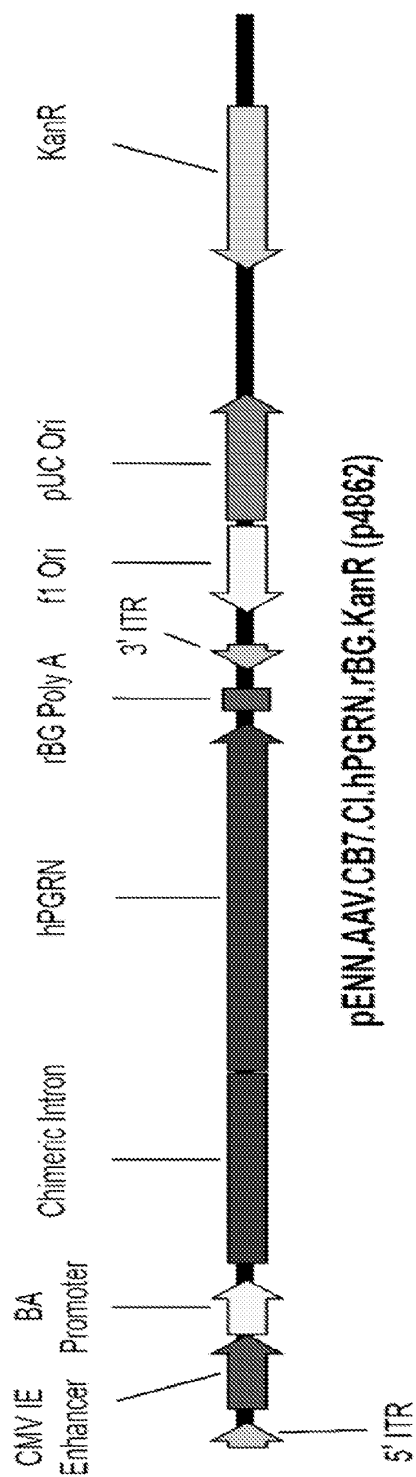


FIG. 3A

Lipofuscin Hippocampus

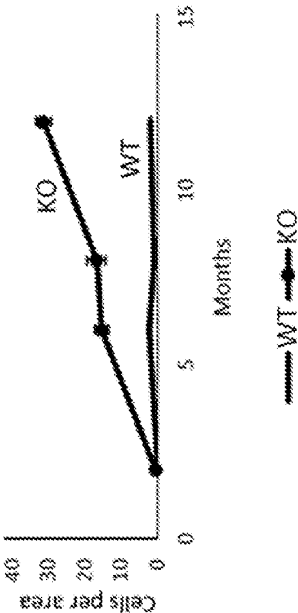


FIG. 3B

Lipofuscin Cortex

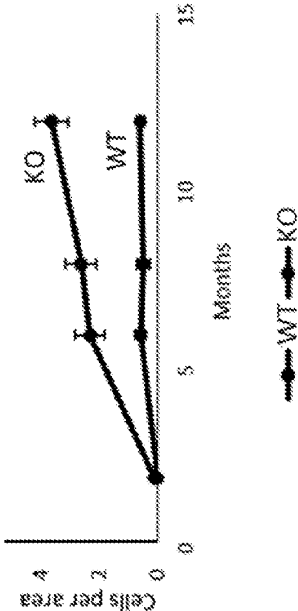


FIG. 3C

Lipofuscin Thalamus

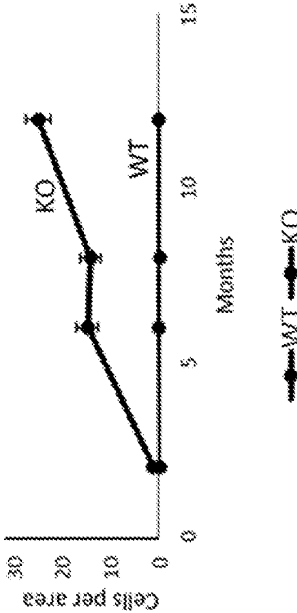


FIG. 3D

Brain Hex activity (ratio to WT)

