

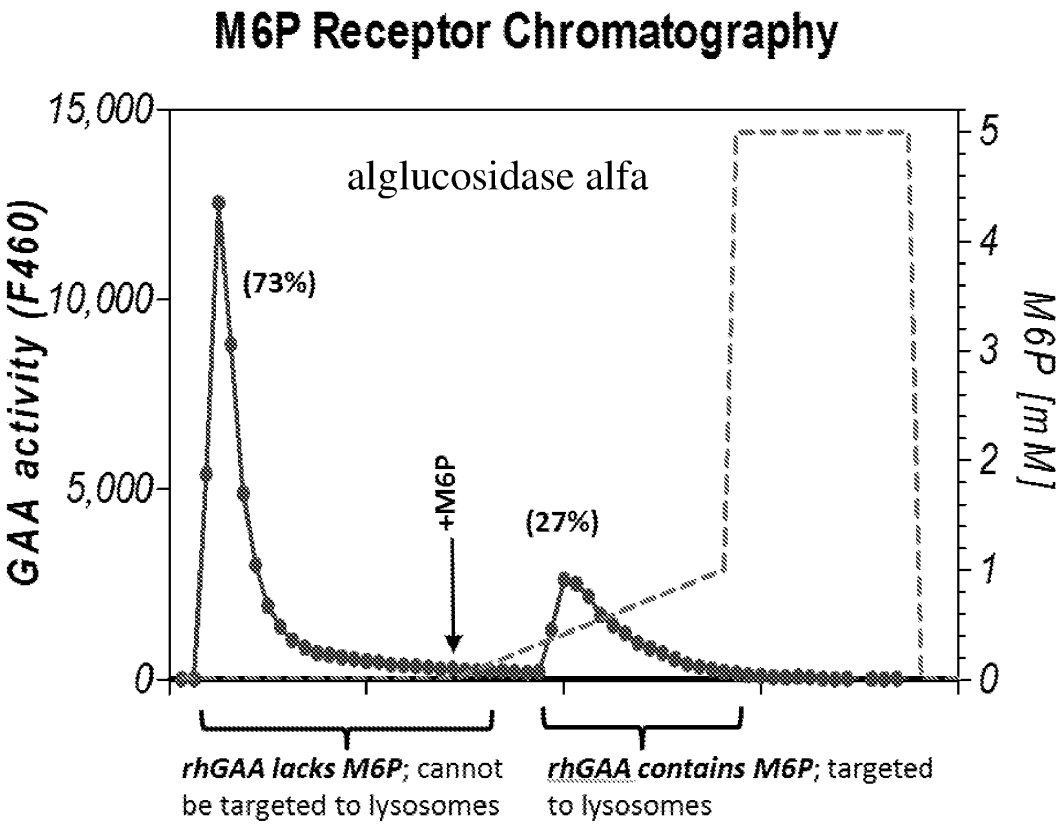


FIG. 1

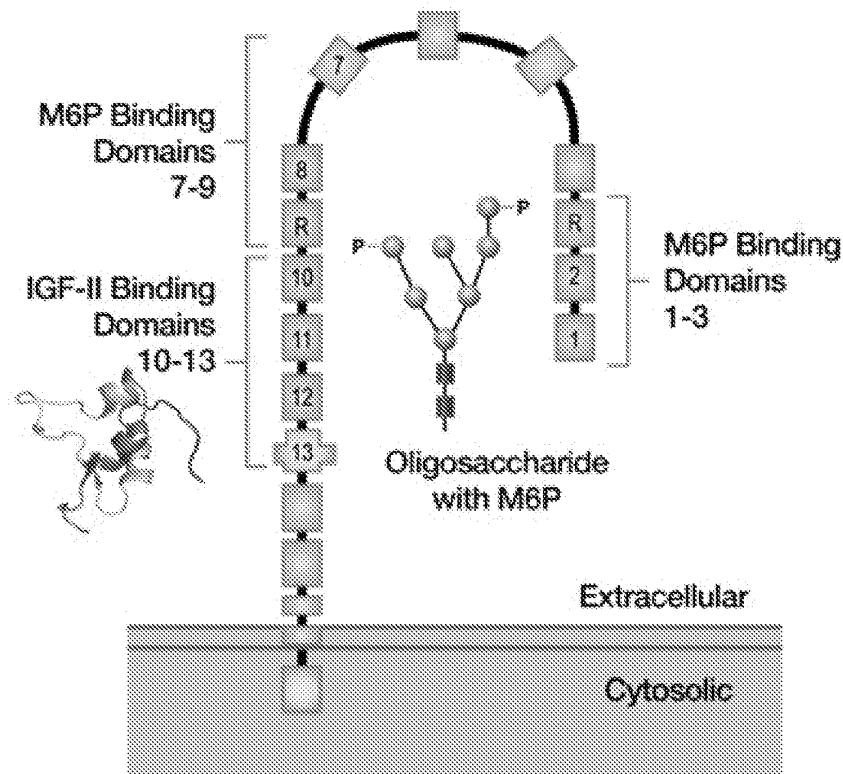


FIG. 2

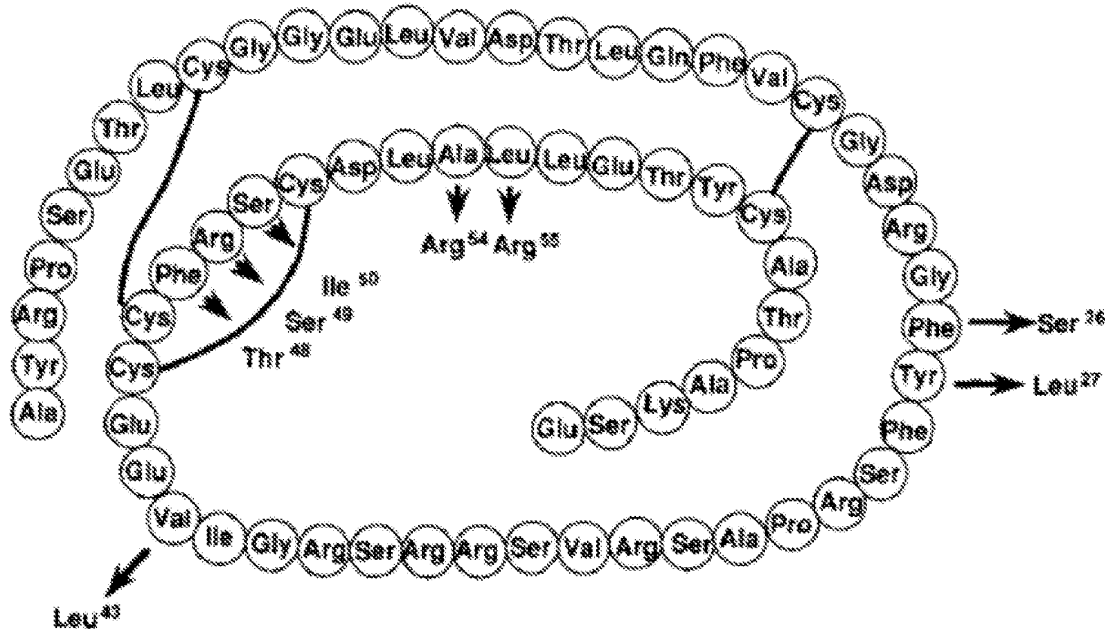


FIG. 3

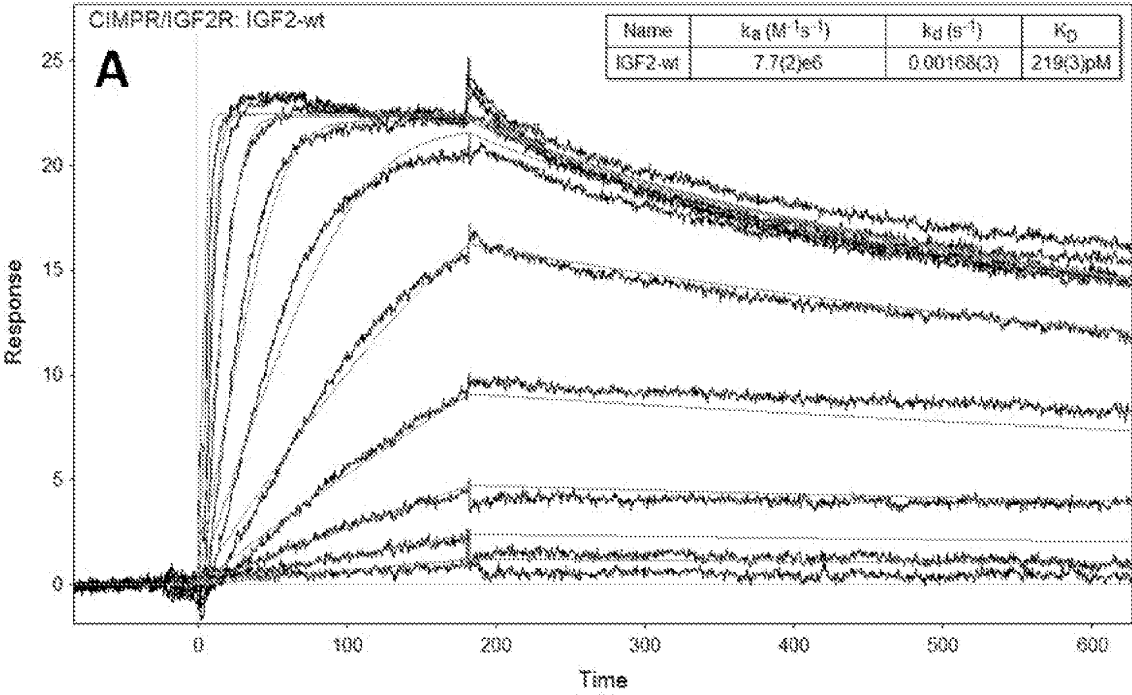


FIG. 4

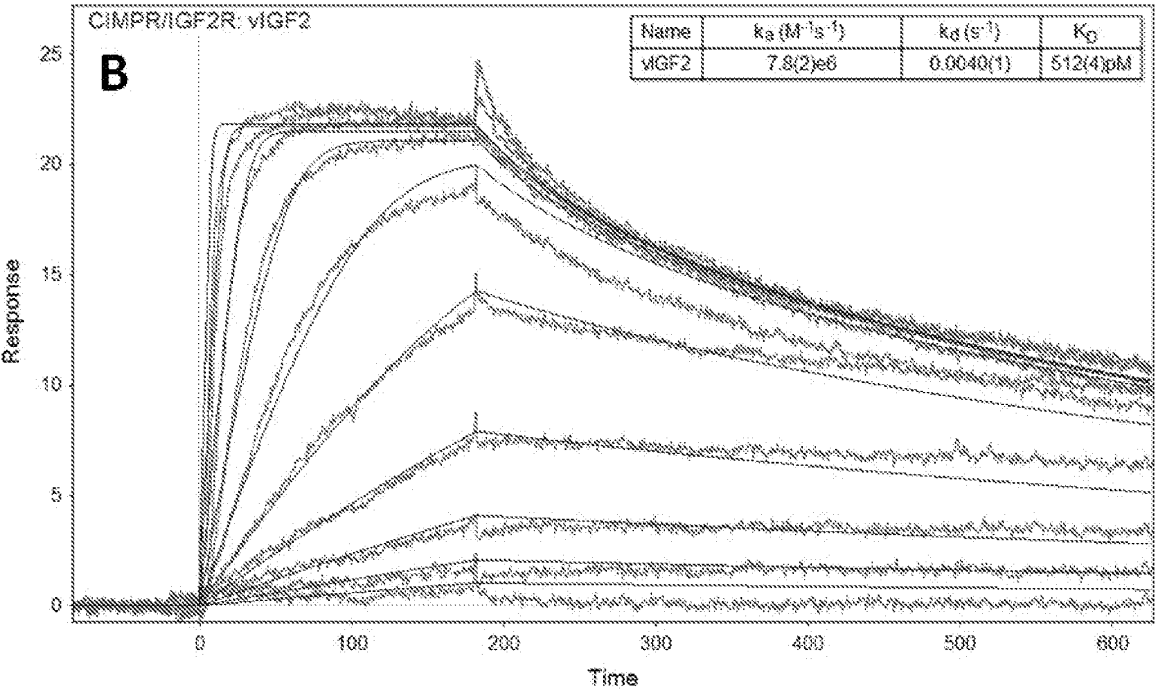
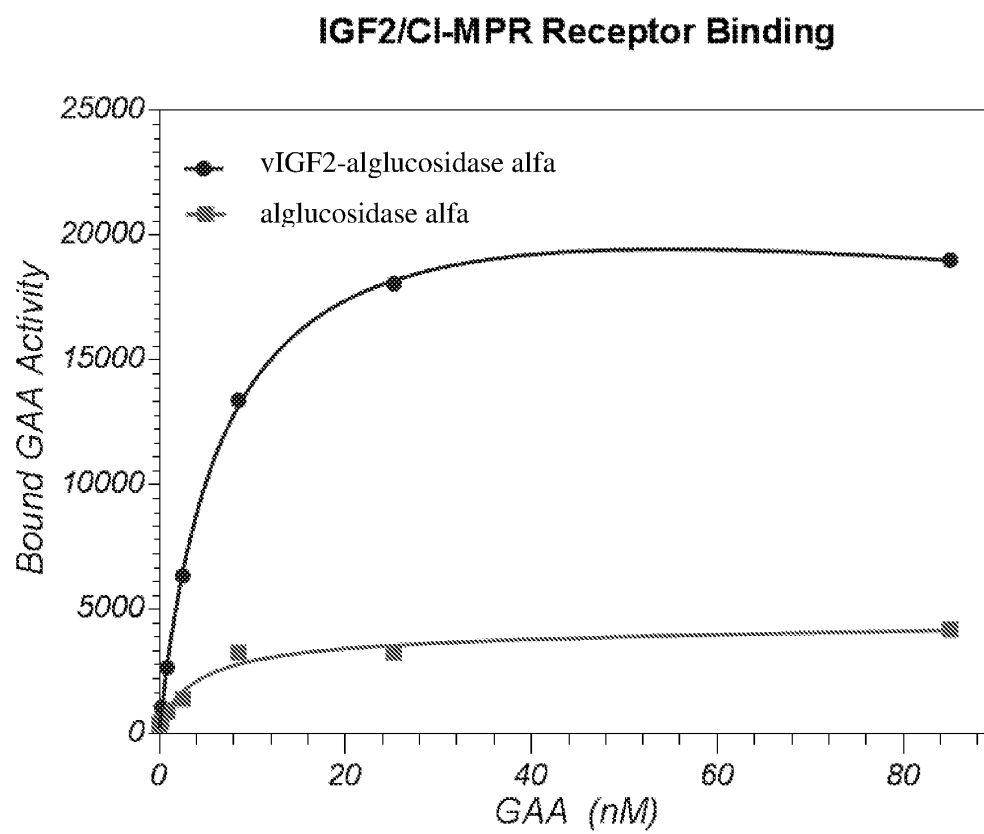