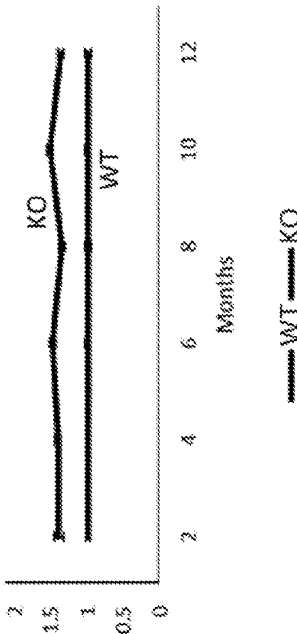


FIG. 4

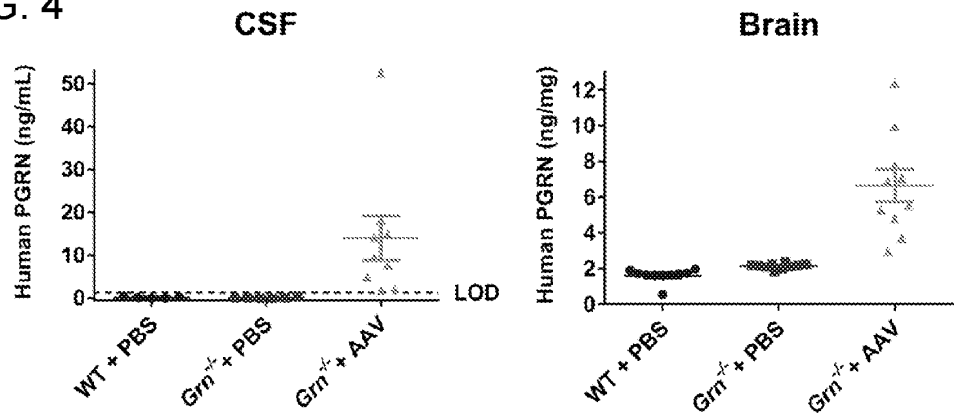


FIG. 5

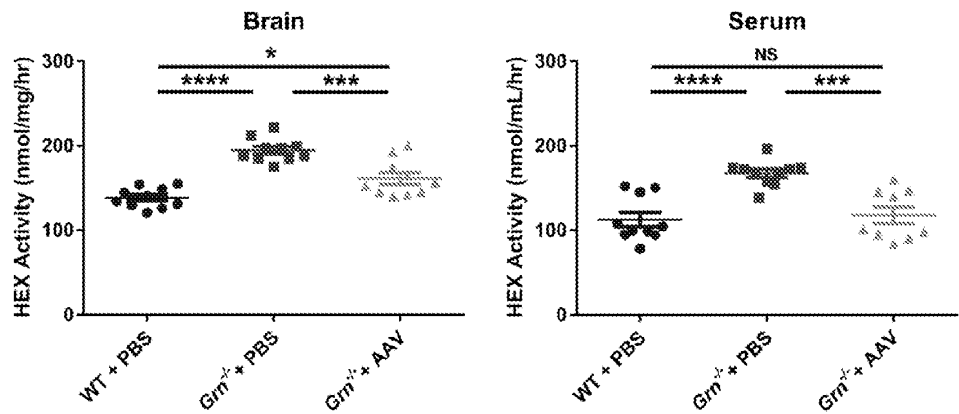


FIG. 6

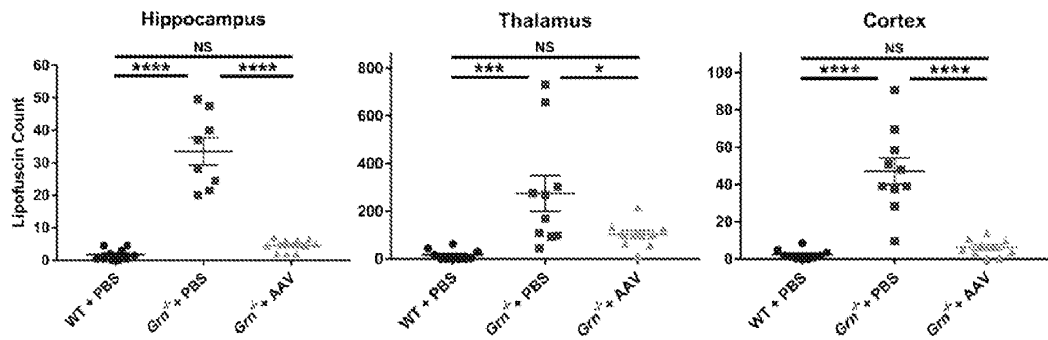


FIG. 7A

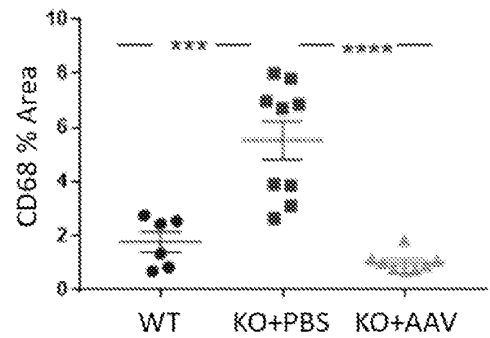


FIG. 7B

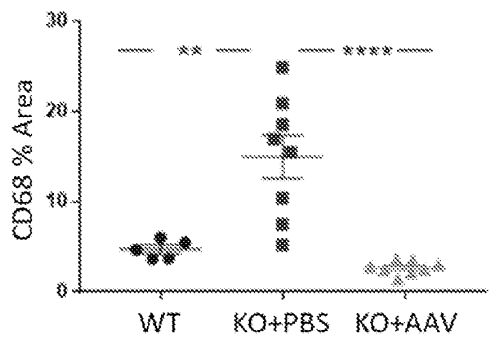


FIG. 7C

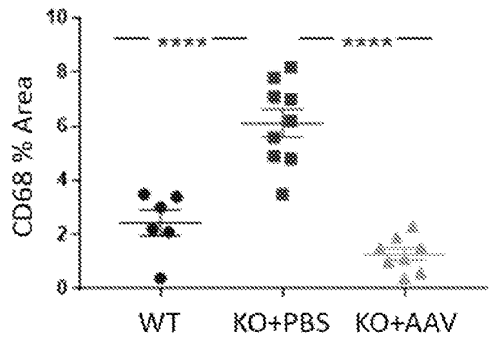


FIG. 8

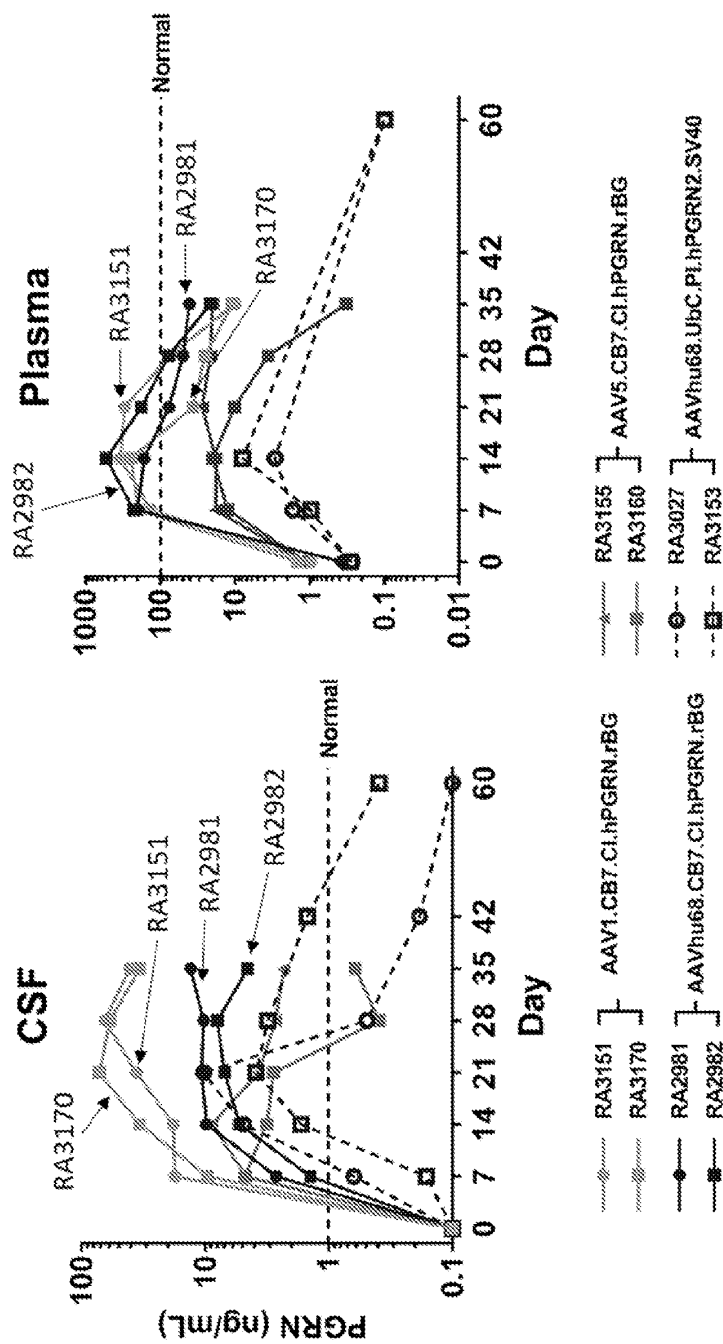


FIG. 9

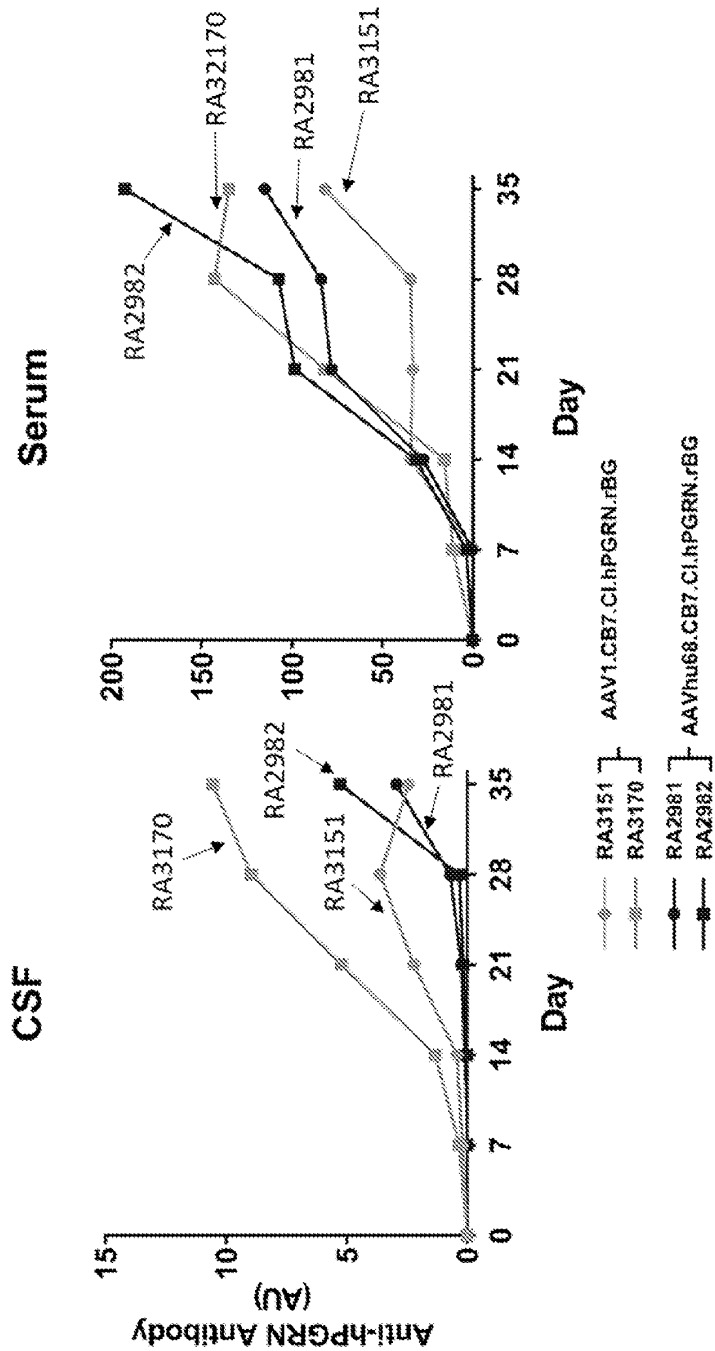


FIG. 10

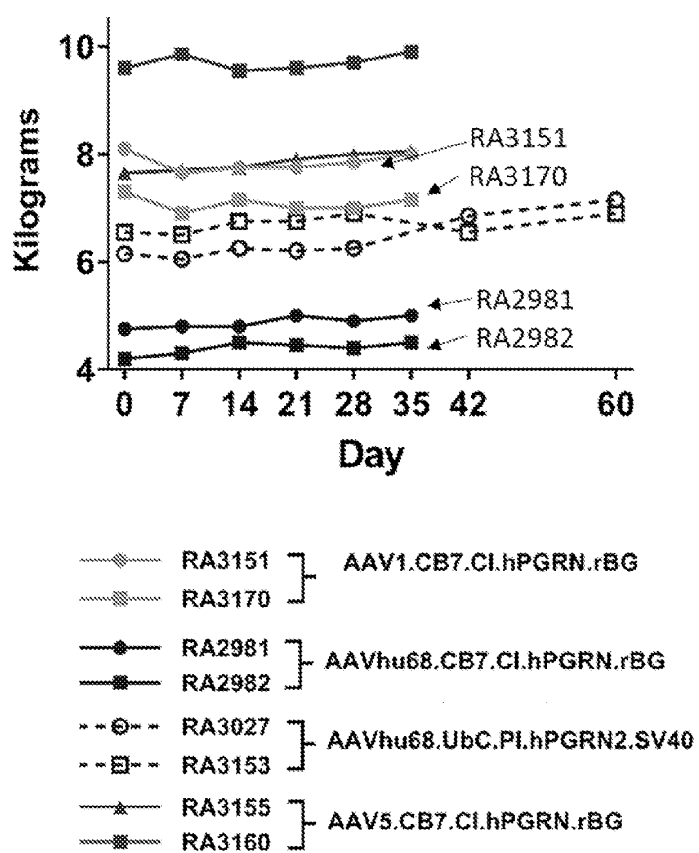
Body Weights

FIG. 11

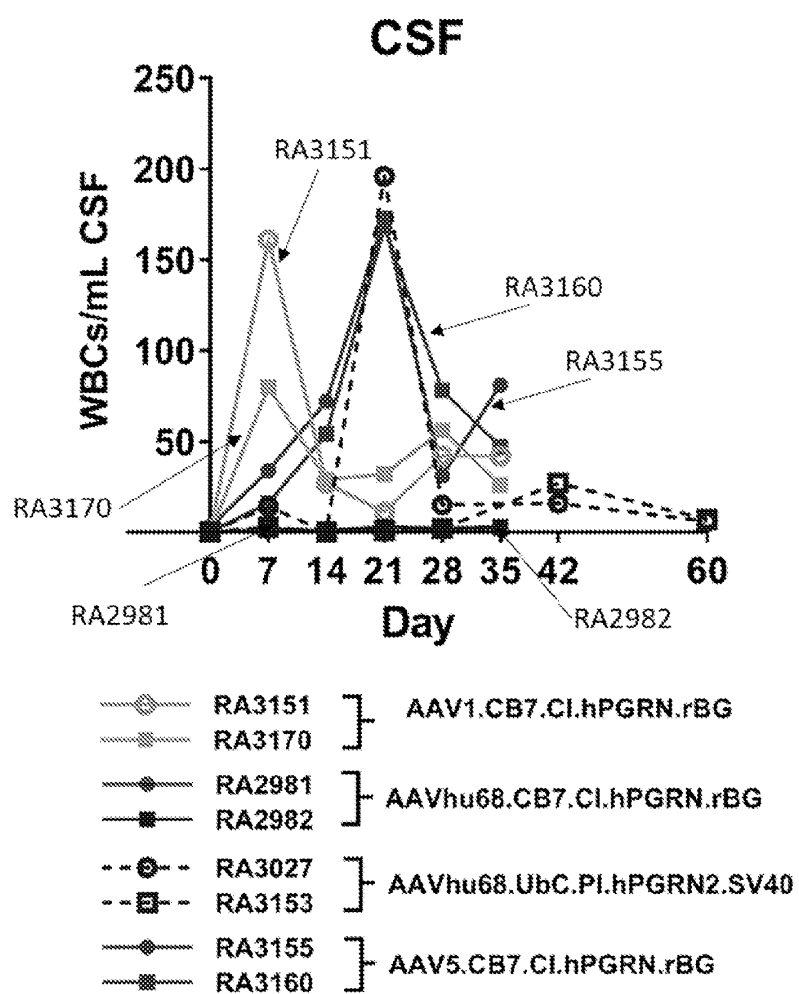


FIG. 12

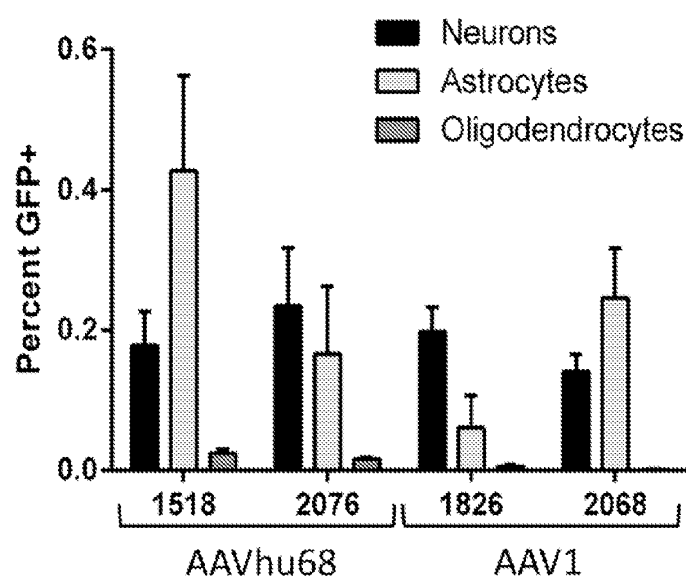


FIG. 13

		Region						
Cell marker	Animal ID	1	2	3	4	5		Average
NeuN	1518	0.13	N/A	0.205	0.34	0.167	0.049	0.178
	2076	0.106	0.227	0.258	0.528	0.053	N/A	0.234
	1826	0.1	0.318	0.195	0.202	0.171	N/A	0.197
	2068	0.218	N/A	0.153	0.141	0.128	0.065	0.141
GFAP	1518	0.152	N/A	0.202	0.914	0.39	0.476	0.427
	2076	0.011	0.064	0.235	0.511	0.011	N/A	0.166
	1826	0.019	0.013	0.021	0.244	0.007	N/A	0.061
	2068	0.066	N/A	0.245	0.13	0.459	0.33	0.246
Olig2	1518	0.02	N/A	0.03	0.04	0.009	0.023	0.024
	2076	0.02	0.023	0.011	0.013	0.013	N/A	0.016
	1826	0	0.001	0.008	0.016	N/A	0.001	0.005
	2068	0.002	0	N/A	0.001	0.002	0.002	0.001

FIG. 14

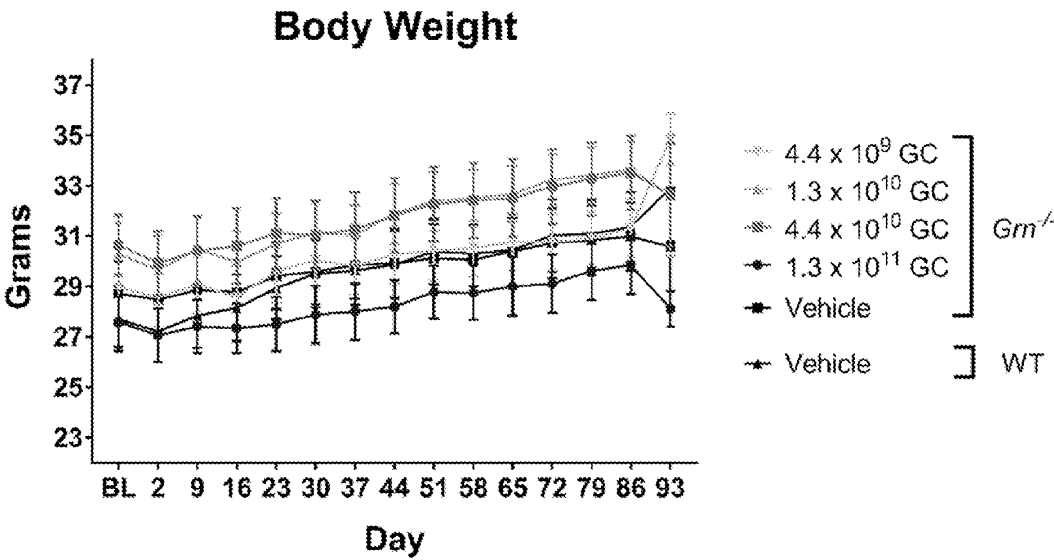


FIG. 15

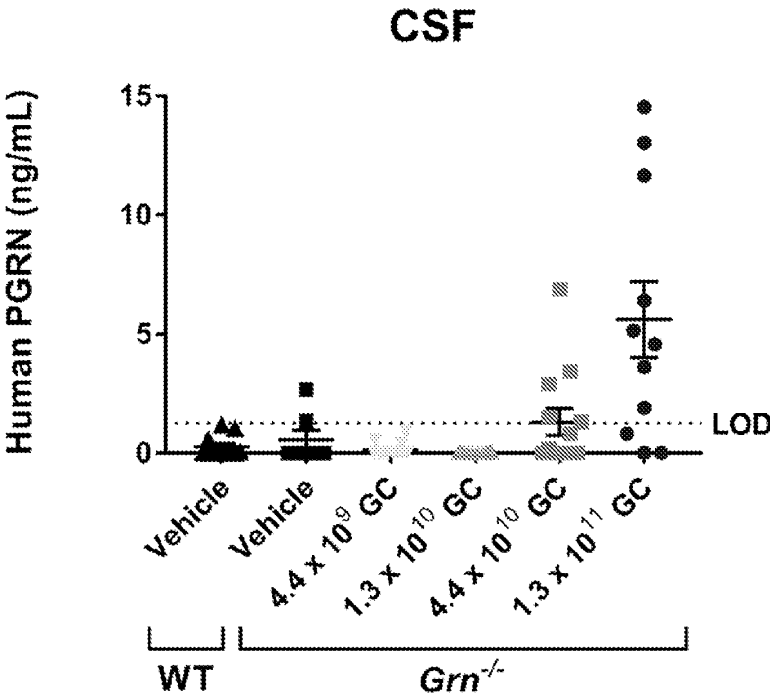
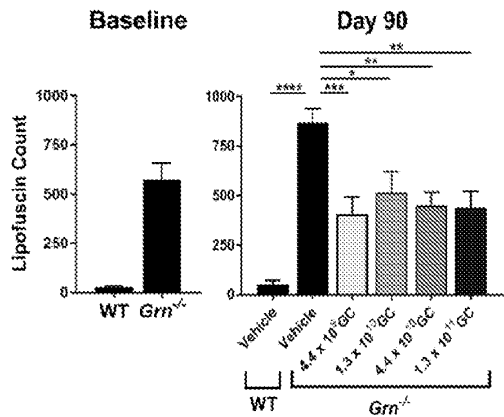


FIG. 16A
Thalamus



Cortex

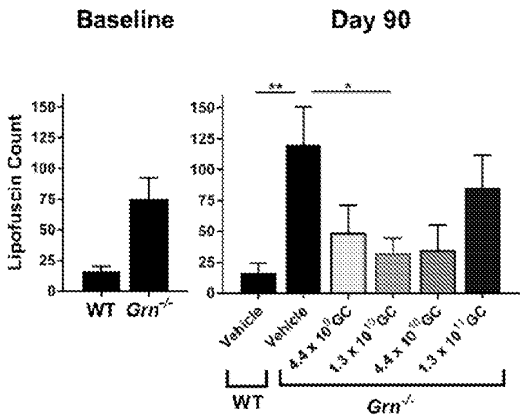


FIG. 16B

Hippocampus

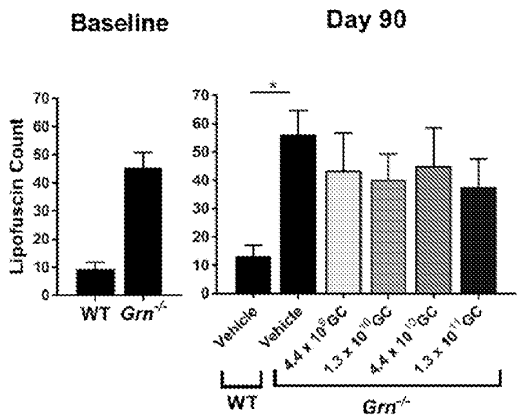
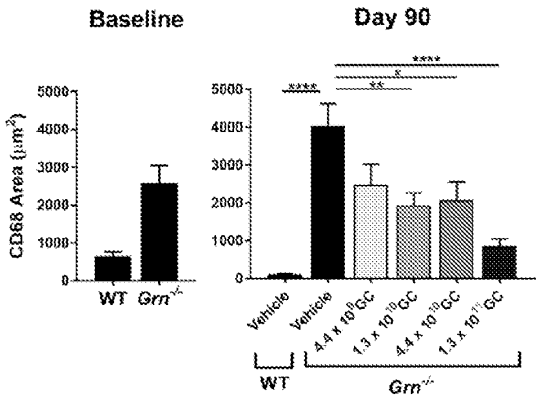