FIG. 5

**FIG. 6**

IGF2/CI-MPR Receptor Binding

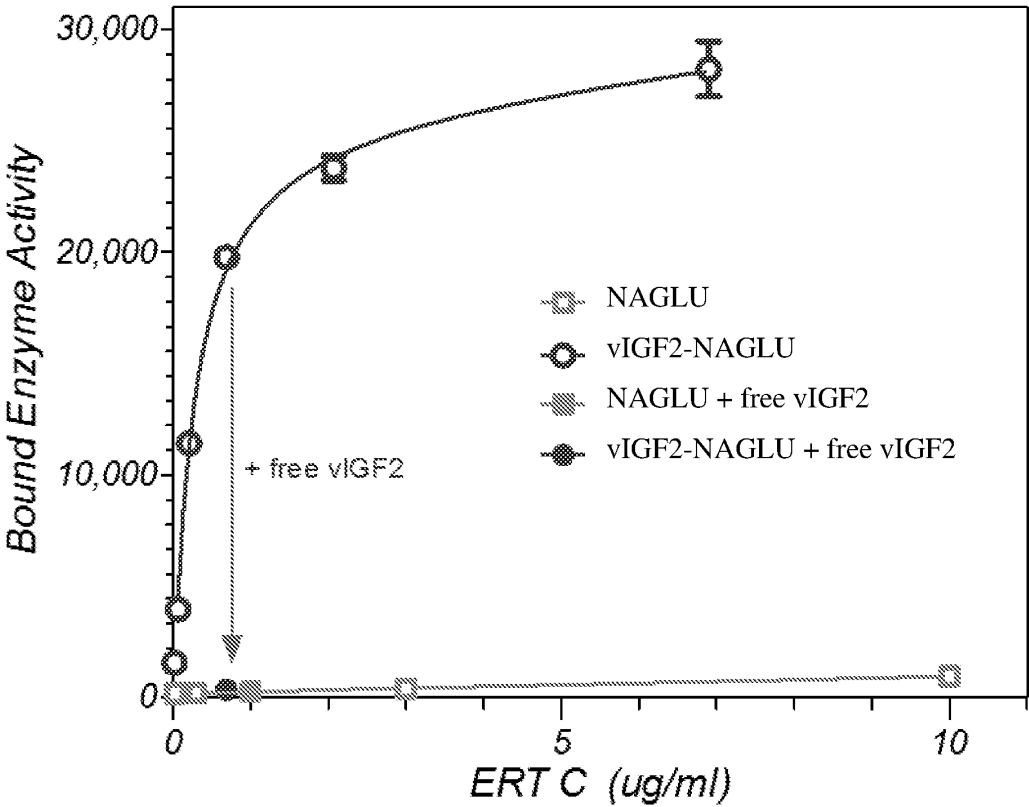


FIG. 7

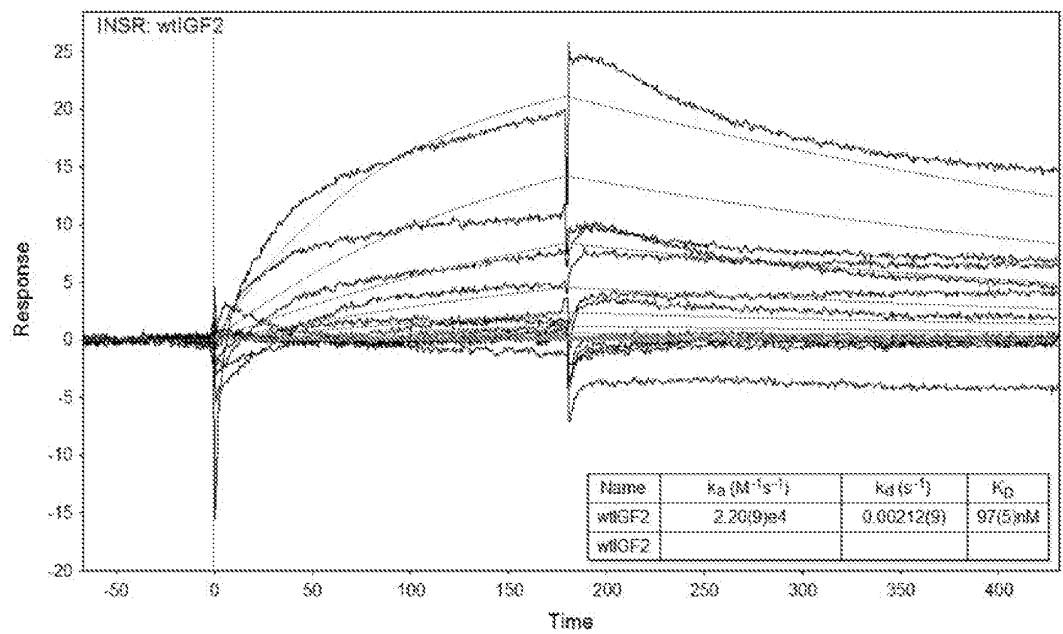


FIG. 8

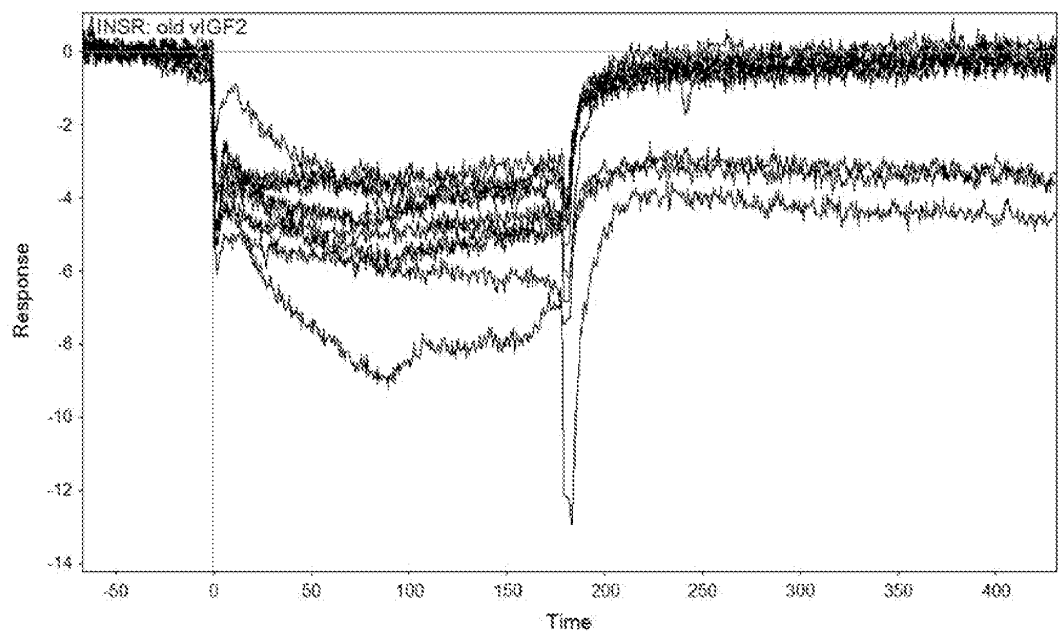


FIG. 9

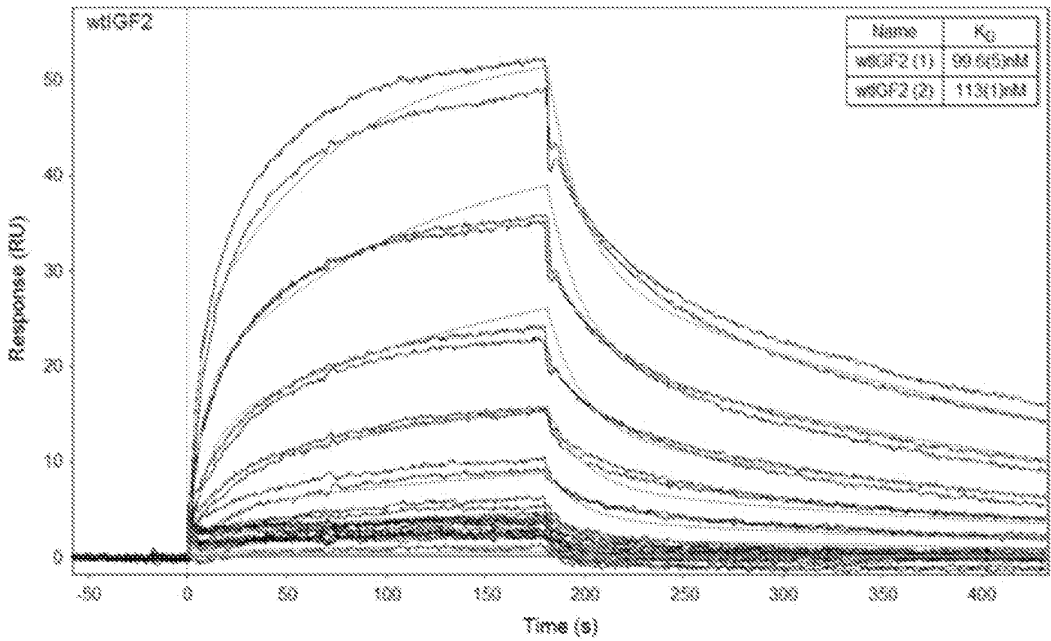


FIG. 10

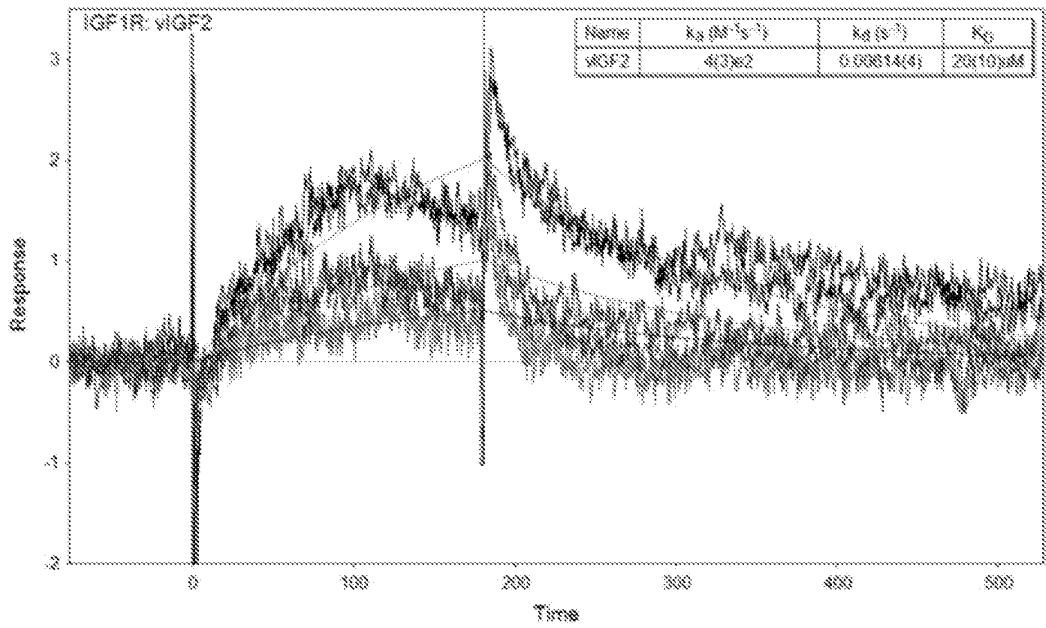


FIG. 11

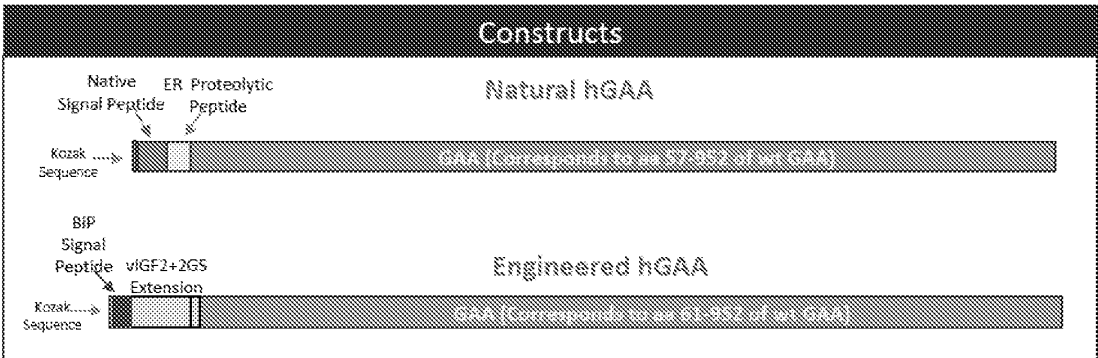


FIG. 12

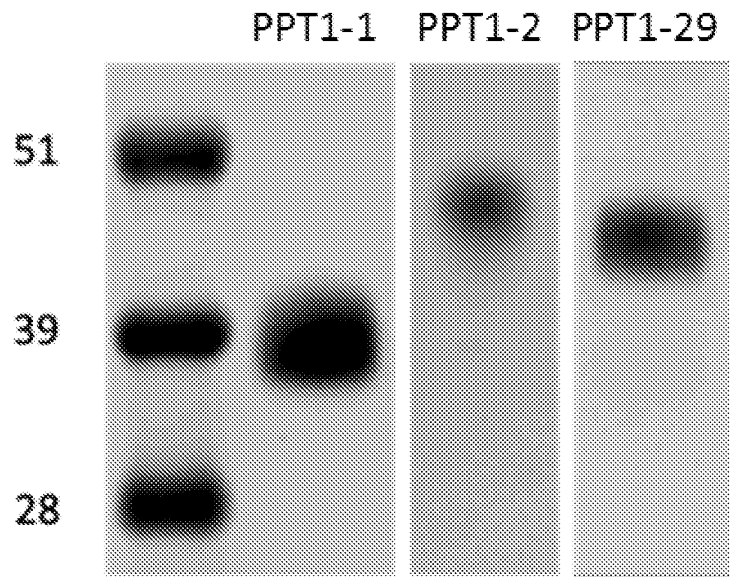


FIG. 13

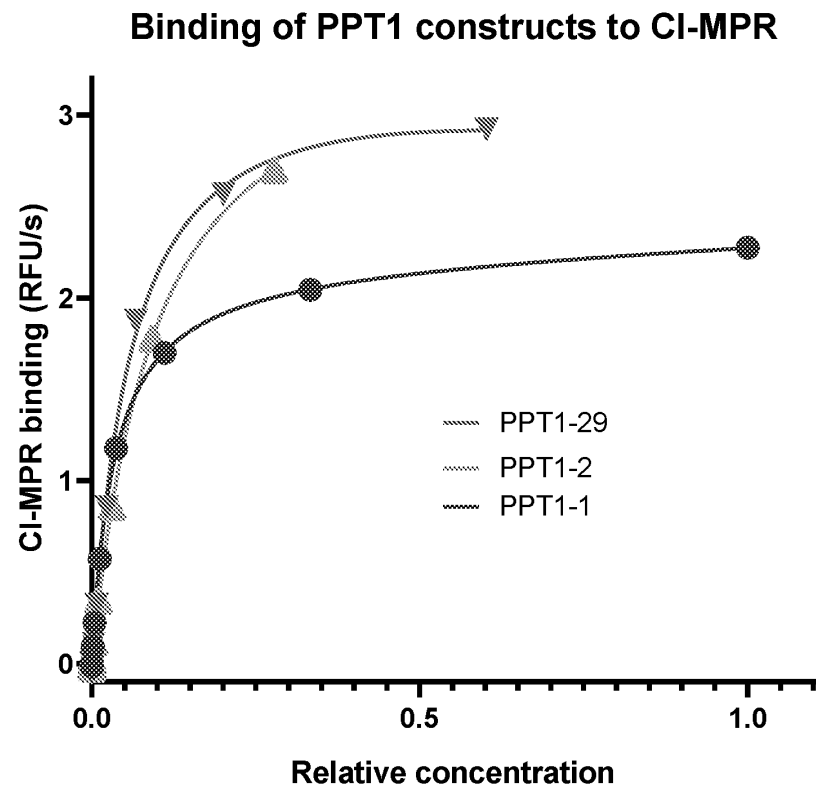


FIG. 14

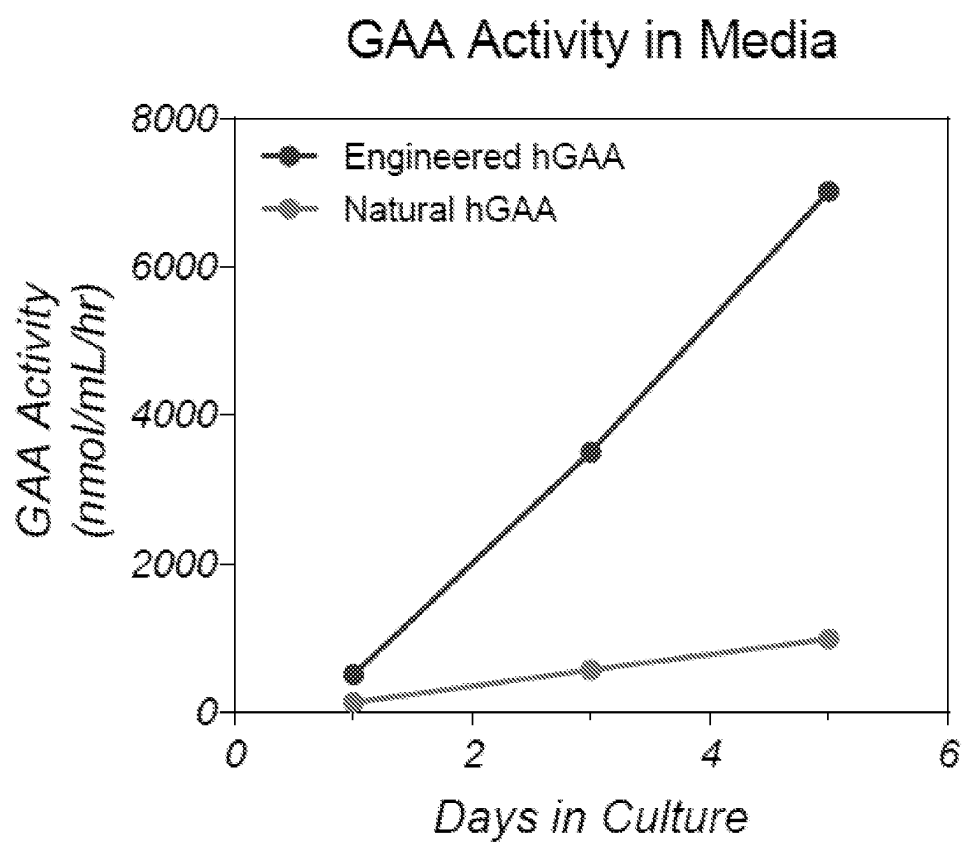


FIG. 15

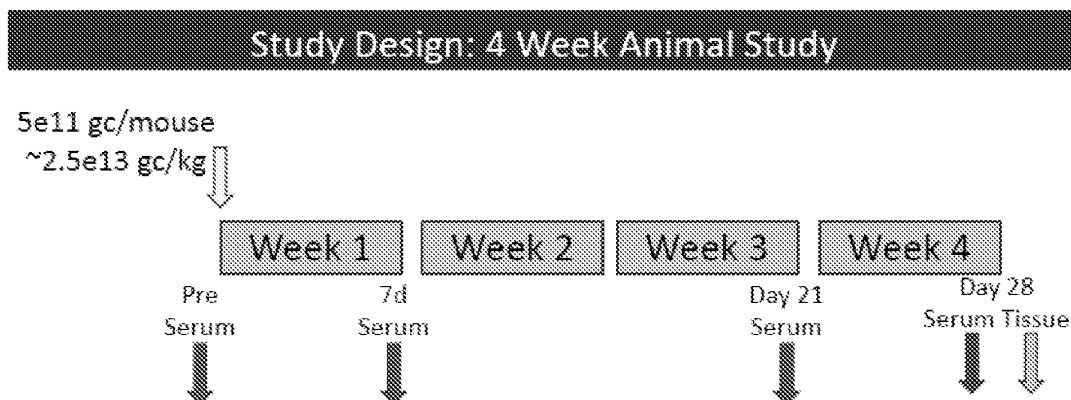


FIG. 16

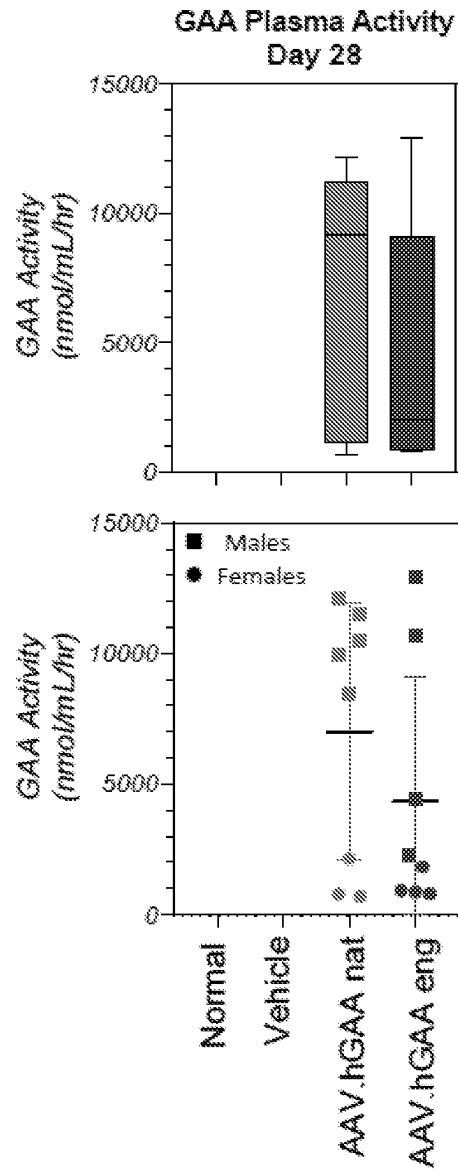


FIG. 17