FIG. 16C

FIG. 17A
Thalamus



Cortex

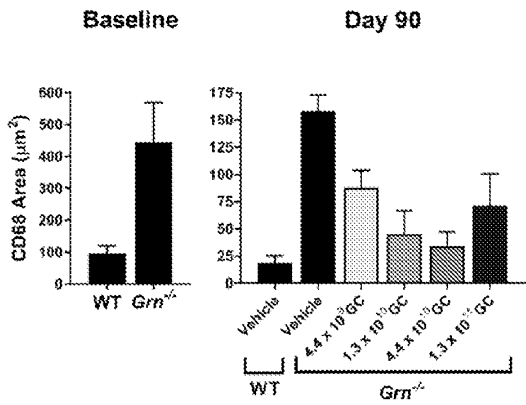


FIG. 17B

Hippocampus

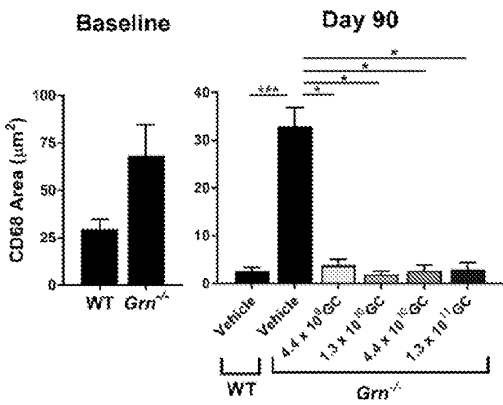


FIG. 17C

FIG. 18

Brain

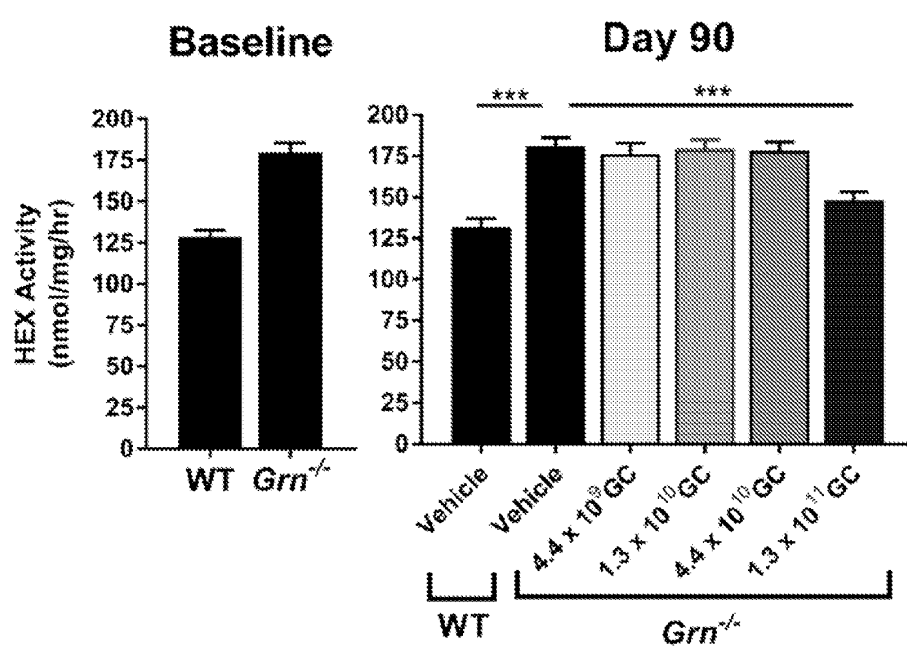


FIG. 19

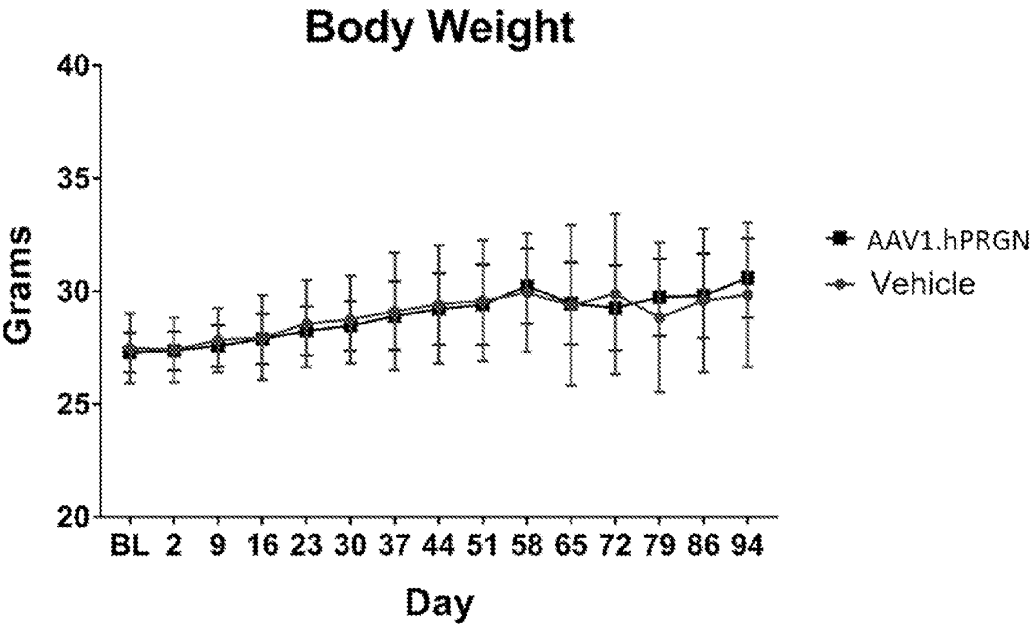


FIG. 20

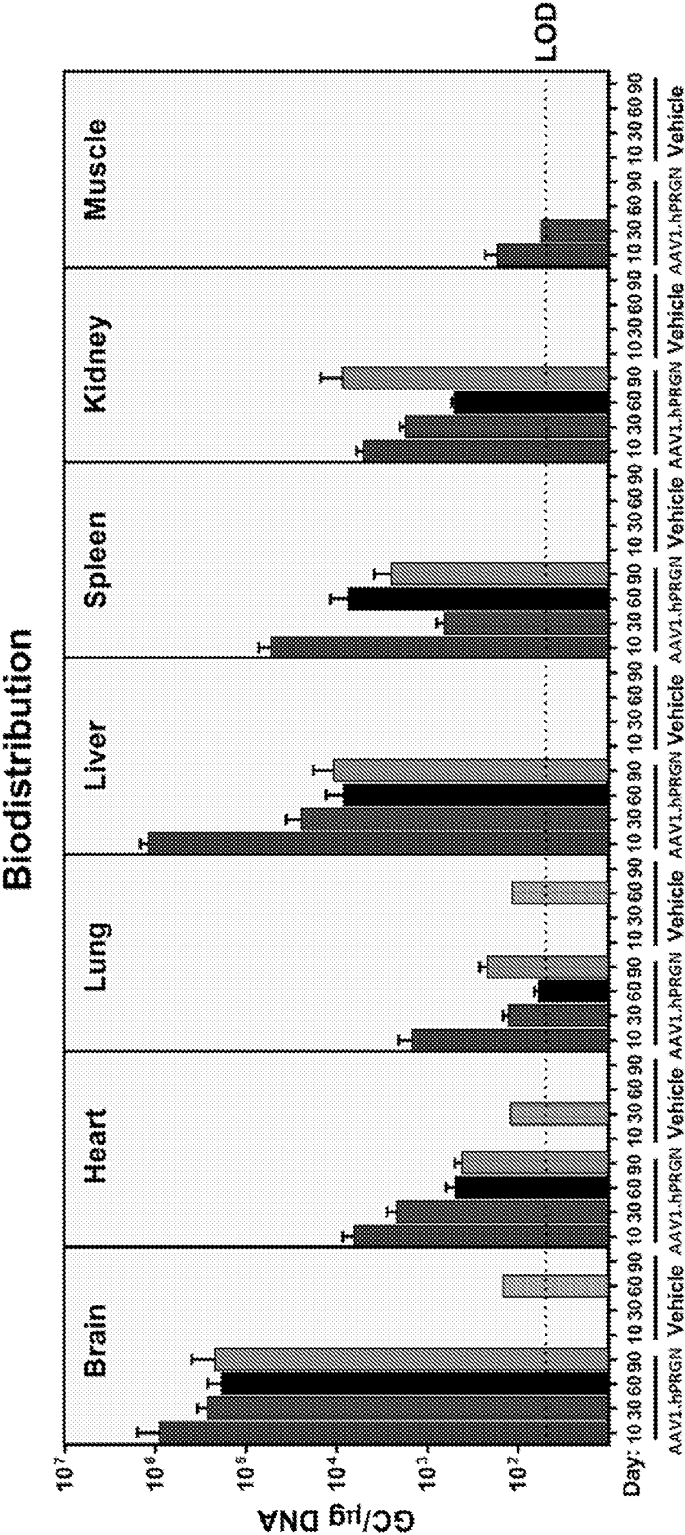


FIG. 21

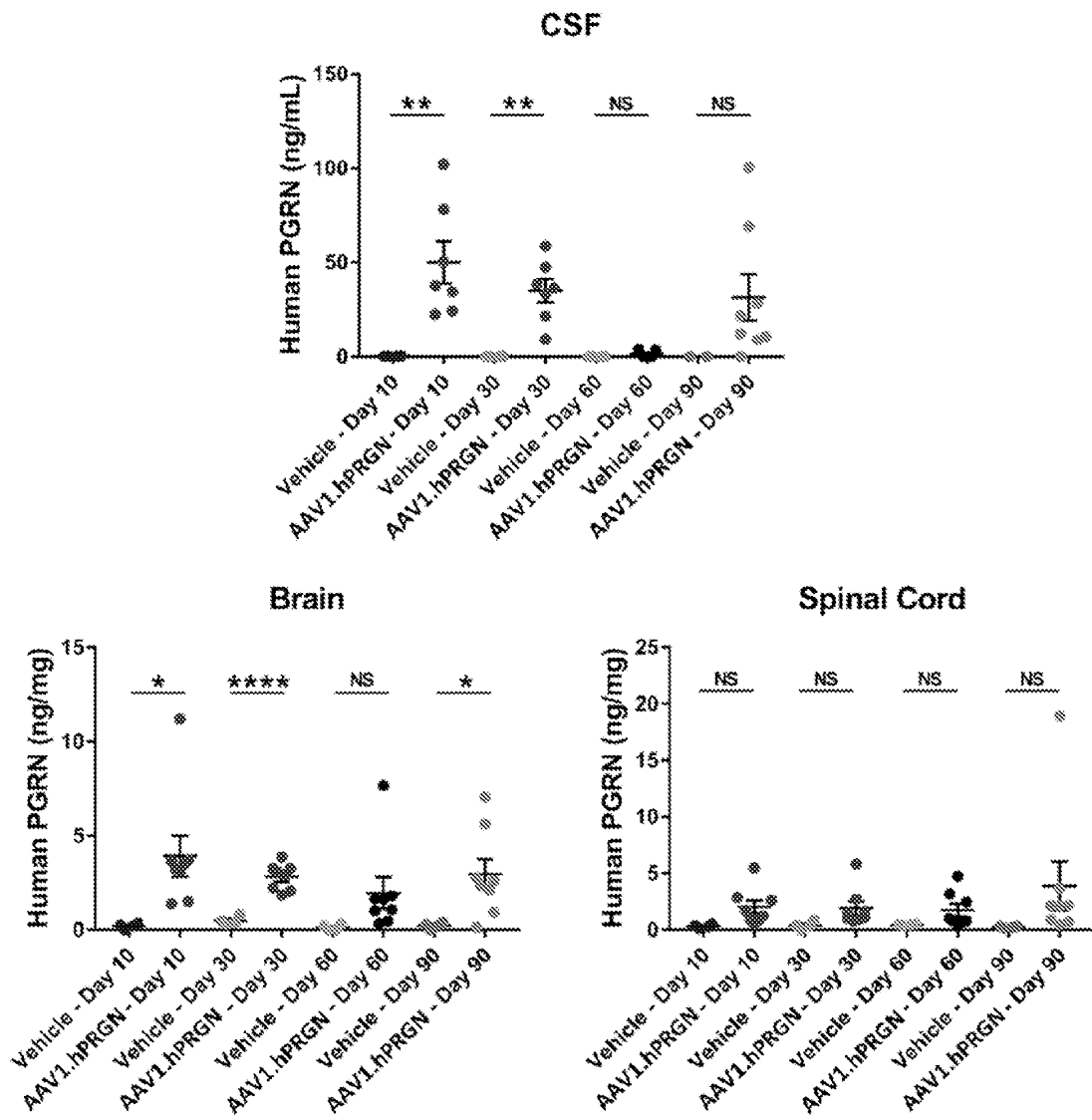


FIG. 22