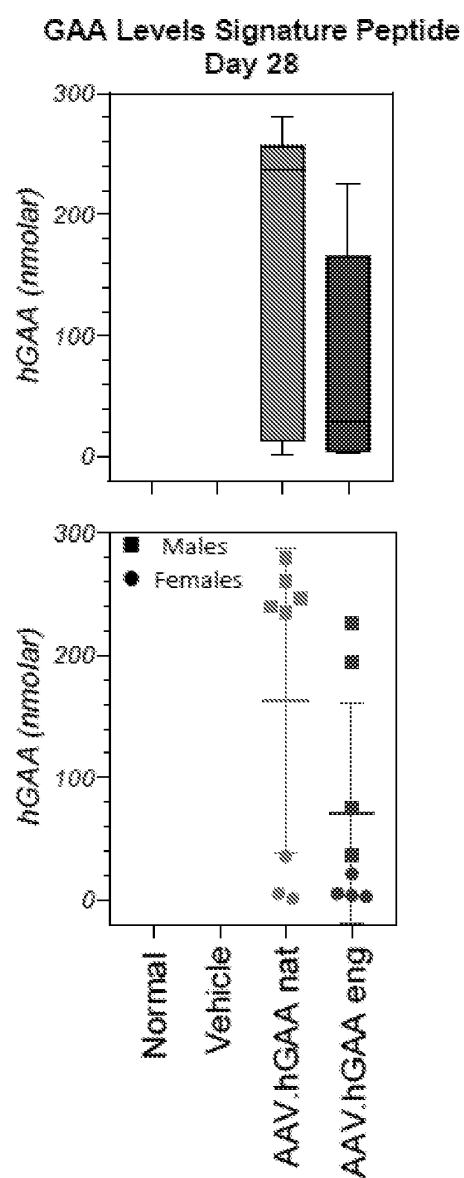


FIG. 18

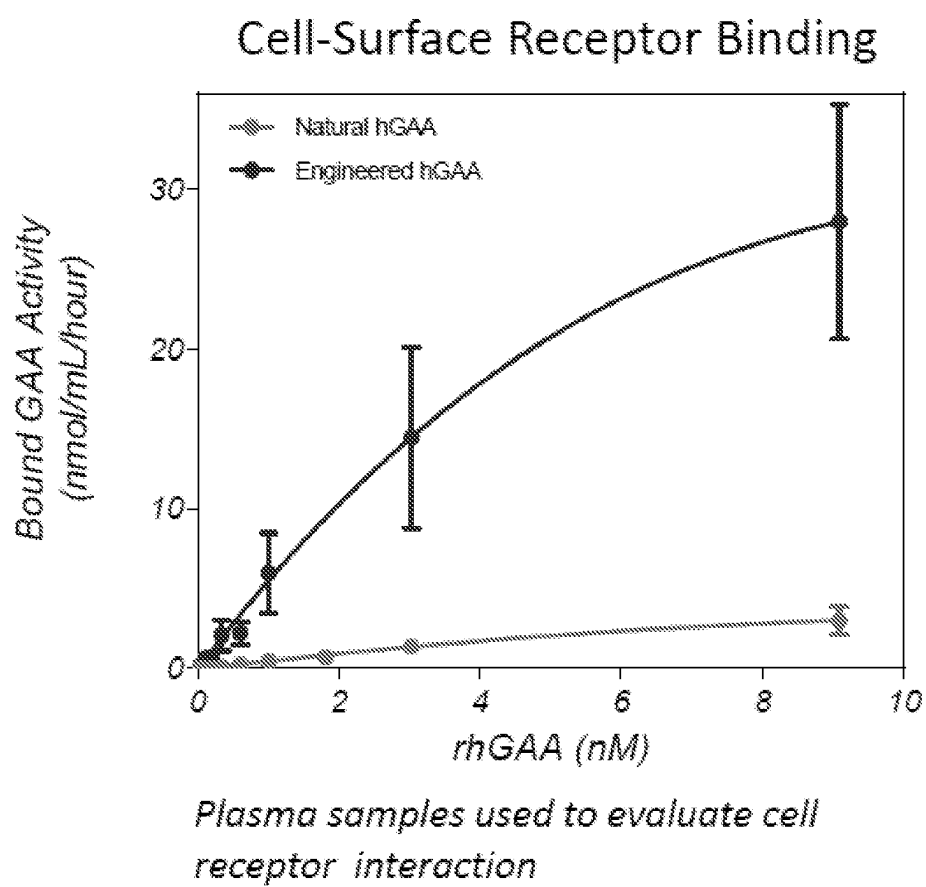


FIG. 19

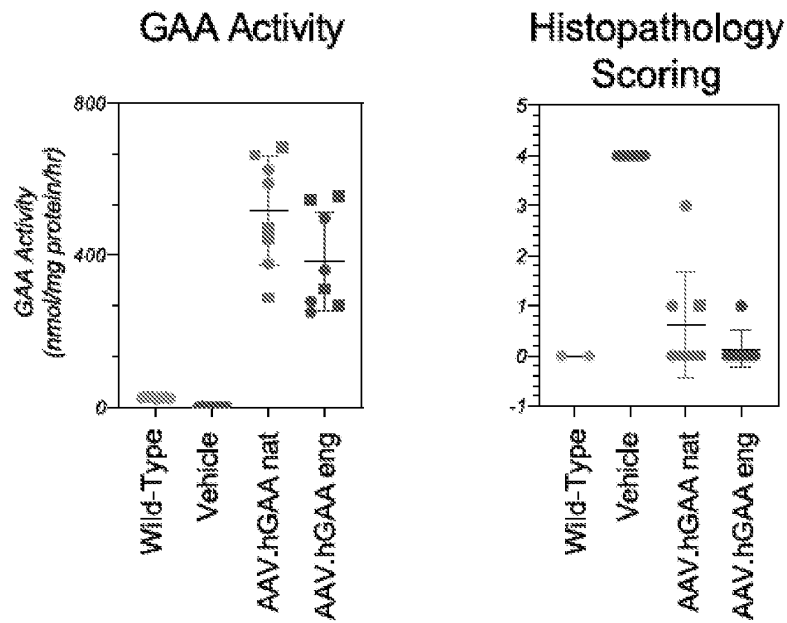


FIG. 20

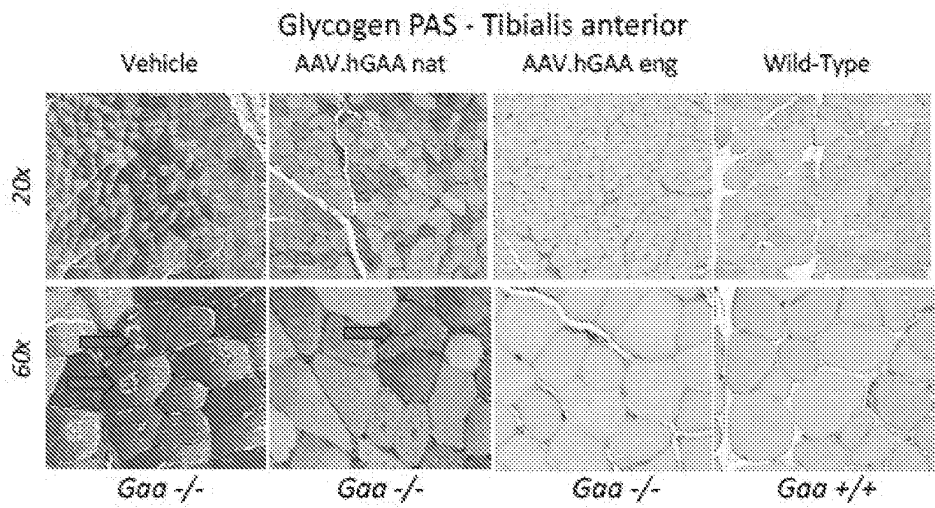


FIG. 21

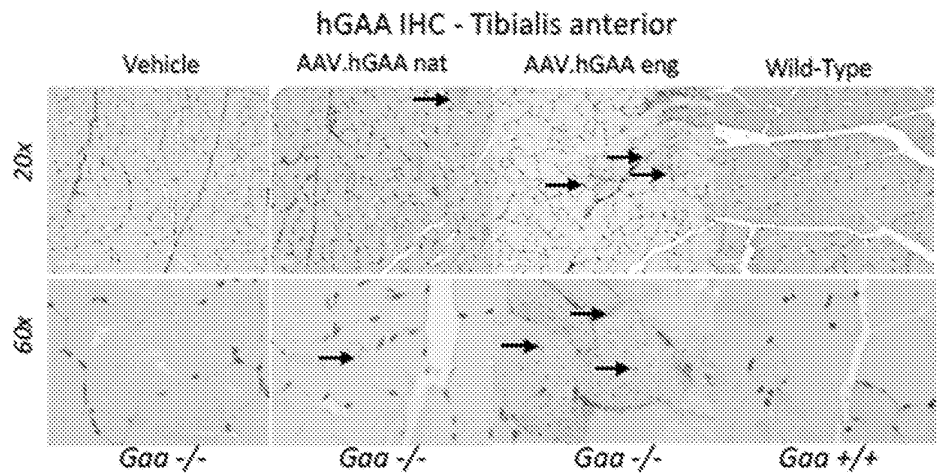


FIG. 22

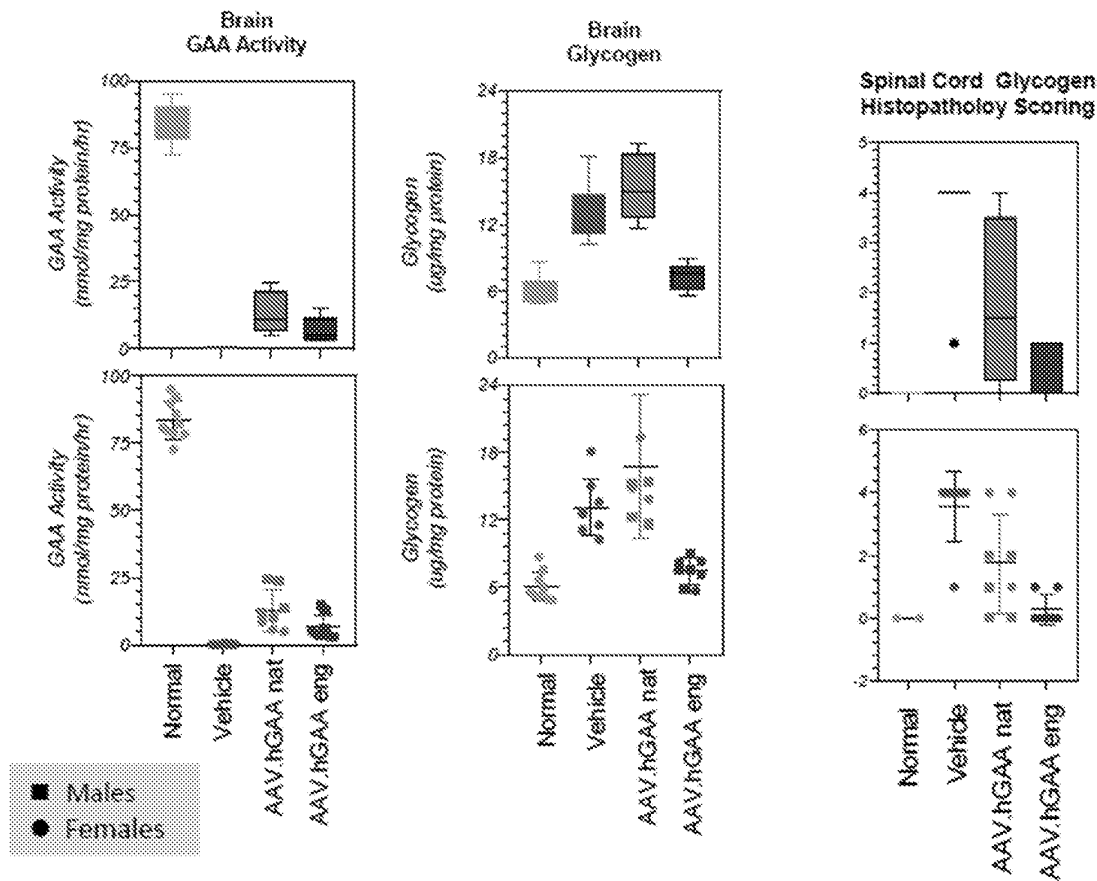


FIG. 23

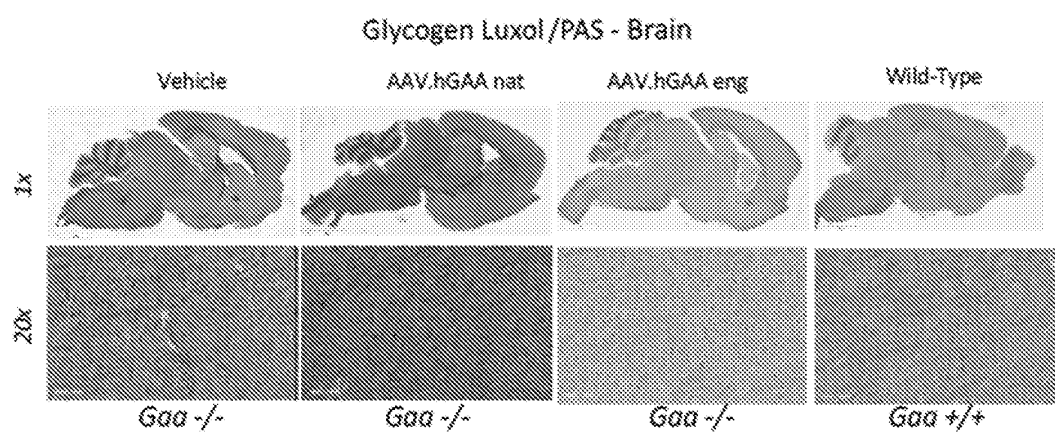


FIG. 24

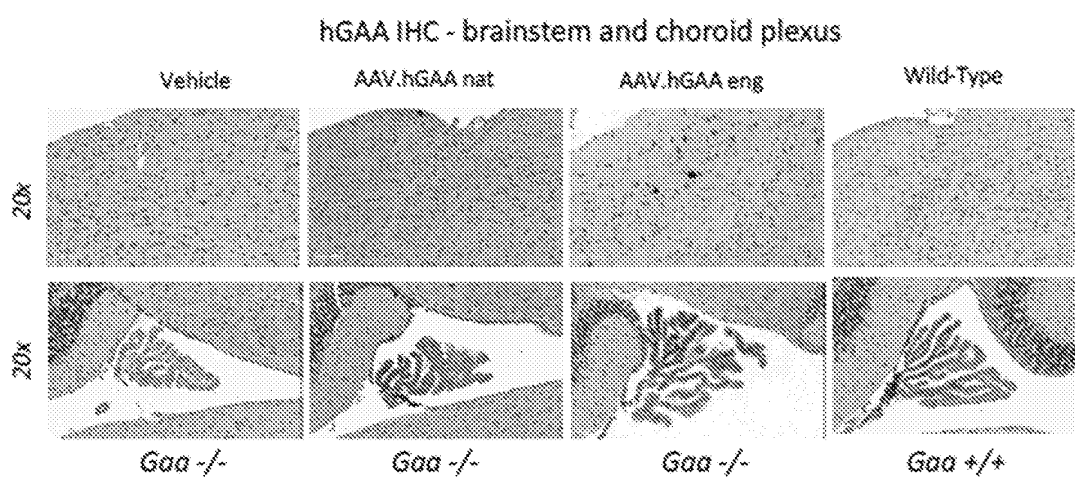


FIG. 25

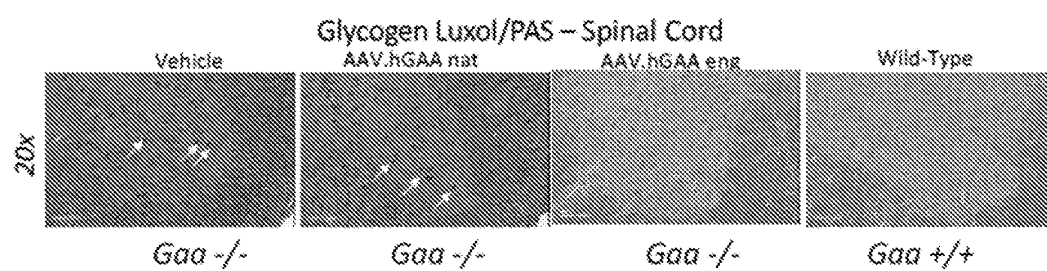


FIG. 26

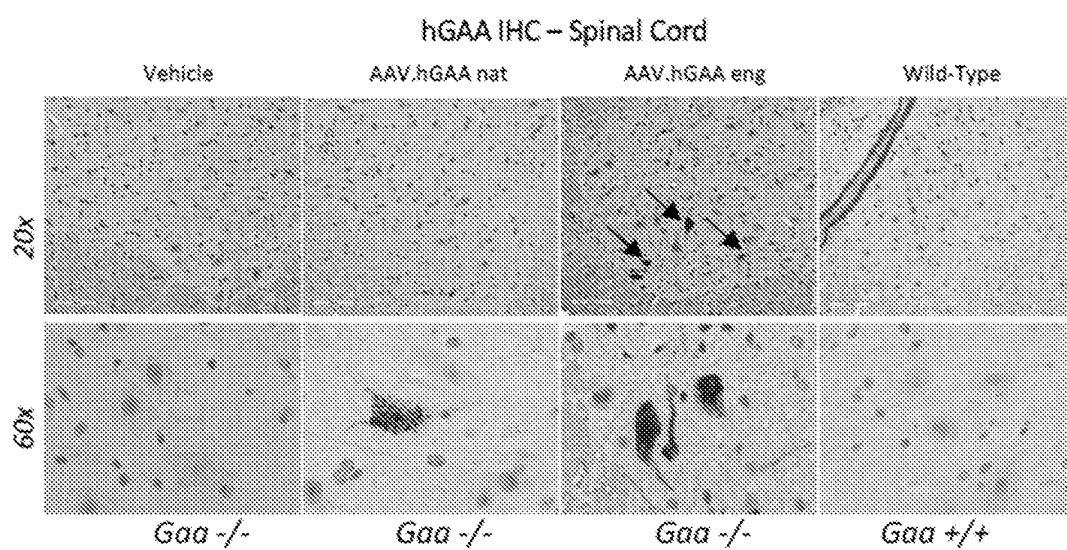


FIG. 27

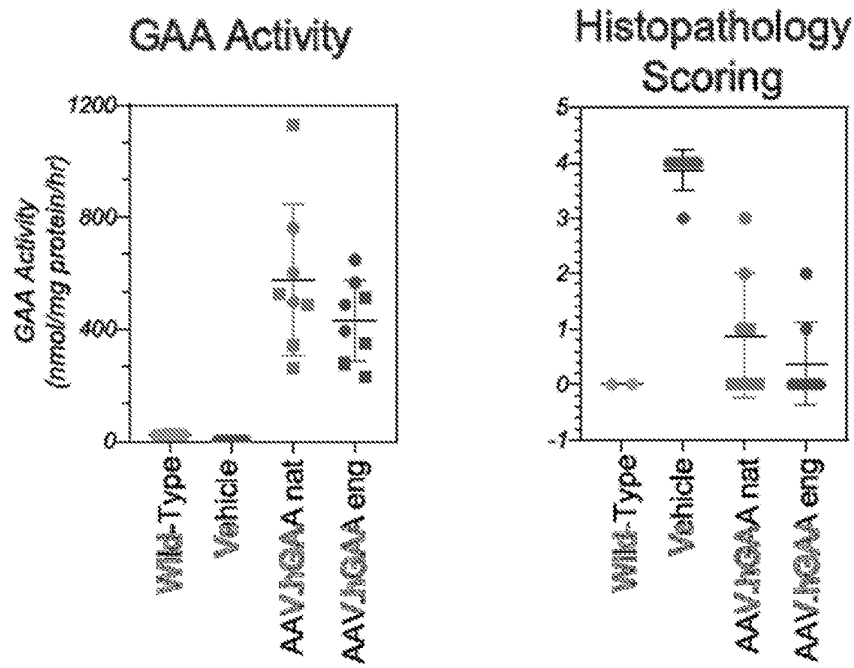


FIG. 28

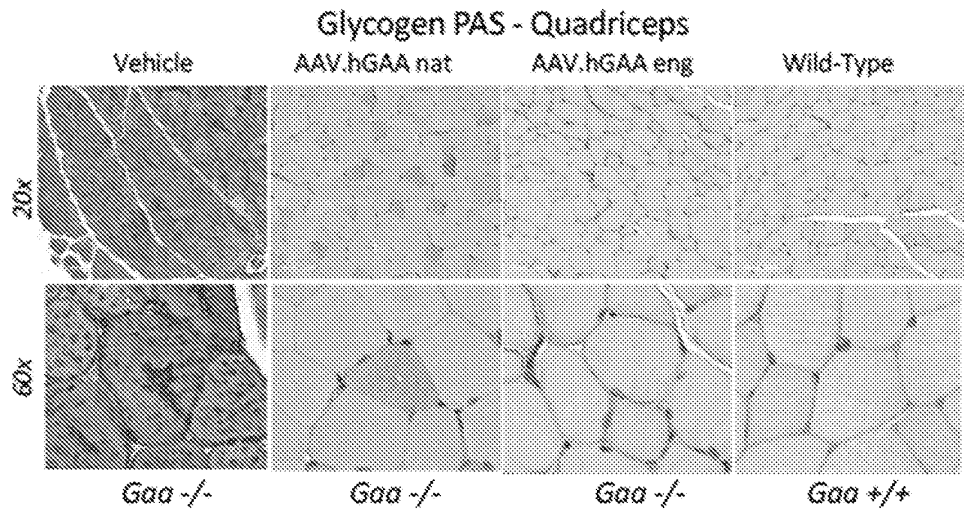


FIG. 29

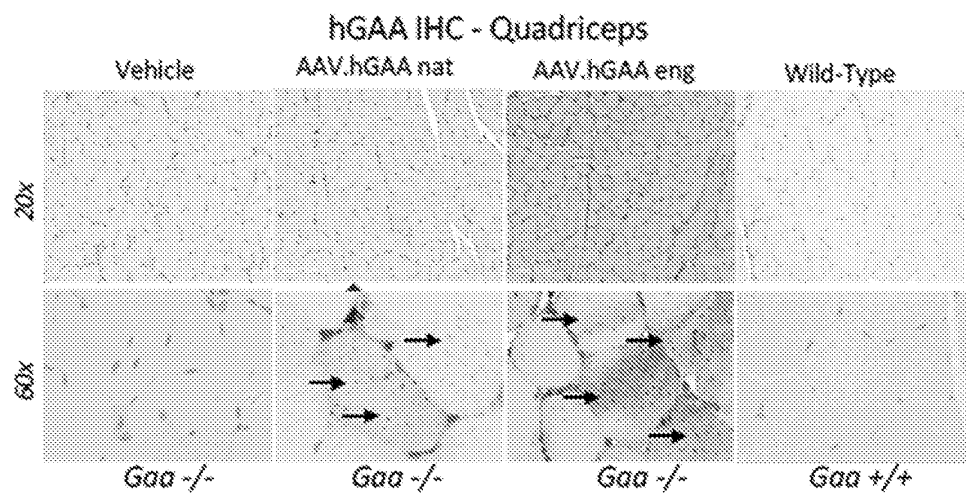