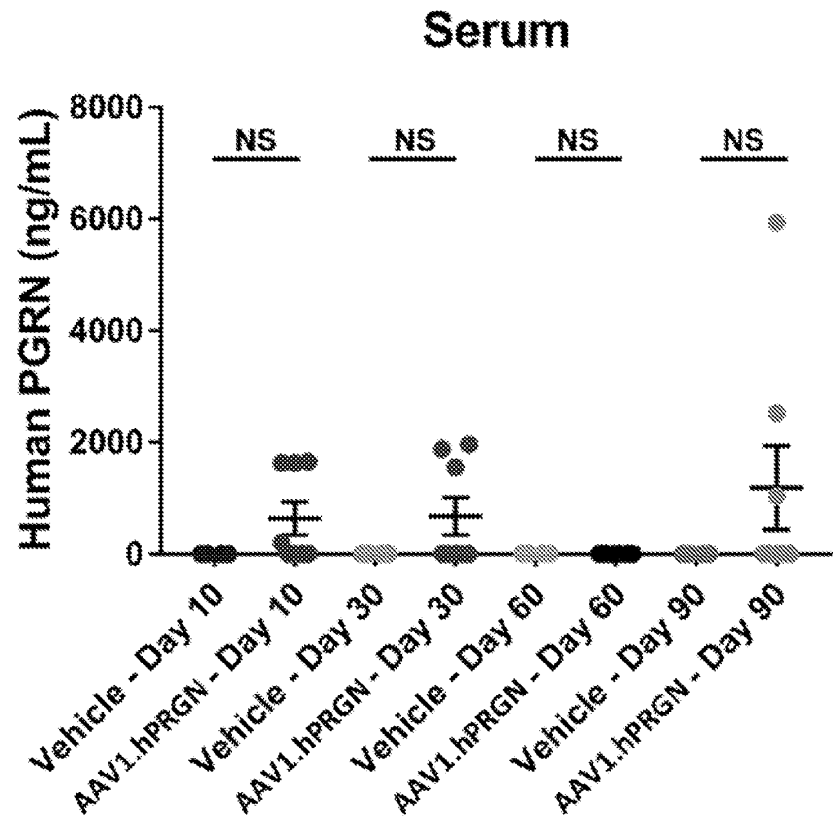


FIG. 23A

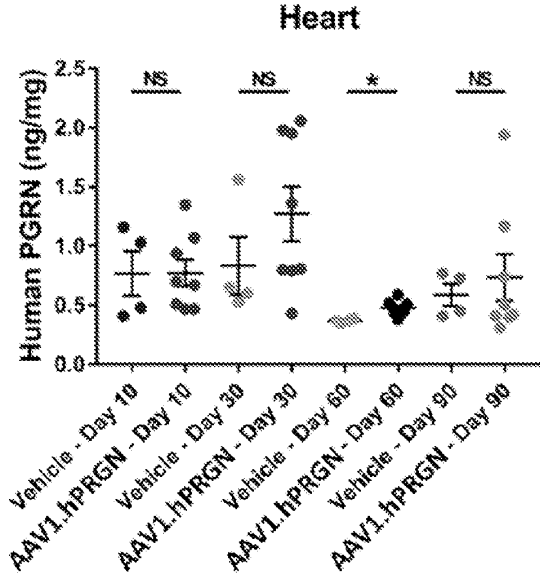


FIG. 23B

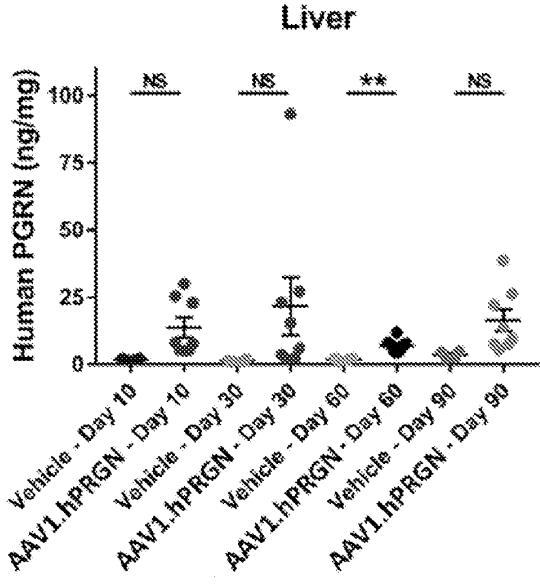


FIG. 23C

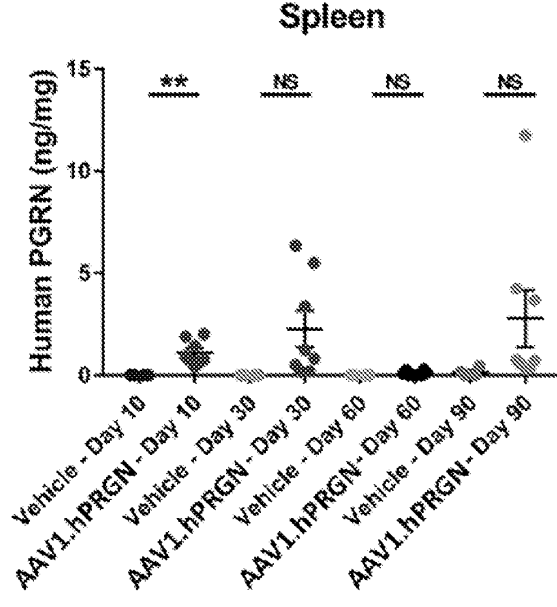


FIG. 23D

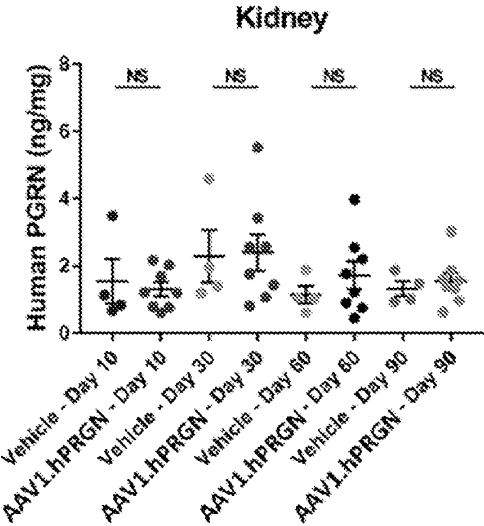


FIG. 23E

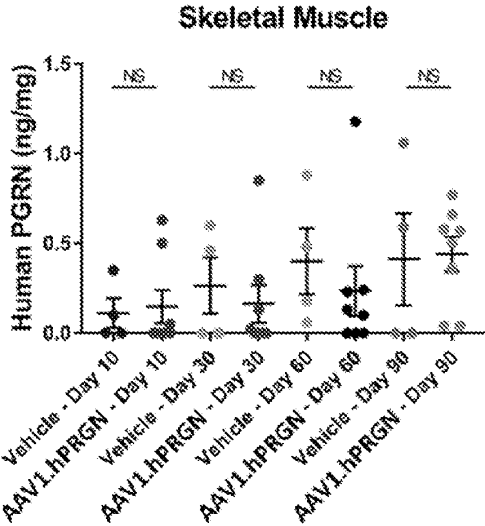


FIG. 23F

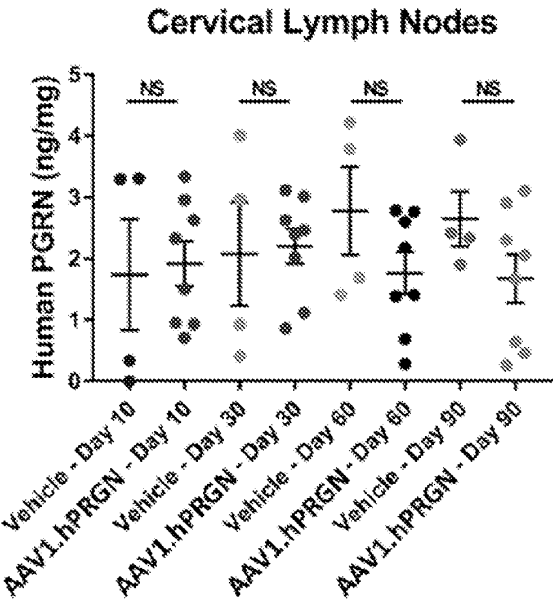
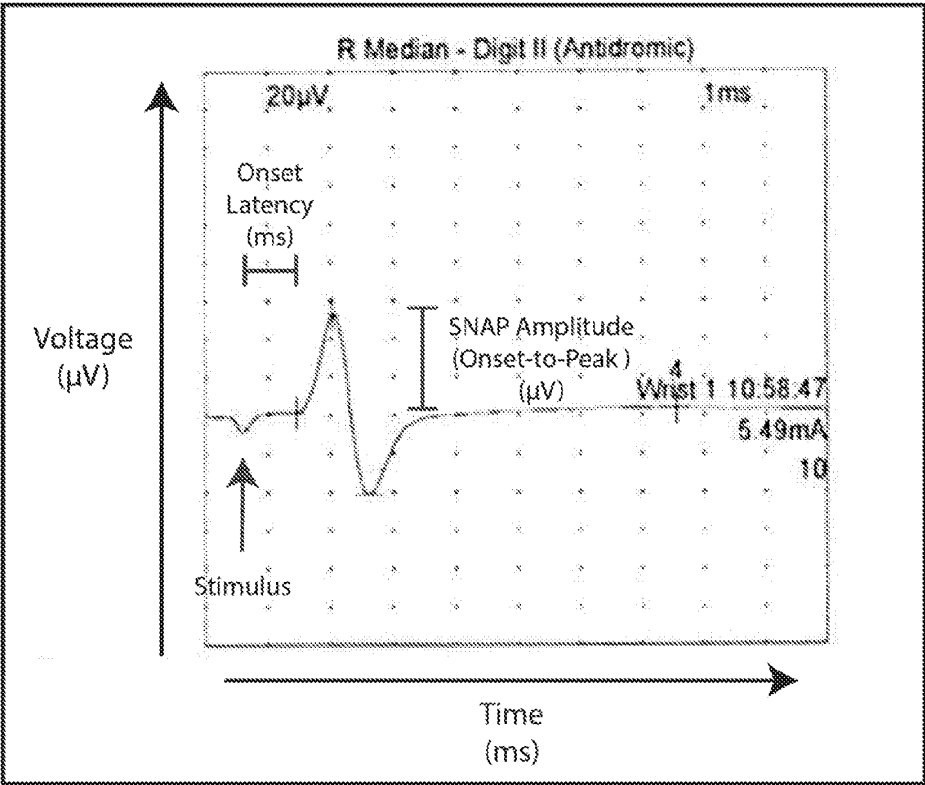


FIG. 24



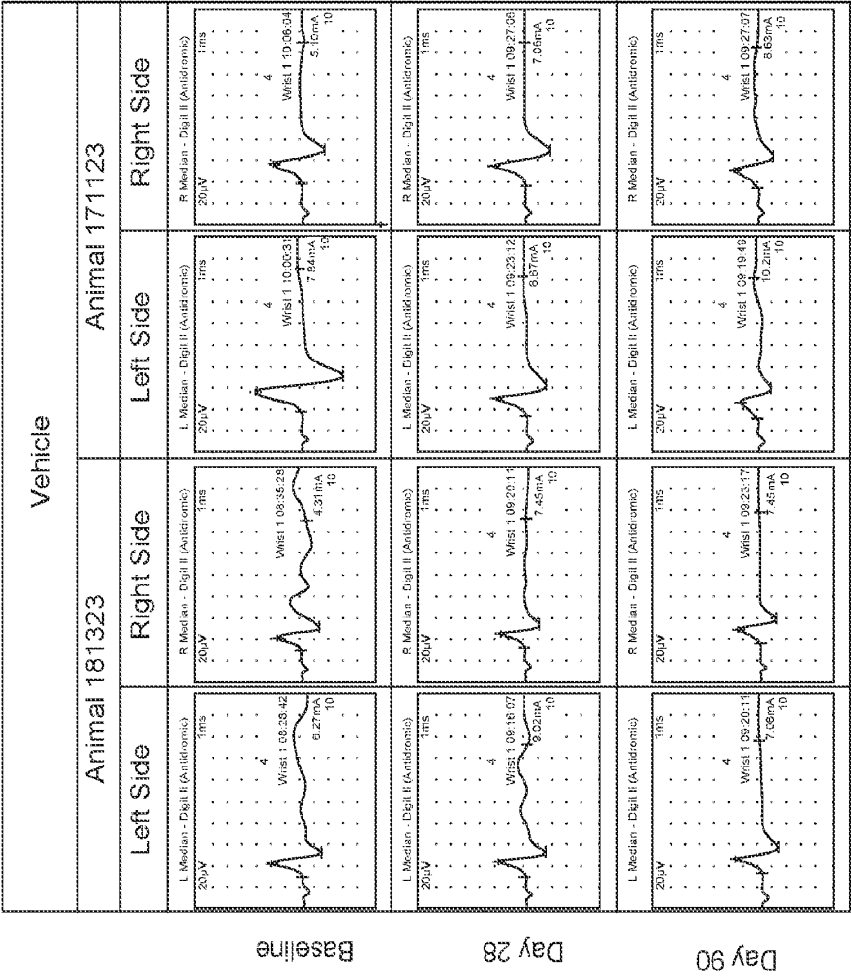


FIG. 25-1

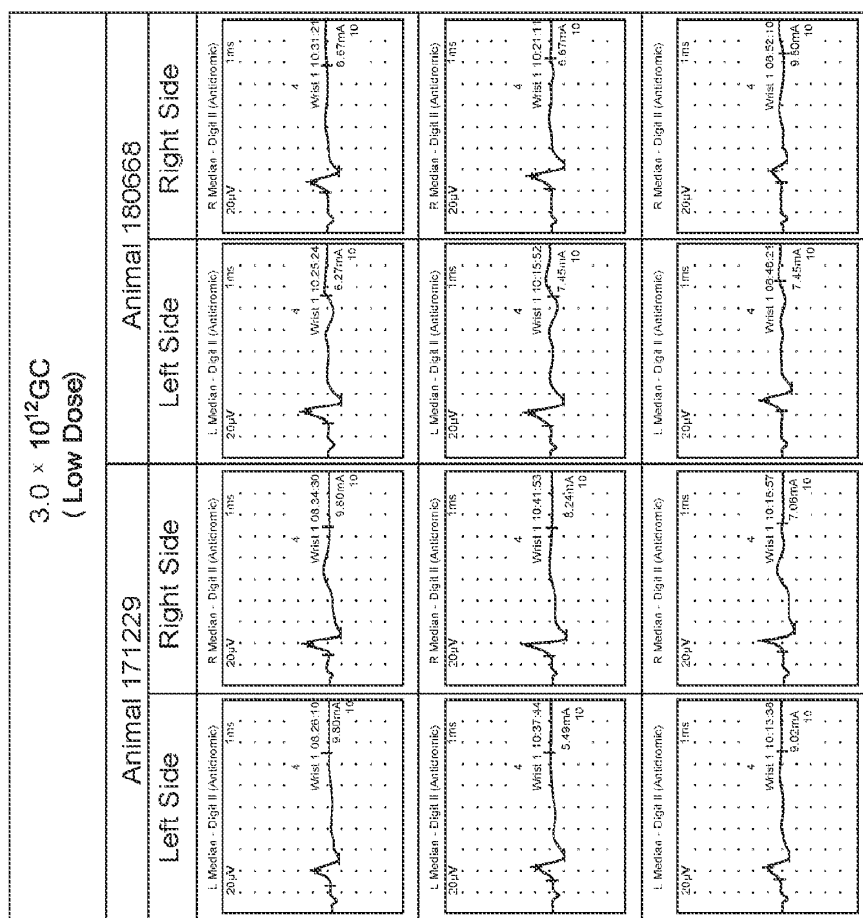


FIG. 25-2

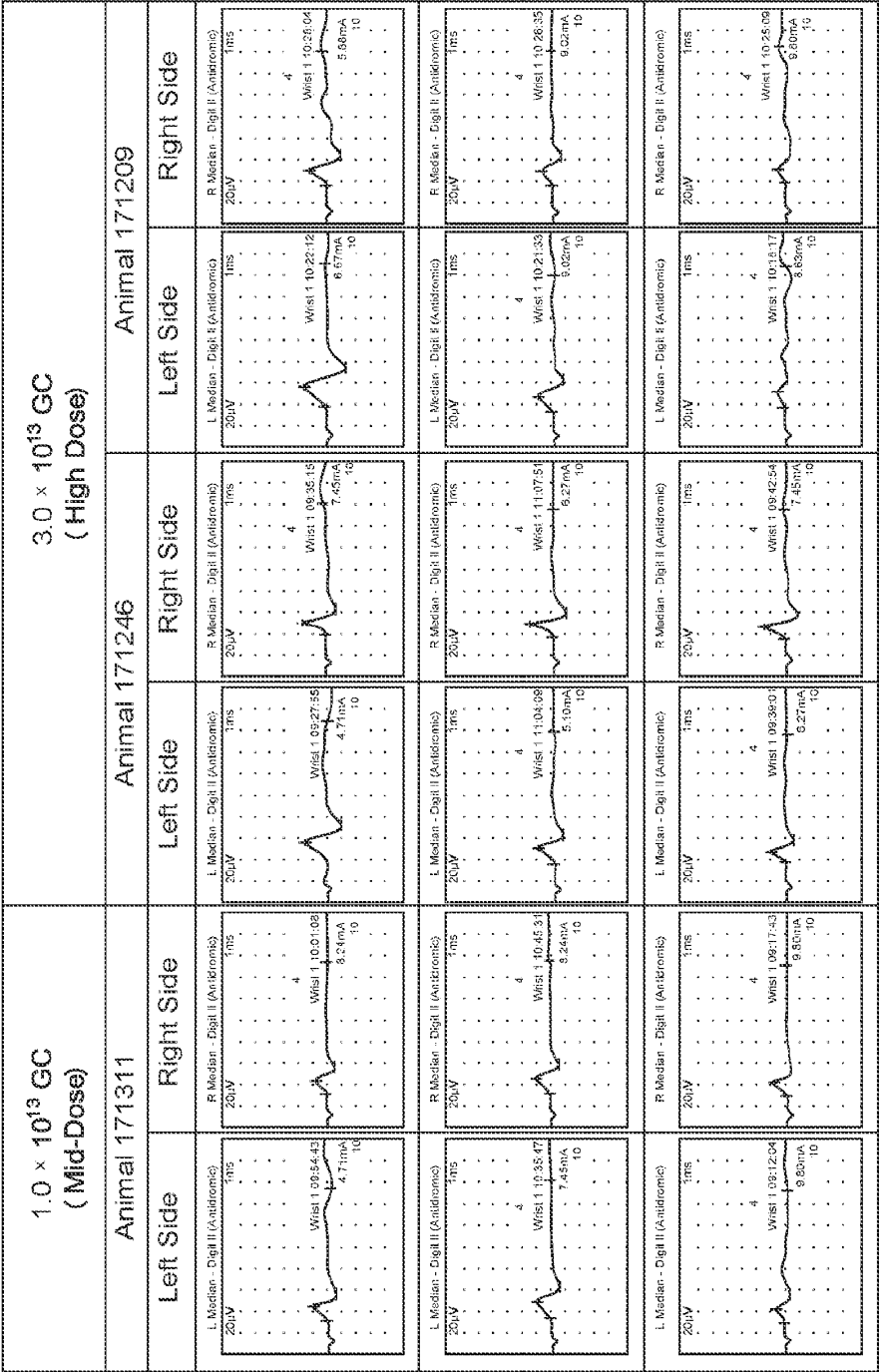


FIG. 25-3

FIG. 26A

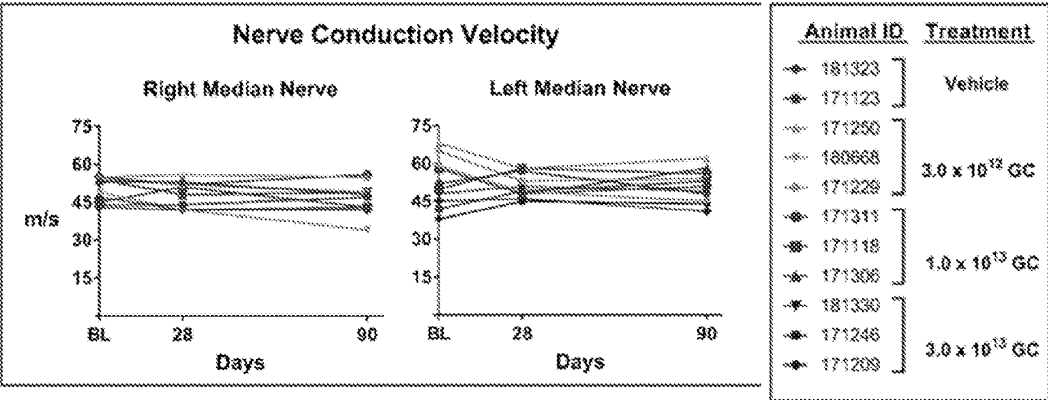
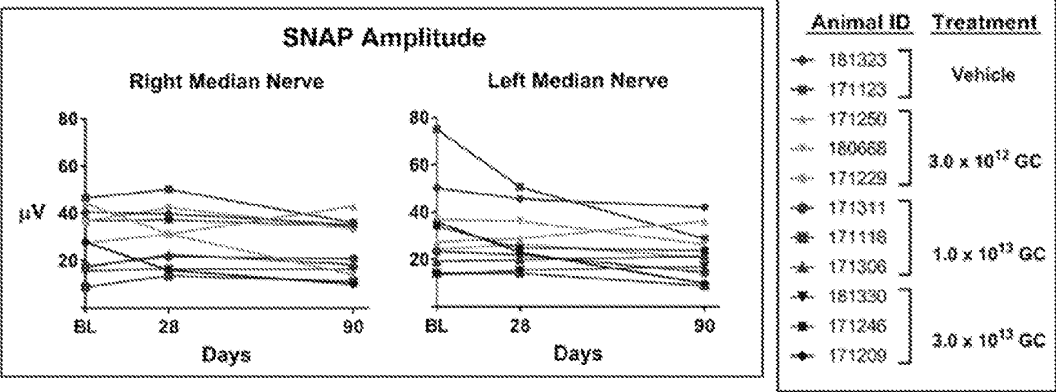