FIG. 30

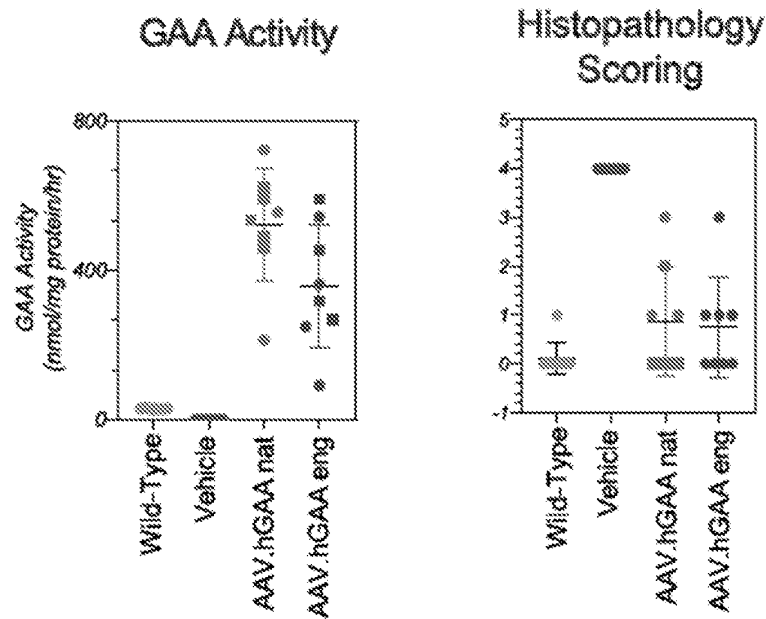


FIG. 31

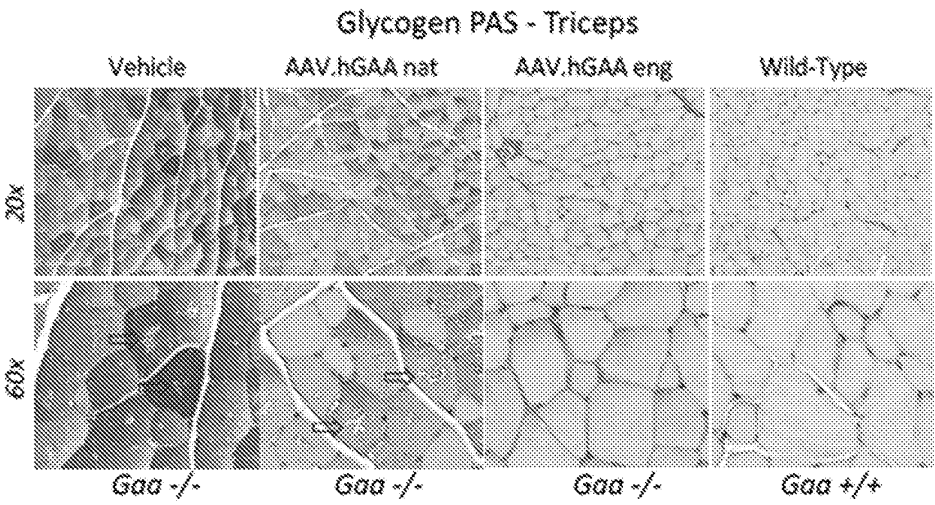


FIG. 32

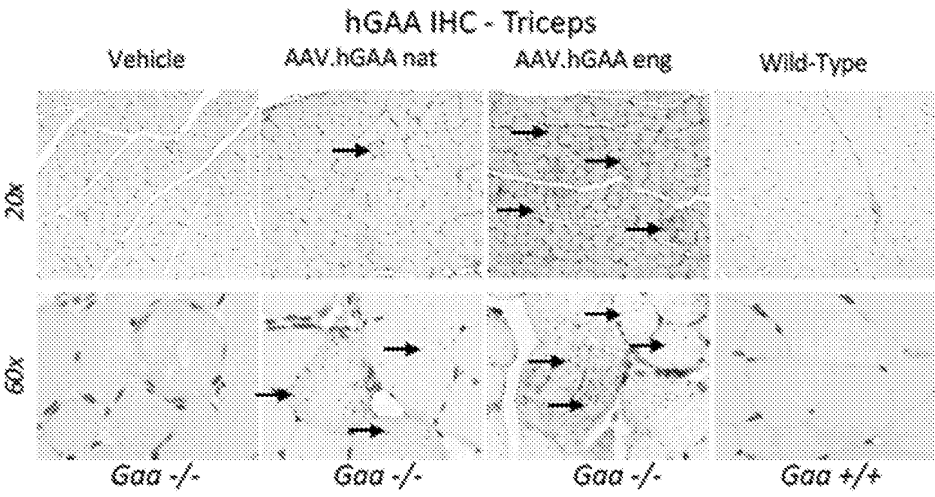


FIG. 33

CLN1 – PPT1

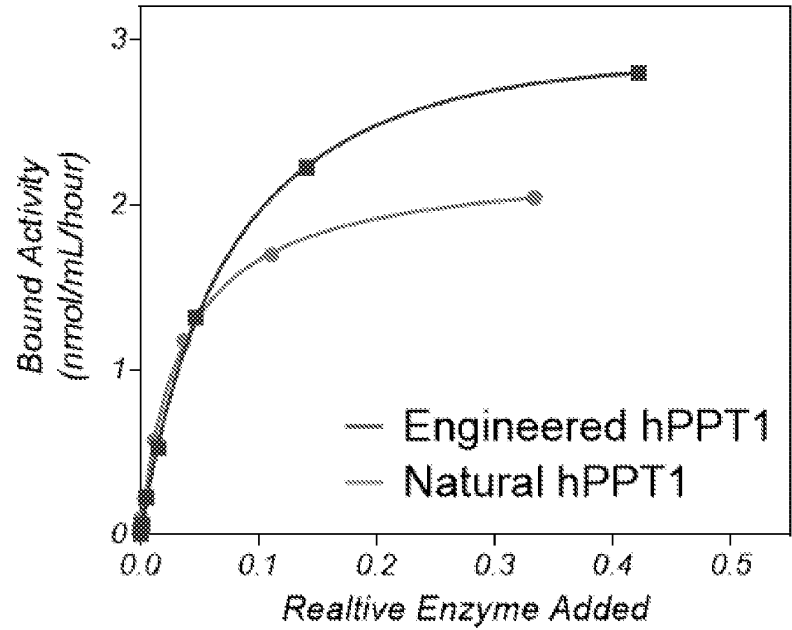


FIG. 34

CLN2 – TTP1

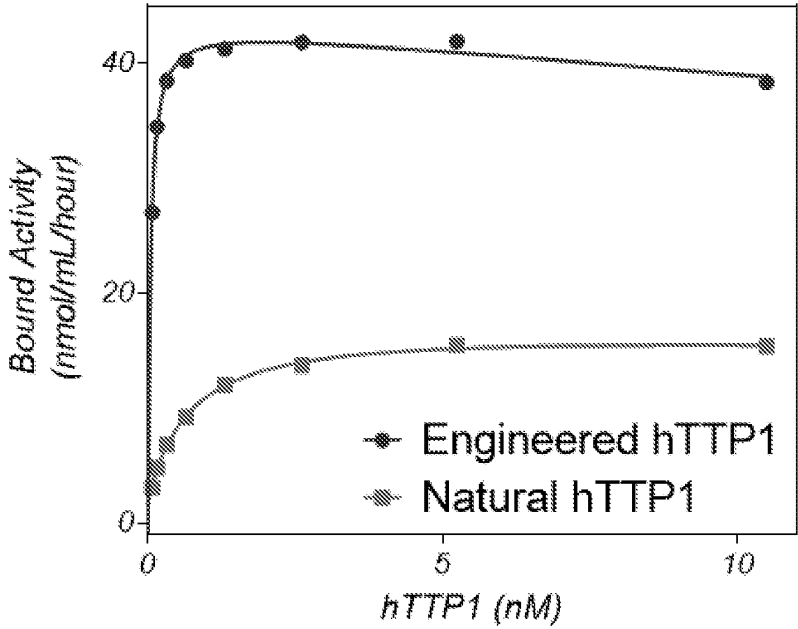


FIG. 35

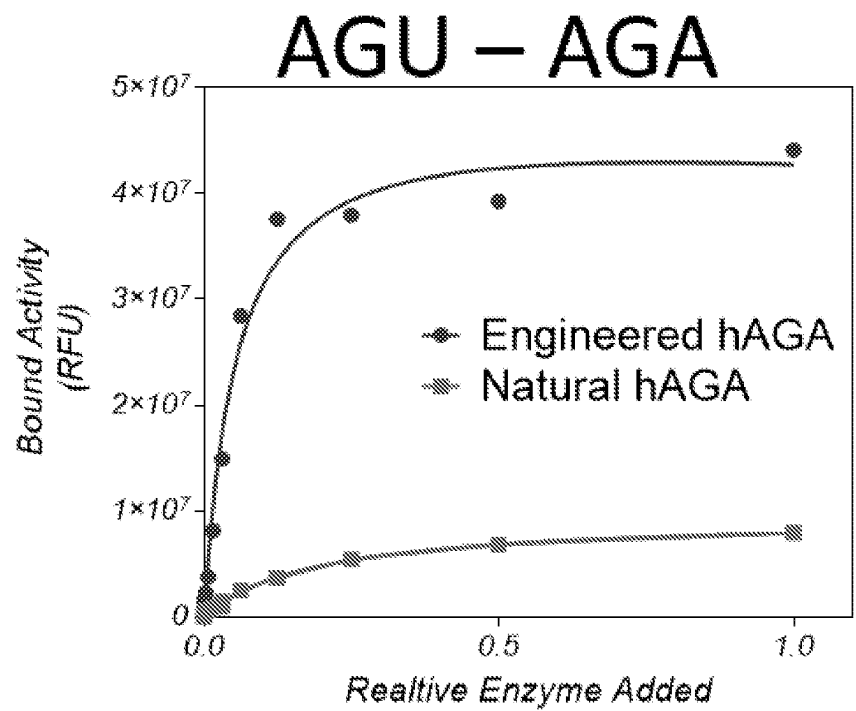


FIG. 36

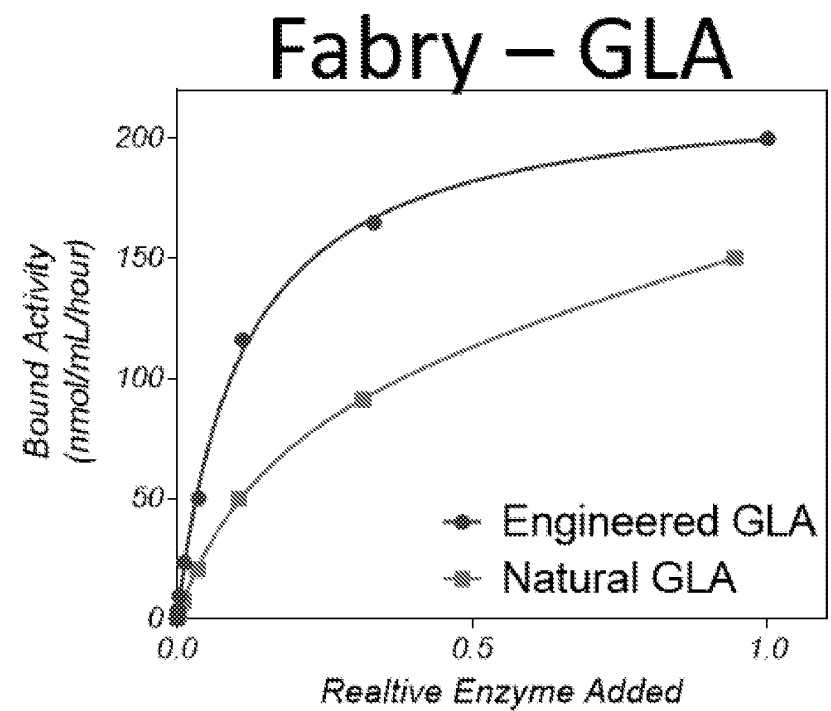


FIG. 37

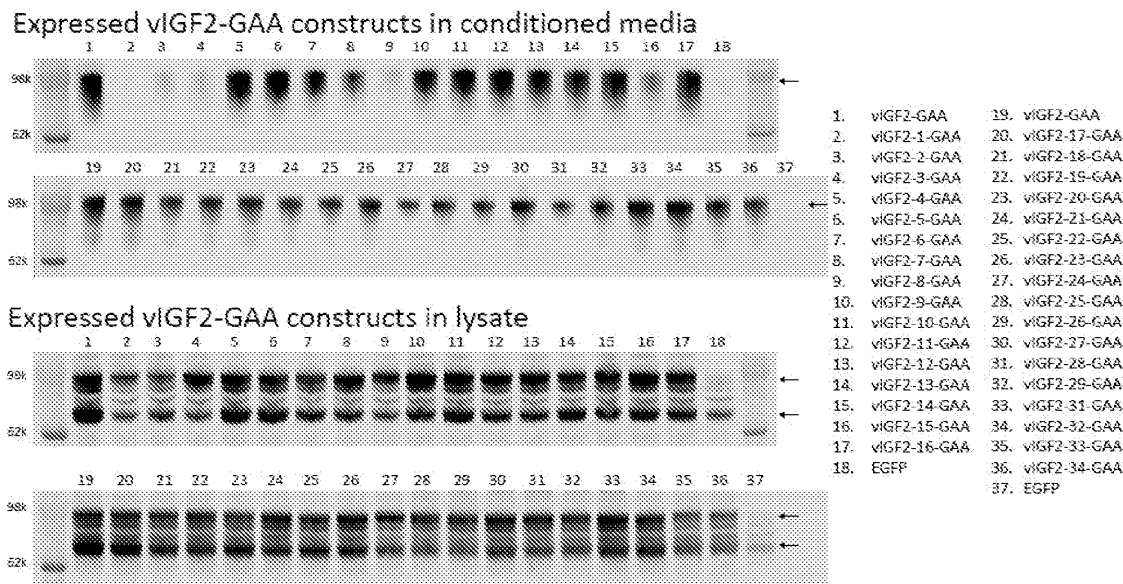


FIG. 38

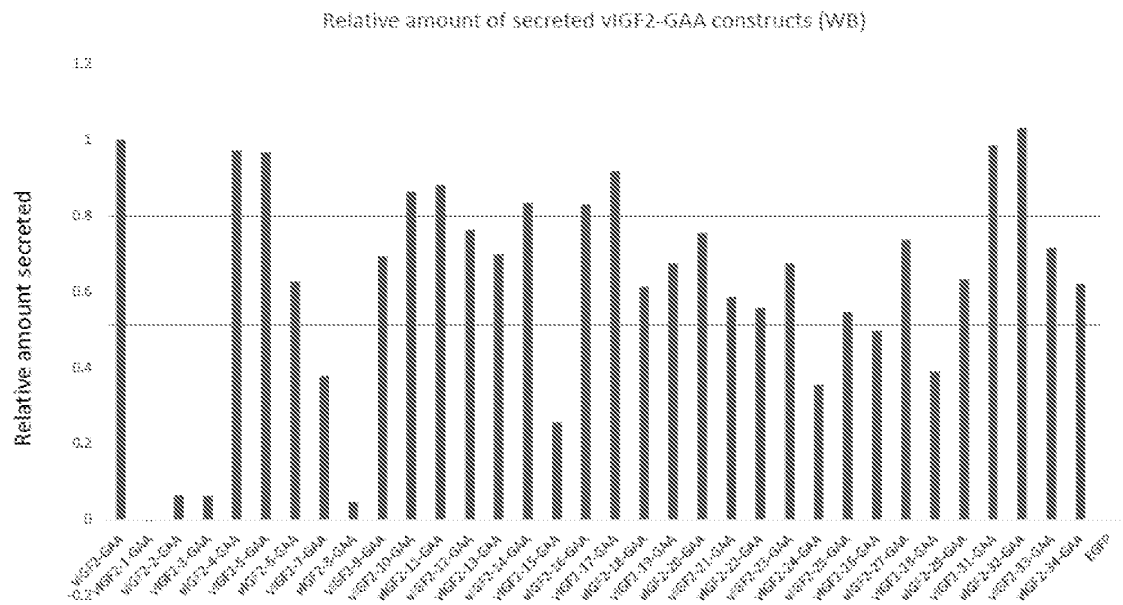


FIG. 39

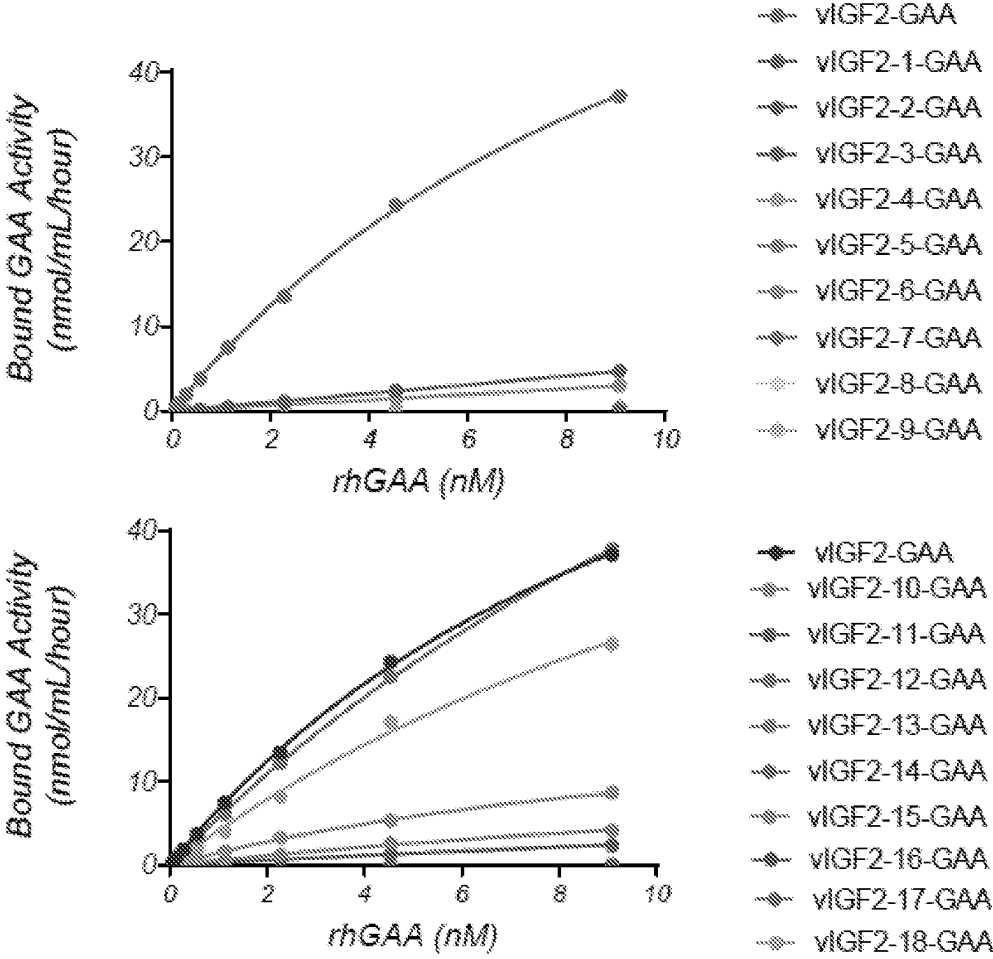


FIG. 40

Construct	B _{max} (nmol/mL/hr)	K _d (nM)	
wIGF2-GAA	85	12	
wIGF2-1-GAA	-	-	
wIGF2-2-GAA	-	-	
wIGF2-3-GAA	-	-	
wIGF2-4-GAA	-	-	
wIGF2-5-GAA	-	-	
wIGF2-6-GAA	-	-	
wIGF2-7-GAA	-	-	
wIGF2-8-GAA	-	-	
wIGF2-9-GAA	-	-	
wIGF2-10-GAA	21	13	
wIGF2-11-GAA	-	-	
wIGF2-12-GAA	-	-	
wIGF2-13-GAA	16	25	
wIGF2-14-GAA	-	-	
wIGF2-15-GAA	-	-	
wIGF2-16-GAA	14	45	
wIGF2-17-GAA	124	21	⚡-----
wIGF2-18-GAA	82	19	⚡-----

FIG. 41

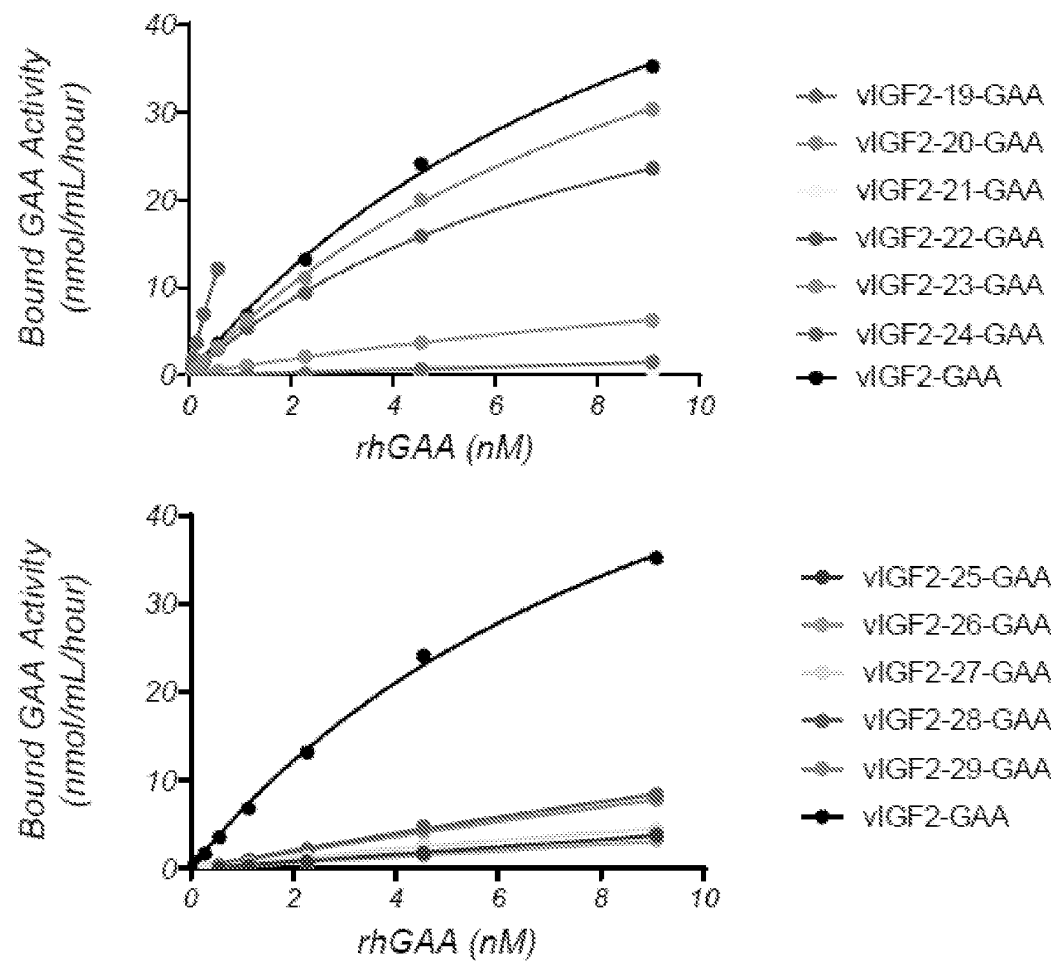


FIG. 42

Construct	Bmax (nmol/mL/hr)	Kd (nM)
vIGF2-GAA	78	11
vIGF2-19-GAA	-	-
vIGF2-20-GAA	-	-
vIGF2-21-GAA	67	11
vIGF2-22-GAA	45	8.7
vIGF2-23-GAA	20	19
vIGF2-24-GAA	50	1.8
vIGF2-25-GAA	-	-
vIGF2-26-GAA	-	-
vIGF2-27-GAA	24	39
vIGF2-28-GAA	66	62
vIGF2-29-GAA	69	70