FIG. 26B

FIG. 27

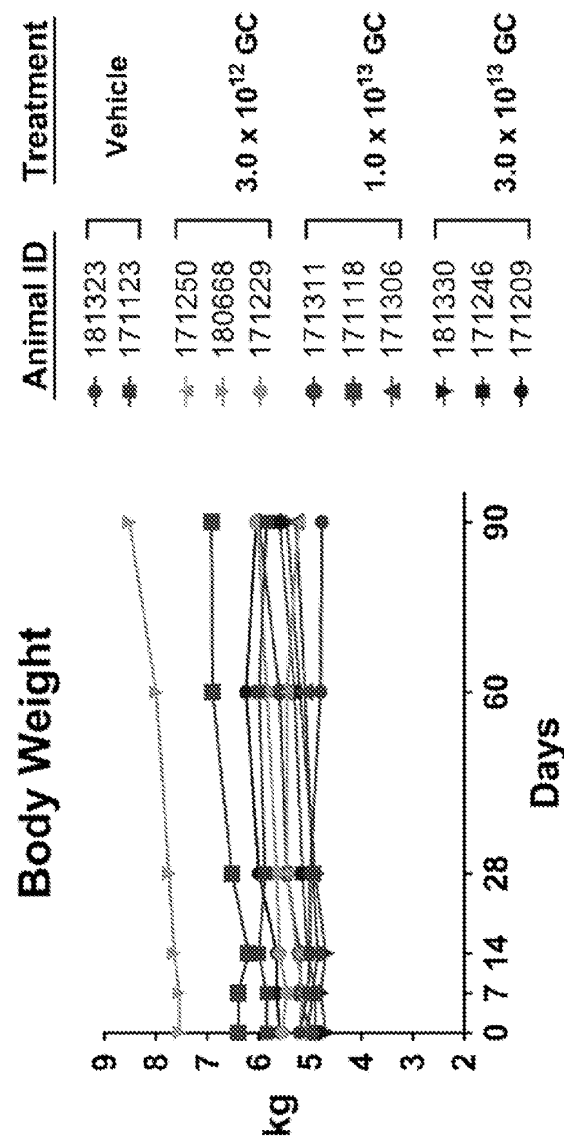


FIG. 28

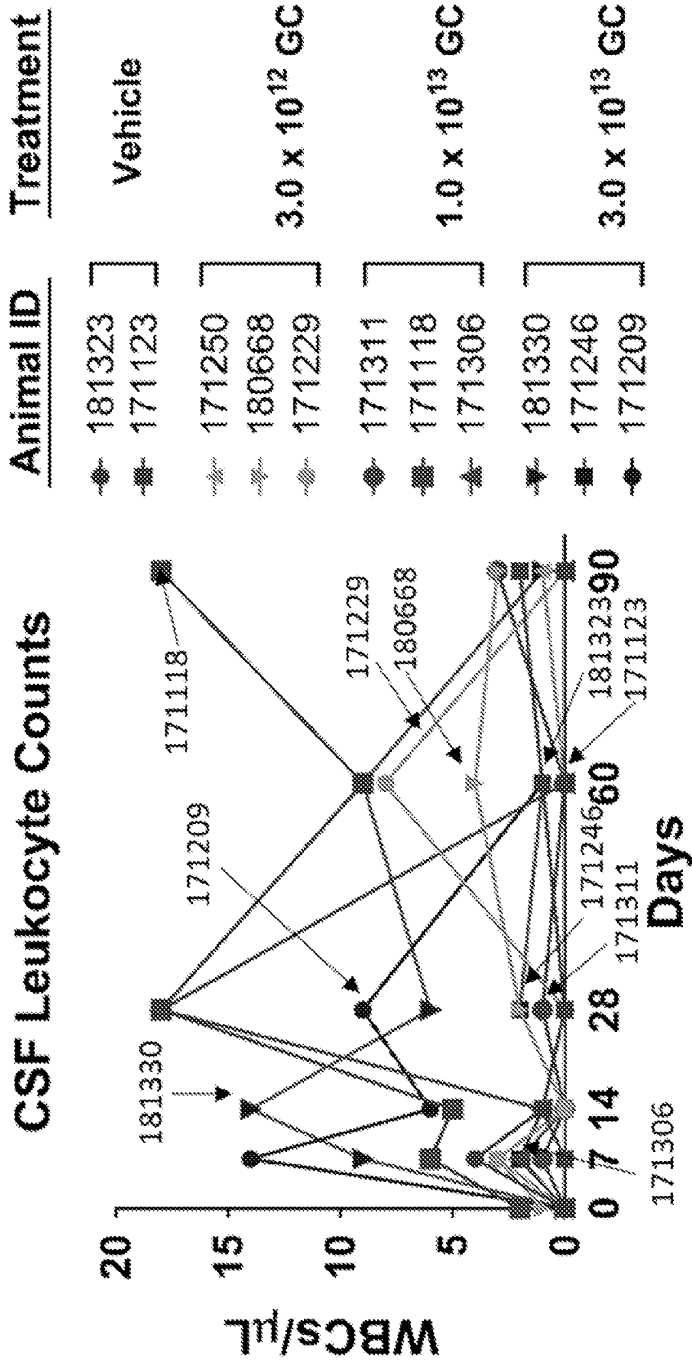


FIG. 29

Group	Treatment	Dose (GC/Animal)	Animal ID	IFN- γ T Cell Response											
				AAV1 (Capsid)						Human PGRN (Transgene)					
				PBMCs			Tissue-Specific Lymphocytes			PBMCs			Tissue-Specific Lymphocytes		
				BL	Day 28	Day 90	Spleen	Liver	Bone Marrow	BL	Day 28	Day 90	Spleen	Liver	Bone Marrow
1	ITFFB	N/A	171123												
			181323												
			171229											X	
2	AAV1.PPRGN	3.0 x 10 ¹²	171250			X						X	X	X	
			180668		X	X	X								
			171118					X							
3	AAV1.PPRGN	1.0 x 10 ¹²	171306		X	X	X					X		X	
			171311												
			171209		X					X			X	X	
4	AAV1.PPRGN	3.0 x 10 ¹²	171246		X	X	X	X				X		X	
			181330											X	

Abbreviations: AAV1, adeno-associated virus serotype 1; BL, baseline; GC, genome copies; ID, identification number; IFN- γ , interferon gamma; ITFFB, intrathecal final formulation buffer; N/A, not applicable; NAb, neutralizing antibody; PBMC, peripheral blood mononuclear cell; PGRN, programulin (protein).