FIG. 43

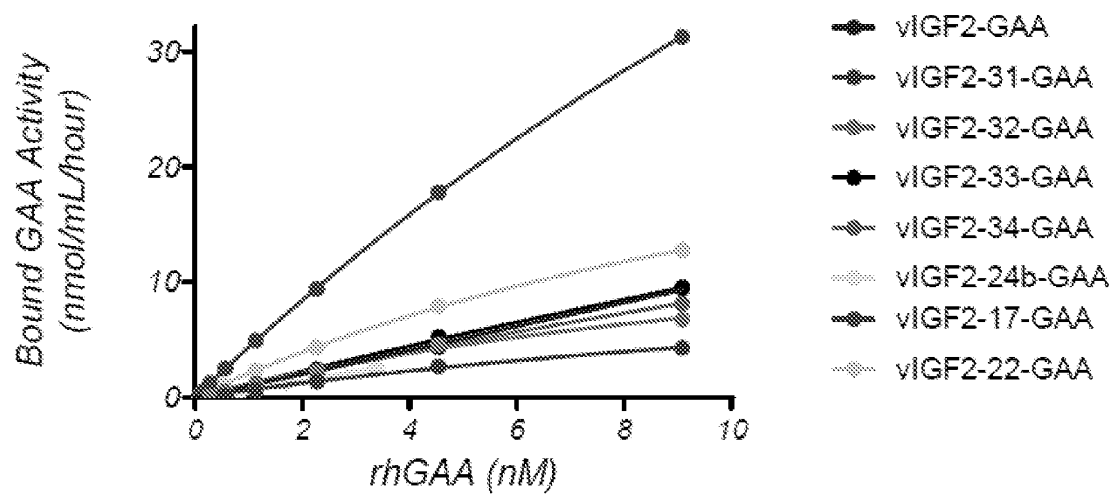


FIG. 44

Construct	Bmax (nmol/mL/hr)	Kd (nM)
vIGF2-GAA	-	-
vIGF2-31-GAA	14	20
vIGF2-32-GAA	18	15
vIGF2-33-GAA	87	74
vIGF2-34-GAA	54	51
vIGF2-17-GAA	132	29
vIGF2-22-GAA	35	16
vIGF2-24b-GAA	-	-

FIG. 45

vIGF2-GAA Cell Uptake (PM25)

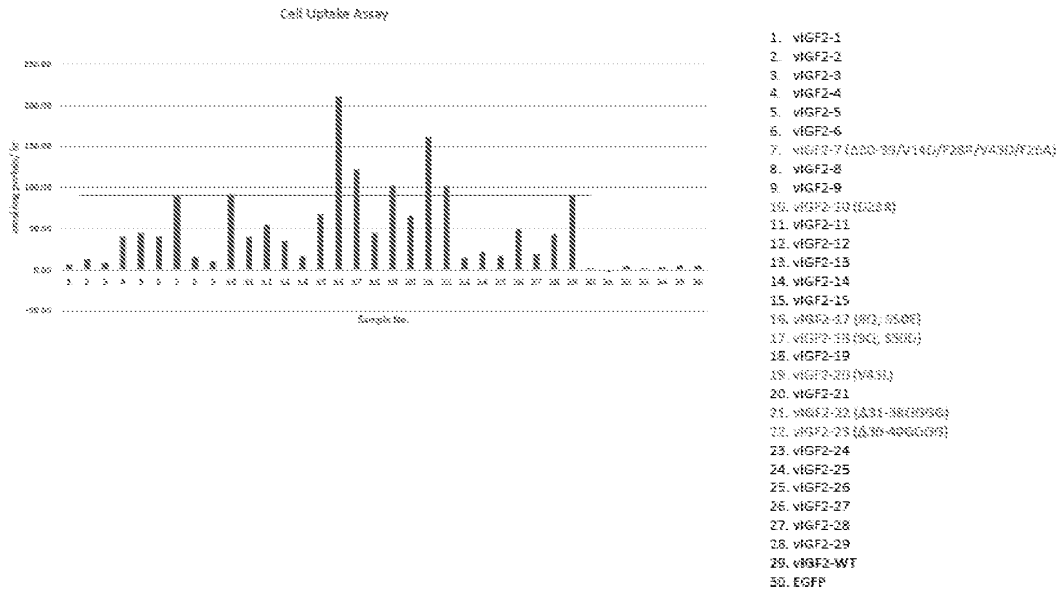


FIG. 46

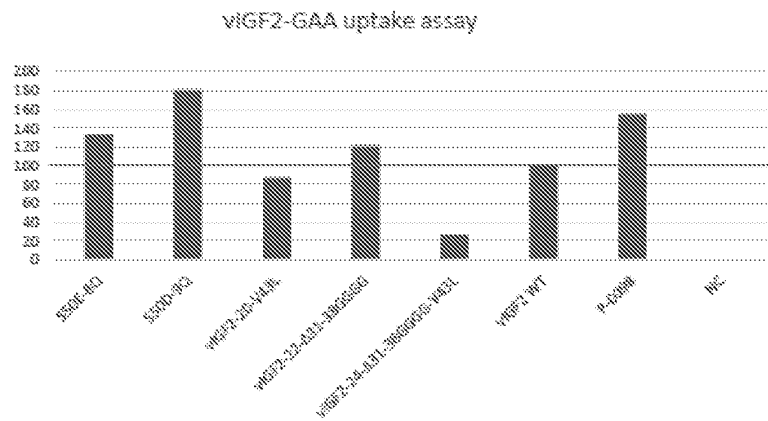


FIG. 47

vIGF2:
vIGF2-31:
vIGF2-32:

Δ1-4, E6R, Y27L, K65R
vIGF2 + Δ31-38GGGG V43L S50D
vIGF2 + Δ31-38GGGG V43L S50E

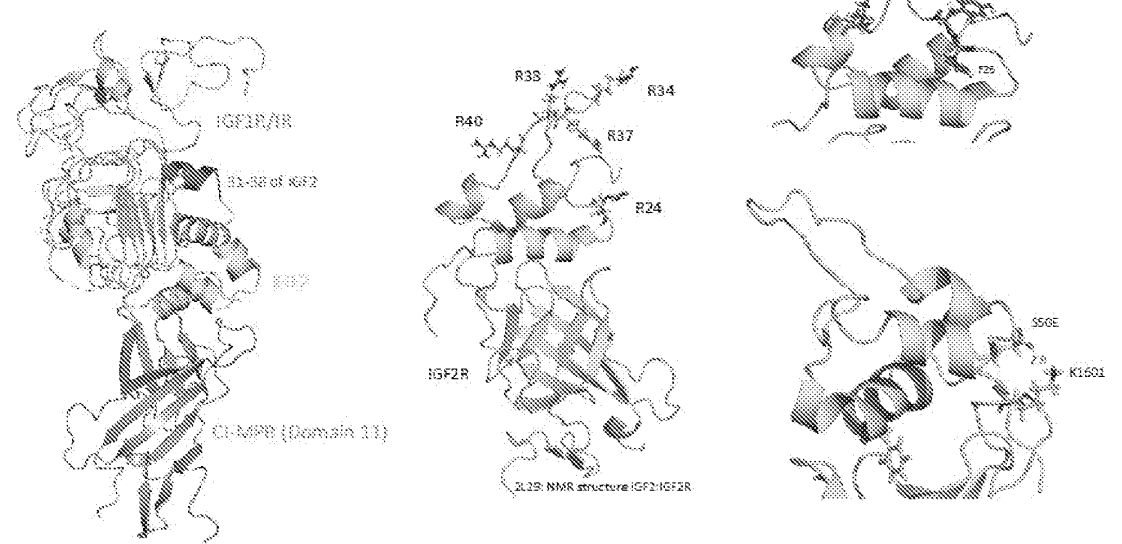


FIG. 48

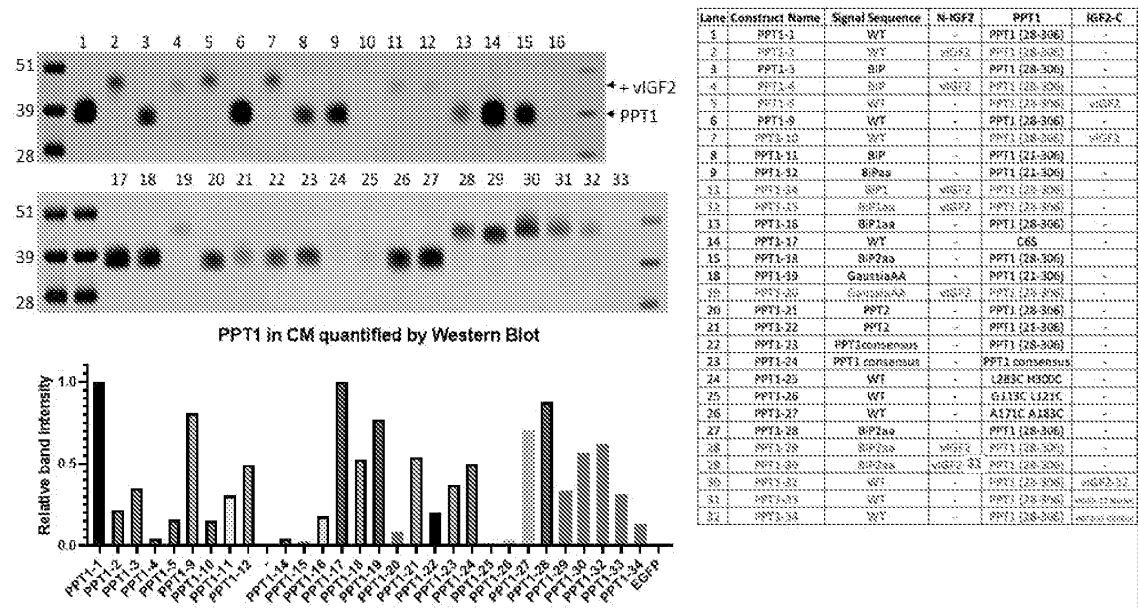


FIG. 49

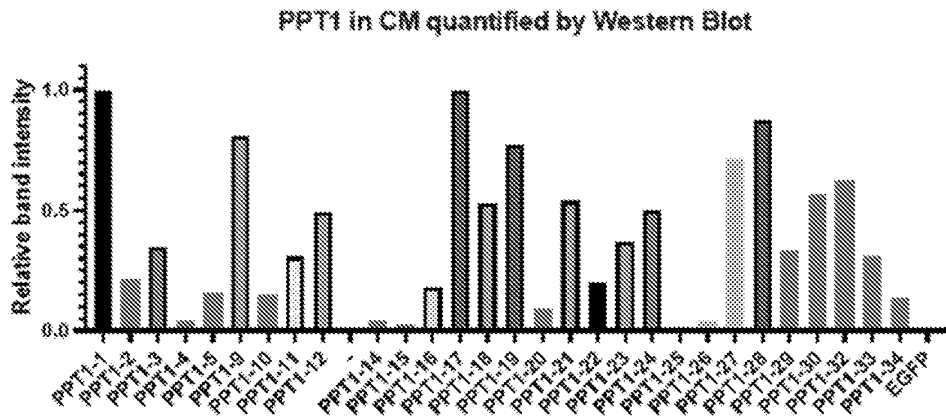


FIG. 50

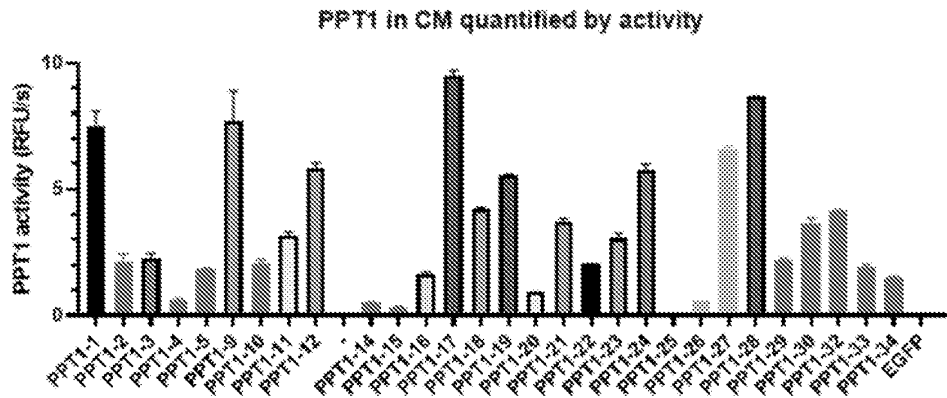


FIG. 51

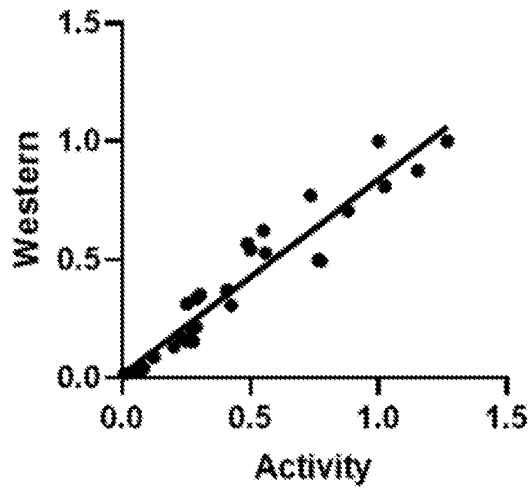


FIG. 52

Binding of PPT1 constructs to CI-MPR in presence of M6P

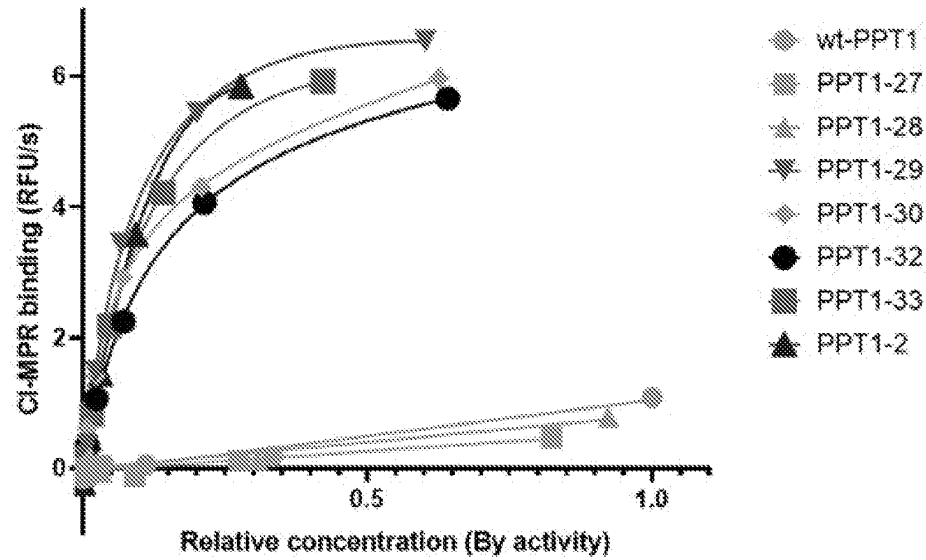


FIG. 53

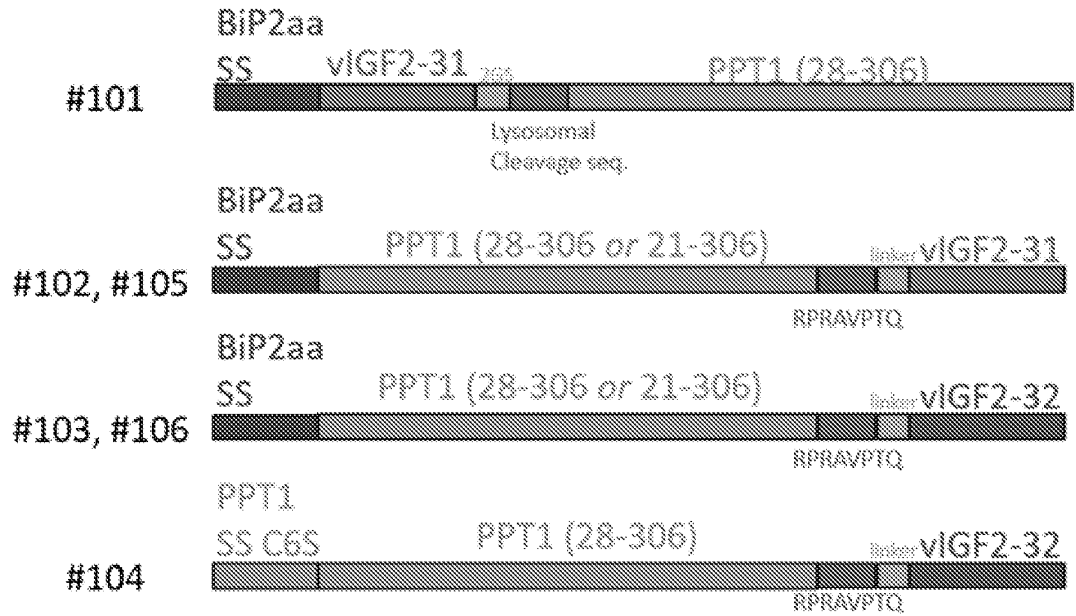


FIG. 54

PPT1 secreted into conditioned media

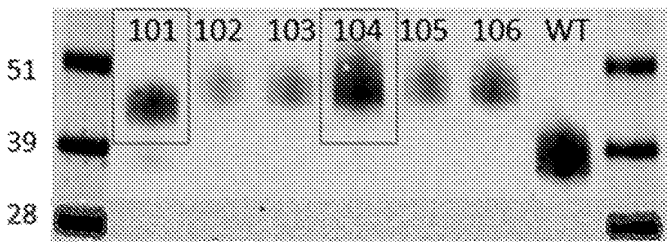


FIG. 55

PPT1 processing in-cell

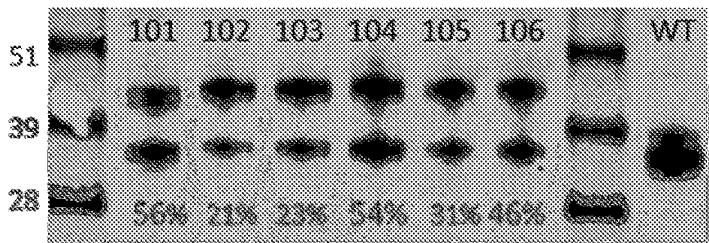


FIG. 56

PPT1 in CM quantified by western blot

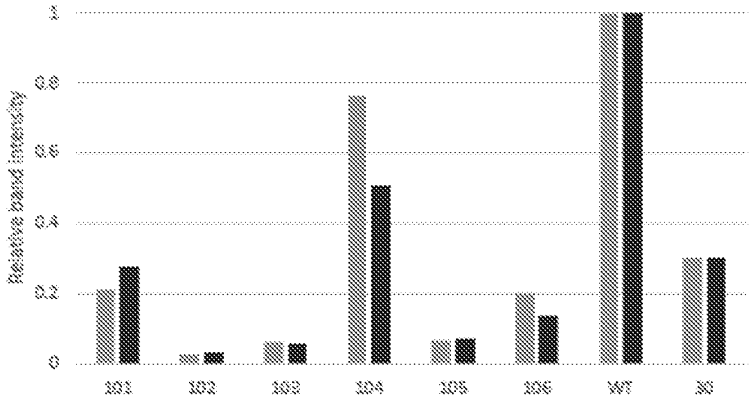


FIG. 57

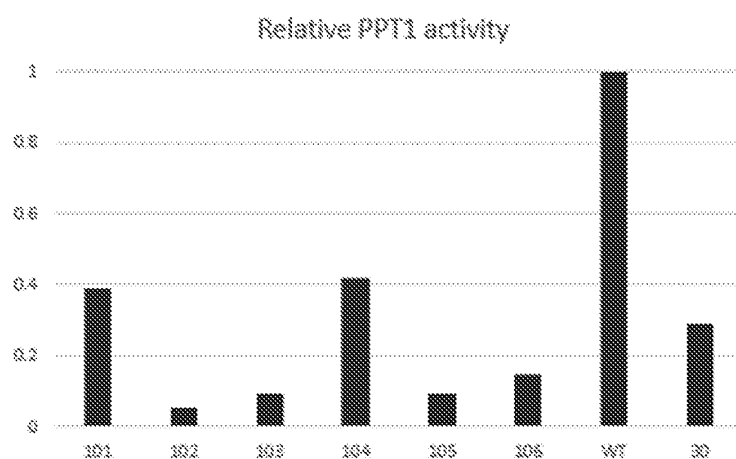


FIG. 58

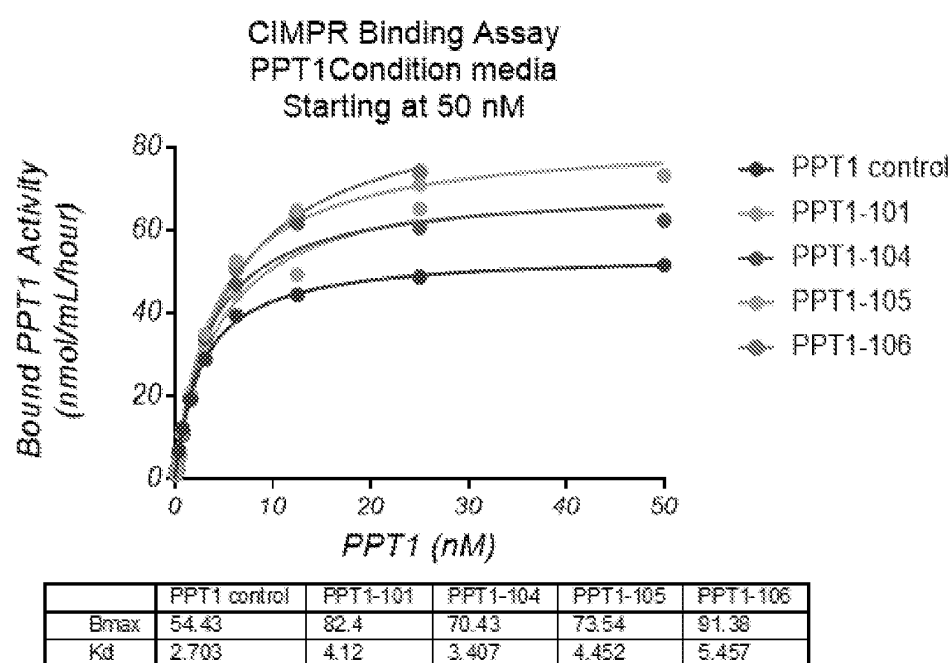


FIG. 59

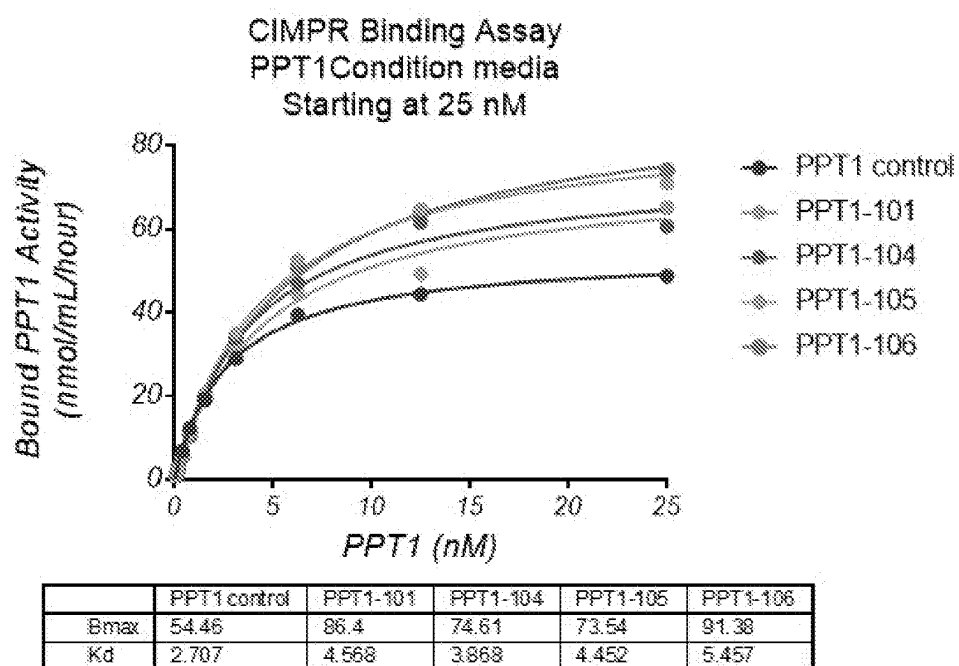


FIG. 60

Consensus

1. vIGF2
2. vIGF2-17
3. vIGF2-20
4. vIGF2-22

		SRTLGGELVDTLQFVCGDRGFLFSRPASRVSRSSRGIVEECCFRSCDLALLETYCATPARS	
1	-----SRTLGGELVDTLQFVCGDRGFLFSRPASRVSRSSRGIVEECCFRSCDLALLETYCATPARS		62
2	-----SRTLGGELVDTLQFVCGDRGFLFSRPASRVSRSSRGIVEECCFRSCDLALLETYCATPARS		62
3	-----SRTLGGELVDTLQFVCGDRGFLFSRPASRVSRSSRGILEECCFRSCDLALLETYCATPARS		62
4	-----SRTLGGELVDTLQFVCGDRGFLFSRGGG-----GSRGIVEECCFRSCDLALLETYCATPARS		58
		EGGGGSGGGGSRPGPRDAQAHGPRRAVPTQCDVPPNSRFDCAPDKAITQECCARGCCYIPAKQGLQGAQMGPWCFFP	
1	EGGGGSGGGGSRPGPRDAQAHGPRRAVPTQCDVPPNSRFDCAPDKAITQECCARGCCYIPAKQGLQGAQMGPWCFFP		142
2	EGGGGSGGGGSRPGPRDAQAHGPRRAVPTQCDVPPNSRFDCAPDKAITQECCARGCCYIPAKQGLQGAQMGPWCFFP		142
3	EGGGGSGGGGSRPGPRDAQAHGPRRAVPTQCDVPPNSRFDCAPDKAITQECCARGCCYIPAKQGLQGAQMGPWCFFP		142
4	EGGGGSGGGGSRPGPRDAQAHGPRRAVPTQCDVPPNSRFDCAPDKAITQECCARGCCYIPAKQGLQGAQMGPWCFFP		138
		PSYPSYKLENLSSSEMGYTATLTRTTPTFFPKDILTLRLDVMETENRLHFTIKDPANRRYEVPLETPHVHSRAPSPLYS	
1	PSYPSYKLENLSSSEMGYTATLTRTTPTFFPKDILTLRLDVMETENRLHFTIKDPANRRYEVPLETPHVHSRAPSPLYS		222
2	PSYPSYKLENLSSSEMGYTATLTRTTPTFFPKDILTLRLDVMETENRLHFTIKDPANRRYEVPLETPHVHSRAPSPLYS		222
3	PSYPSYKLENLSSSEMGYTATLTRTTPTFFPKDILTLRLDVMETENRLHFTIKDPANRRYEVPLETPHVHSRAPSPLYS		222
4	PSYPSYKLENLSSSEMGYTATLTRTTPTFFPKDILTLRLDVMETENRLHFTIKDPANRRYEVPLETPHVHSRAPSPLYS		218
		VEFSEEPFGVIVRRQLDGRVLLNTTVAPLFFADQFLQLSTSLPSQYITGLAEHLSPLMLSTSWTRITLWNRDLAPTGAN	
1	VEFSEEPFGVIVRRQLDGRVLLNTTVAPLFFADQFLQLSTSLPSQYITGLAEHLSPLMLSTSWTRITLWNRDLAPTGAN		302
2	VEFSEEPFGVIVRRQLDGRVLLNTTVAPLFFADQFLQLSTSLPSQYITGLAEHLSPLMLSTSWTRITLWNRDLAPTGAN		302
3	VEFSEEPFGVIVRRQLDGRVLLNTTVAPLFFADQFLQLSTSLPSQYITGLAEHLSPLMLSTSWTRITLWNRDLAPTGAN		302
4	VEFSEEPFGVIVRRQLDGRVLLNTTVAPLFFADQFLQLSTSLPSQYITGLAEHLSPLMLSTSWTRITLWNRDLAPTGAN		298
		LYGSHPPFYLALEDGGSAHGVLNLSNANDVVLQPSPALSWRSTGGILDVYIFLGPEPKSVVQYLDVVGYPFMPYWG LG	
1	LYGSHPPFYLALEDGGSAHGVLNLSNANDVVLQPSPALSWRSTGGILDVYIFLGPEPKSVVQYLDVVGYPFMPYWG LG		382
2	LYGSHPPFYLALEDGGSAHGVLNLSNANDVVLQPSPALSWRSTGGILDVYIFLGPEPKSVVQYLDVVGYPFMPYWG LG		382
3	LYGSHPPFYLALEDGGSAHGVLNLSNANDVVLQPSPALSWRSTGGILDVYIFLGPEPKSVVQYLDVVGYPFMPYWG LG		382
4	LYGSHPPFYLALEDGGSAHGVLNLSNANDVVLQPSPALSWRSTGGILDVYIFLGPEPKSVVQYLDVVGYPFMPYWG LG		378
		FHLCRWGSSTAIRQVVENMTRAHFLDVQWNLQDYMDSRRDFTFNKDGFRDFPANVQELHQGGRRYMMIVDPAISSSG	
1	FHLCRWGSSTAIRQVVENMTRAHFLDVQWNLQDYMDSRRDFTFNKDGFRDFPANVQELHQGGRRYMMIVDPAISSSG		462
2	FHLCRWGSSTAIRQVVENMTRAHFLDVQWNLQDYMDSRRDFTFNKDGFRDFPANVQELHQGGRRYMMIVDPAISSSG		462
3	FHLCRWGSSTAIRQVVENMTRAHFLDVQWNLQDYMDSRRDFTFNKDGFRDFPANVQELHQGGRRYMMIVDPAISSSG		462
4	FHLCRWGSSTAIRQVVENMTRAHFLDVQWNLQDYMDSRRDFTFNKDGFRDFPANVQELHQGGRRYMMIVDPAISSSG		456
		PAGSYRPHYDEGLRRGVFITNETGQPLIGKVWPGSTAFPDFTNPALAWWEDMVAEFHQVFPDGMWIDMNEPSNFIRGSE	
1	PAGSYRPHYDEGLRRGVFITNETGQPLIGKVWPGSTAFPDFTNPALAWWEDMVAEFHQVFPDGMWIDMNEPSNFIRGSE		542
2	PAGSYRPHYDEGLRRGVFITNETGQPLIGKVWPGSTAFPDFTNPALAWWEDMVAEFHQVFPDGMWIDMNEPSNFIRGSE		542
3	PAGSYRPHYDEGLRRGVFITNETGQPLIGKVWPGSTAFPDFTNPALAWWEDMVAEFHQVFPDGMWIDMNEPSNFIRGSE		542
4	PAGSYRPHYDEGLRRGVFITNETGQPLIGKVWPGSTAFPDFTNPALAWWEDMVAEFHQVFPDGMWIDMNEPSNFIRGSE		538