FIG. 30

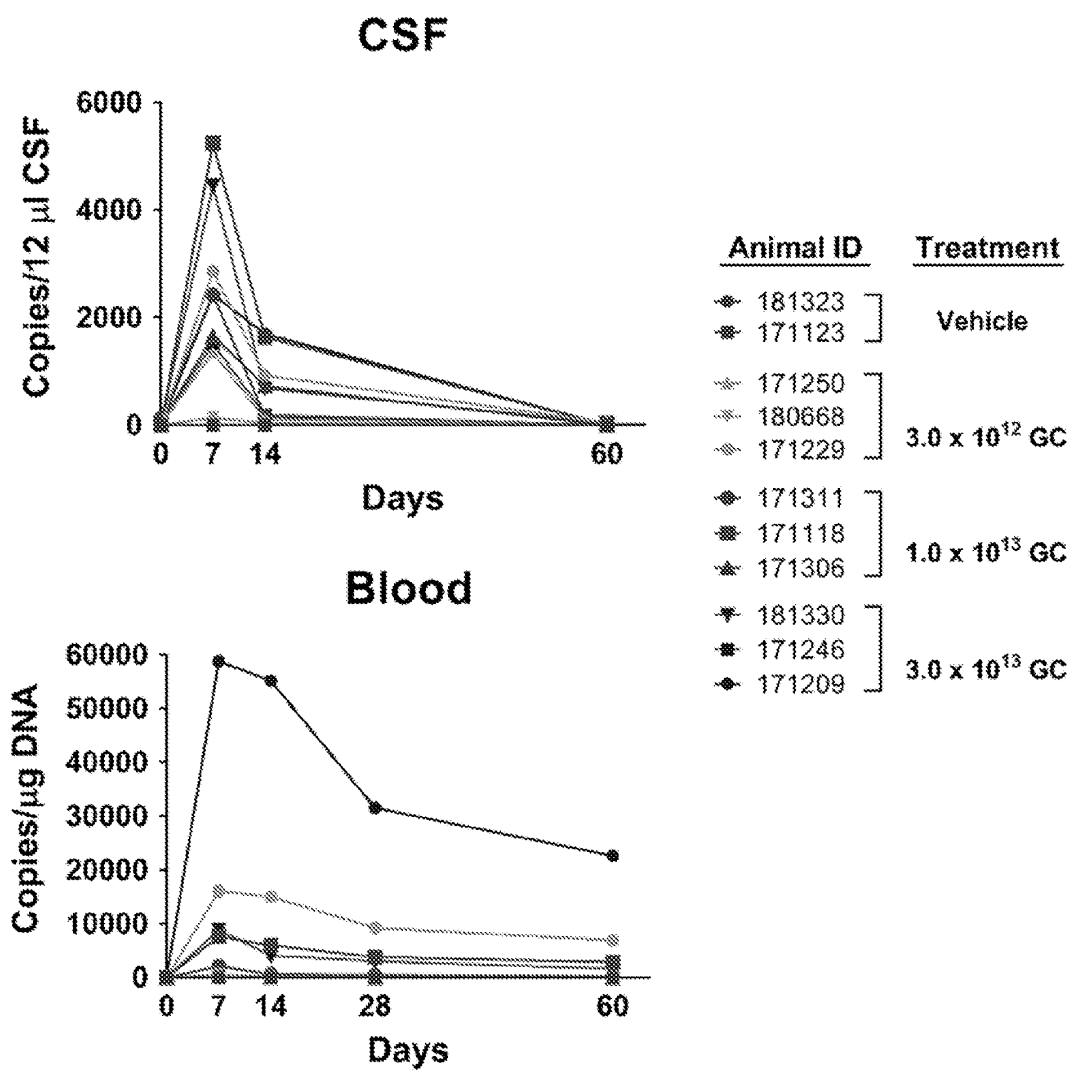


FIG. 31

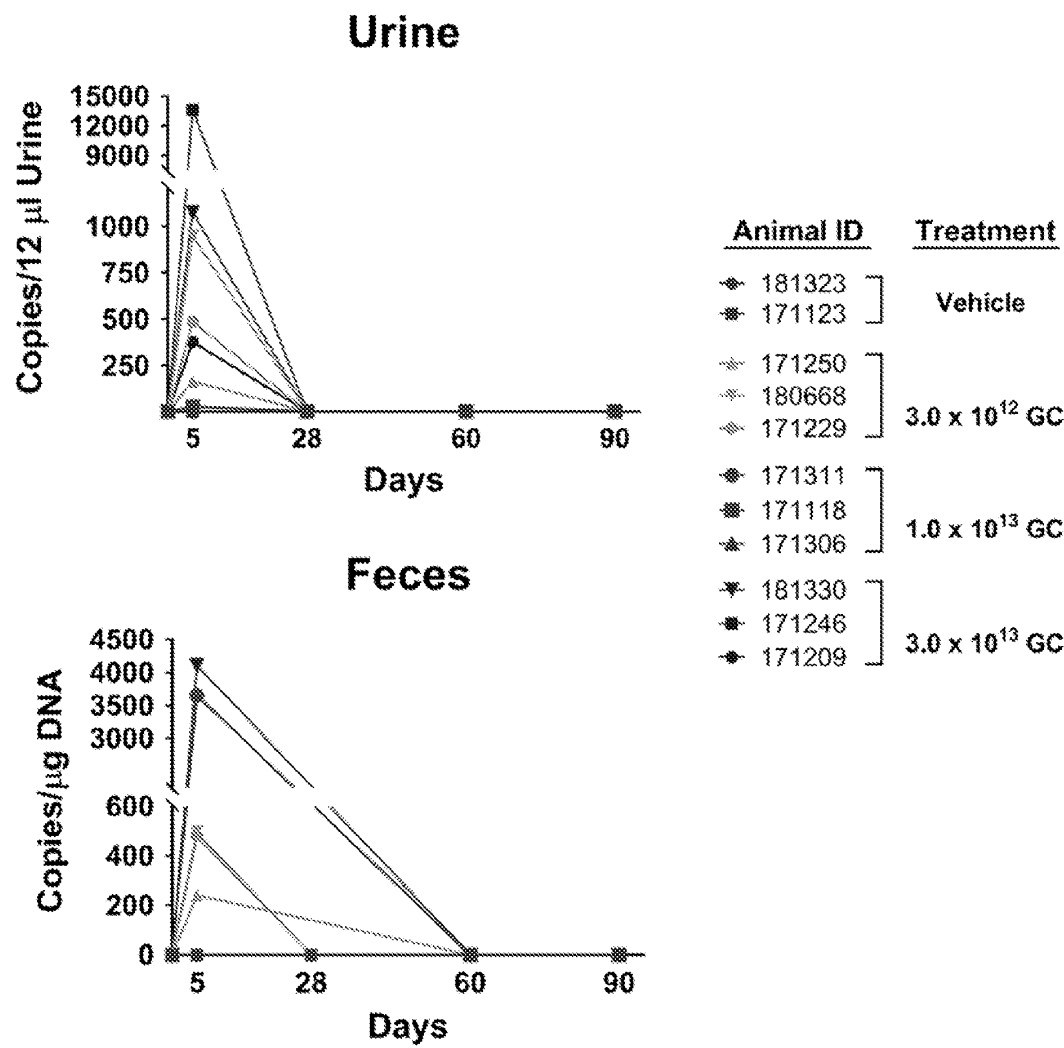


FIG. 32
Human PGRN Protein

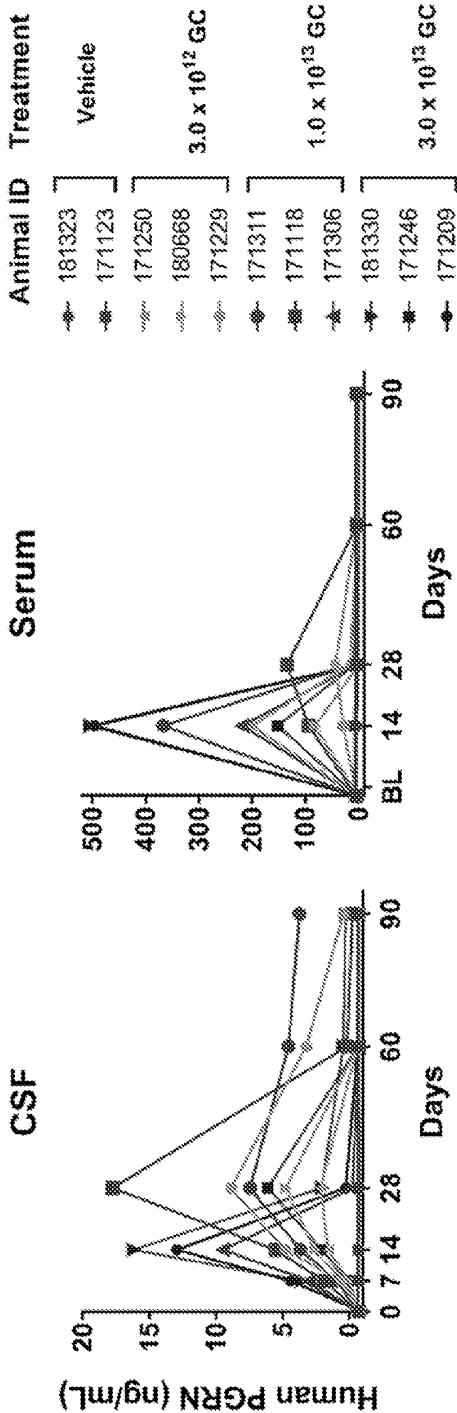


FIG. 33

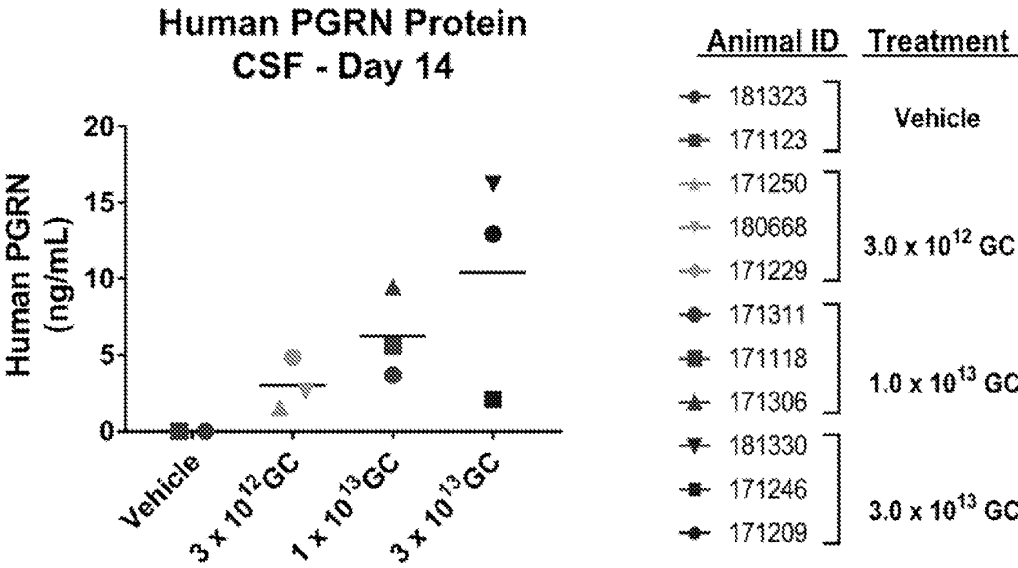


FIG. 34

Anti-Human PGRN Antibodies

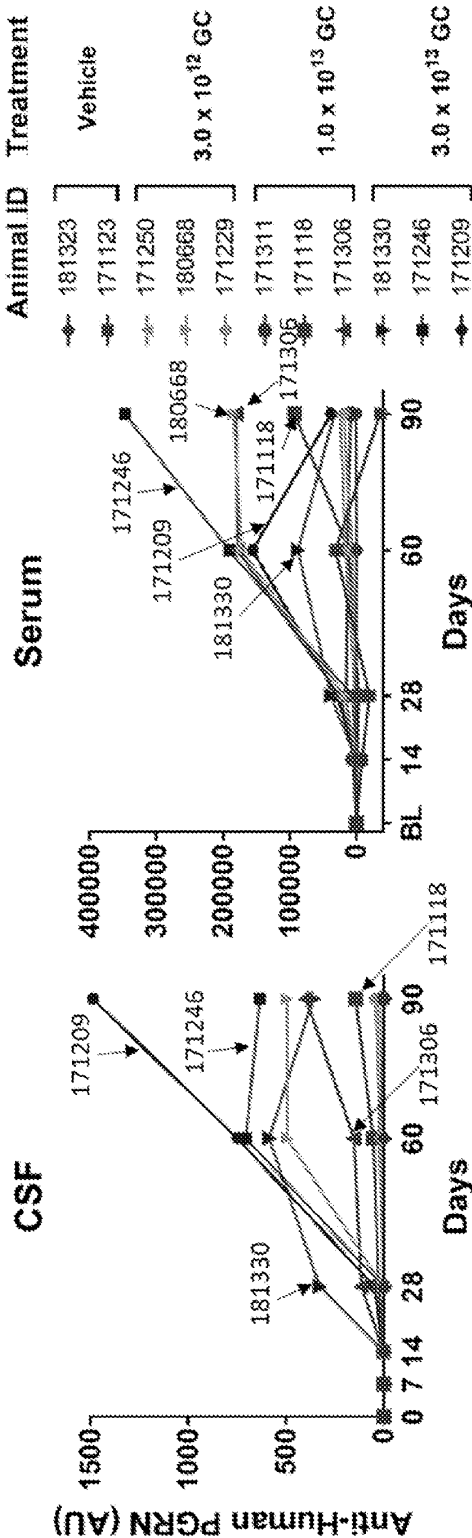


FIG. 35