FIG. 61

	DGCPNNELENPPYVPGVGGTLQAATICASSHQFLSTHYNLHNLVGLTEAIAASHRALVKARGTRPFVISRSTFAGHGRYA	
1	DGCPNNELENPPYVPGVGGTLQAATICASSHQFLSTHYNLHNLVGLTEAIAASHRALVKARGTRPFVISRSTFAGHGRYA	622
2	DGCPNNELENPPYVPGVGGTLQAATICASSHQFLSTHYNLHNLVGLTEAIAASHRALVKARGTRPFVISRSTFAGHGRYA	622
3	DGCPNNELENPPYVPGVGGTLQAATICASSHQFLSTHYNLHNLVGLTEAIAASHRALVKARGTRPFVISRSTFAGHGRYA	622
4	DGCPNNELENPPYVPGVGGTLQAATICASSHQFLSTHYNLHNLVGLTEAIAASHRALVKARGTRPFVISRSTFAGHGRYA	618
	GHWTGDVWSSWEQLASSVPEILQFNLLGVPLVGADVCGFLGNTSEELCVRWTLGAFYPMRNNHNSLLSLPQEPYSFSEP	
1	GHWTGDVWSSWEQLASSVPEILQFNLLGVPLVGADVCGFLGNTSEELCVRWTLGAFYPMRNNHNSLLSLPQEPYSFSEP	702
2	GHWTGDVWSSWEQLASSVPEILQFNLLGVPLVGADVCGFLGNTSEELCVRWTLGAFYPMRNNHNSLLSLPQEPYSFSEP	702
3	GHWTGDVWSSWEQLASSVPEILQFNLLGVPLVGADVCGFLGNTSEELCVRWTLGAFYPMRNNHNSLLSLPQEPYSFSEP	702
4	GHWTGDVWSSWEQLASSVPEILQFNLLGVPLVGADVCGFLGNTSEELCVRWTLGAFYPMRNNHNSLLSLPQEPYSFSEP	698
	AQQAMRKALTLRYALLPHLYTLFHQAHVAGETVARPLFLEFPKDSSTWTVDHQLLWGEALLITPVLQAGKAEVTGYFPLG	
1	AQQAMRKALTLRYALLPHLYTLFHQAHVAGETVARPLFLEFPKDSSTWTVDHQLLWGEALLITPVLQAGKAEVTGYFPLG	782
2	AQQAMRKALTLRYALLPHLYTLFHQAHVAGETVARPLFLEFPKDSSTWTVDHQLLWGEALLITPVLQAGKAEVTGYFPLG	782
3	AQQAMRKALTLRYALLPHLYTLFHQAHVAGETVARPLFLEFPKDSSTWTVDHQLLWGEALLITPVLQAGKAEVTGYFPLG	782
4	AQQAMRKALTLRYALLPHLYTLFHQAHVAGETVARPLFLEFPKDSSTWTVDHQLLWGEALLITPVLQAGKAEVTGYFPLG	778
	TWYDLQTVPVEALGSLPPPPAAPREPAIHSEGQWVTLPAPLDTINVHLRAGYIIPLQGPGLTTTESRQQPMALAVALTKG	
1	TWYDLQTVPVEALGSLPPPPAAPREPAIHSEGQWVTLPAPLDTINVHLRAGYIIPLQGPGLTTTESRQQPMALAVALTKG	862
2	TWYDLQTVPVEALGSLPPPPAAPREPAIHSEGQWVTLPAPLDTINVHLRAGYIIPLQGPGLTTTESRQQPMALAVALTKG	862
3	TWYDLQTVPVEALGSLPPPPAAPREPAIHSEGQWVTLPAPLDTINVHLRAGYIIPLQGPGLTTTESRQQPMALAVALTKG	862
4	TWYDLQTVPVEALGSLPPPPAAPREPAIHSEGQWVTLPAPLDTINVHLRAGYIIPLQGPGLTTTESRQQPMALAVALTKG	858
	GEARGELFWDDGESLEVLERGAYTQVIFLARNTIVNELVRVTSEGAGLQLQKVTVLGVATAPQQVLSNGVPVSNFTYSP	
1	GEARGELFWDDGESLEVLERGAYTQVIFLARNTIVNELVRVTSEGAGLQLQKVTVLGVATAPQQVLSNGVPVSNFTYSP	942
2	GEARGELFWDDGESLEVLERGAYTQVIFLARNTIVNELVRVTSEGAGLQLQKVTVLGVATAPQQVLSNGVPVSNFTYSP	942
3	GEARGELFWDDGESLEVLERGAYTQVIFLARNTIVNELVRVTSEGAGLQLQKVTVLGVATAPQQVLSNGVPVSNFTYSP	942
4	GEARGELFWDDGESLEVLERGAYTQVIFLARNTIVNELVRVTSEGAGLQLQKVTVLGVATAPQQVLSNGVPVSNFTYSP	938
	DTKVLDICVSLLMGEQFLVSWC	
1	DTKVLDICVSLLMGEQFLVSWC	964
2	DTKVLDICVSLLMGEQFLVSWC	964
3	DTKVLDICVSLLMGEQFLVSWC	964
4	DTKVLDICVSLLMGEQFLVSWC	963

FIG. 61 (cont)

FIG. 62

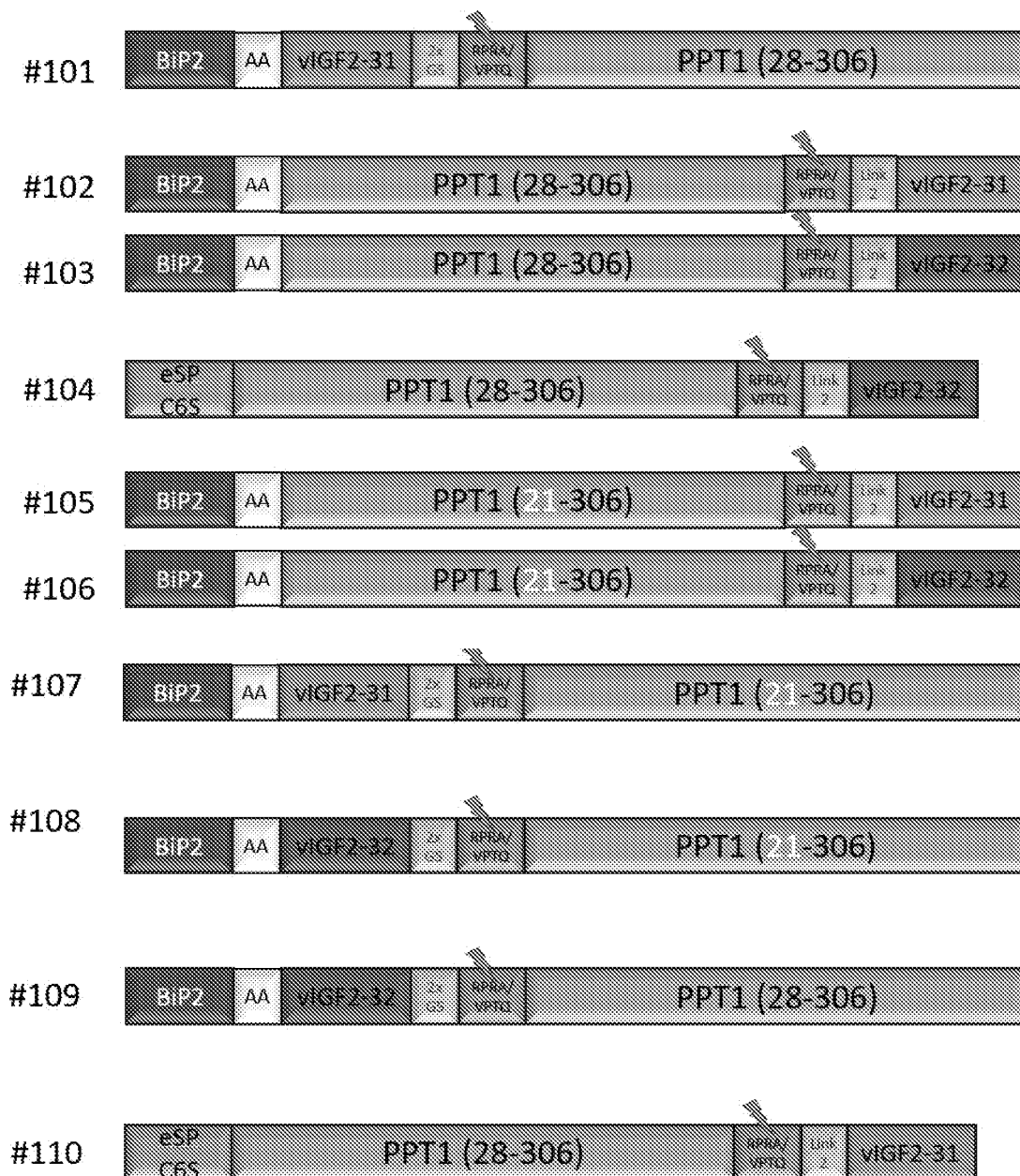


FIG. 62 (Cont)

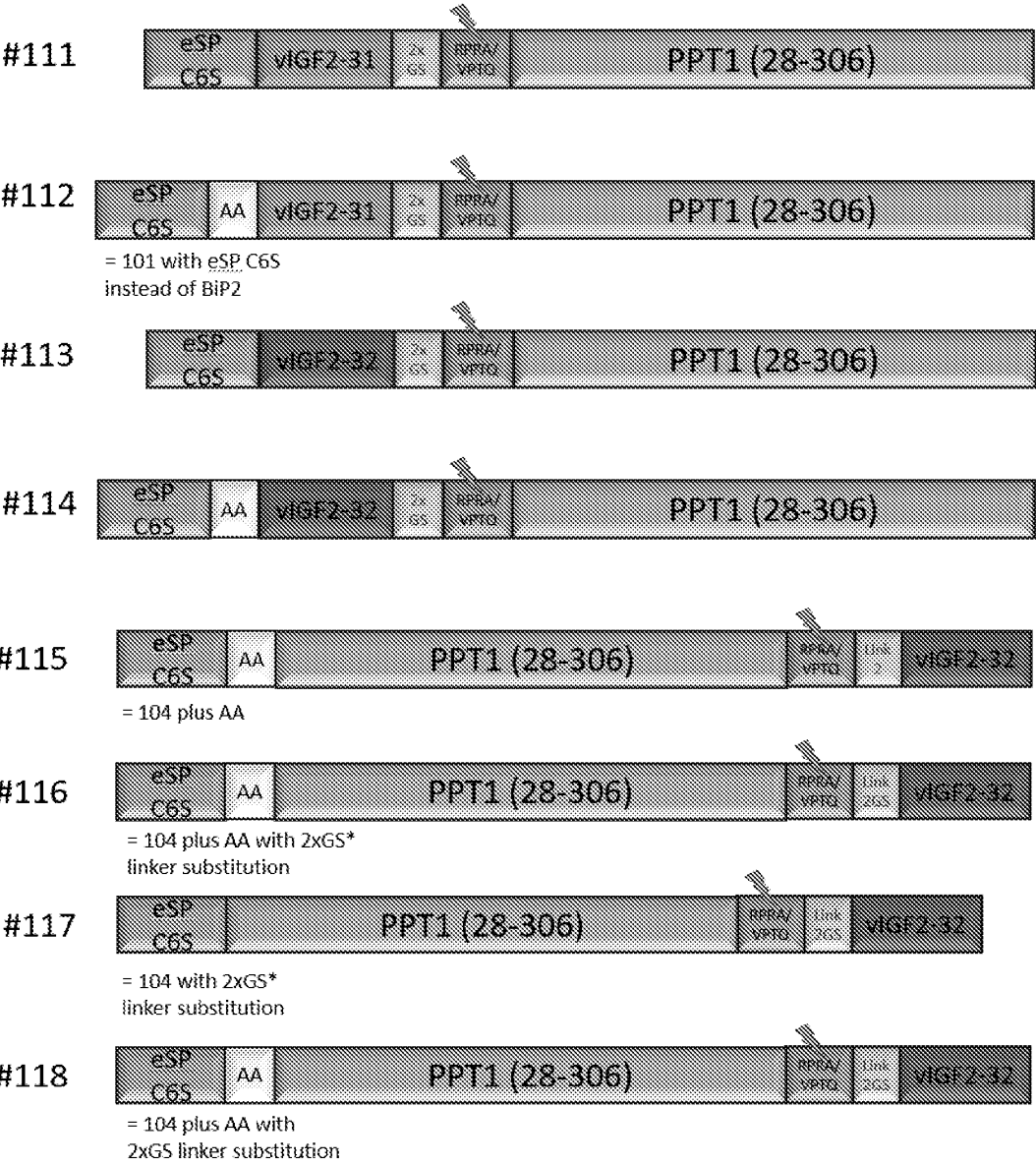


FIG. 62 (Cont)

FIG. 63

PPT1 Screen (normalized by average)

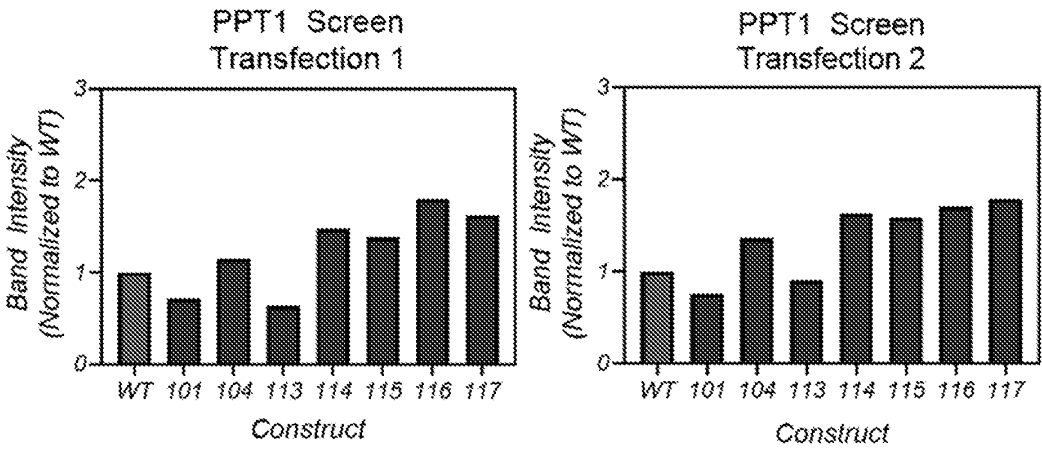
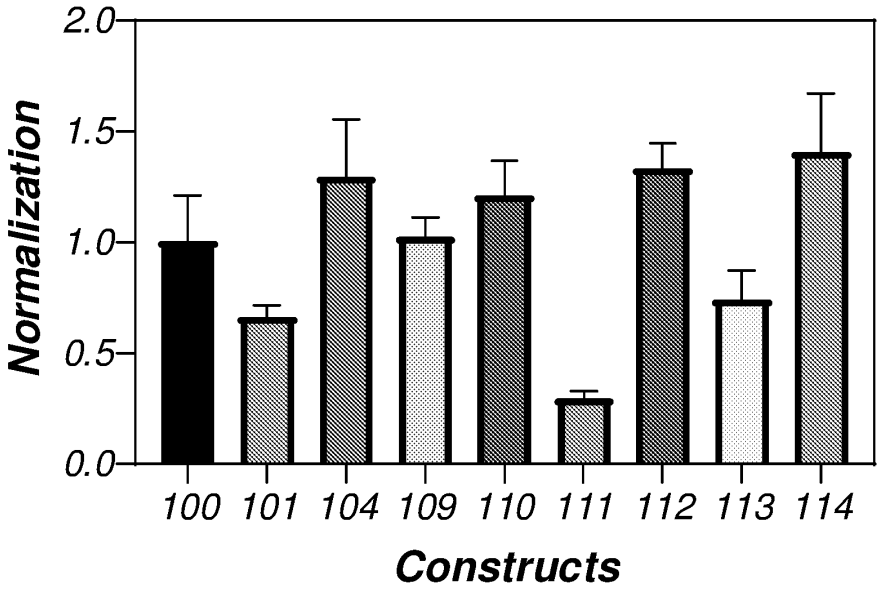
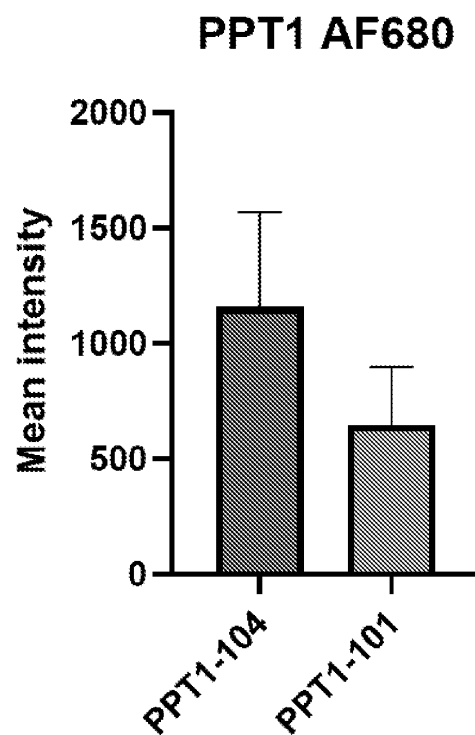


FIG. 64

A



B

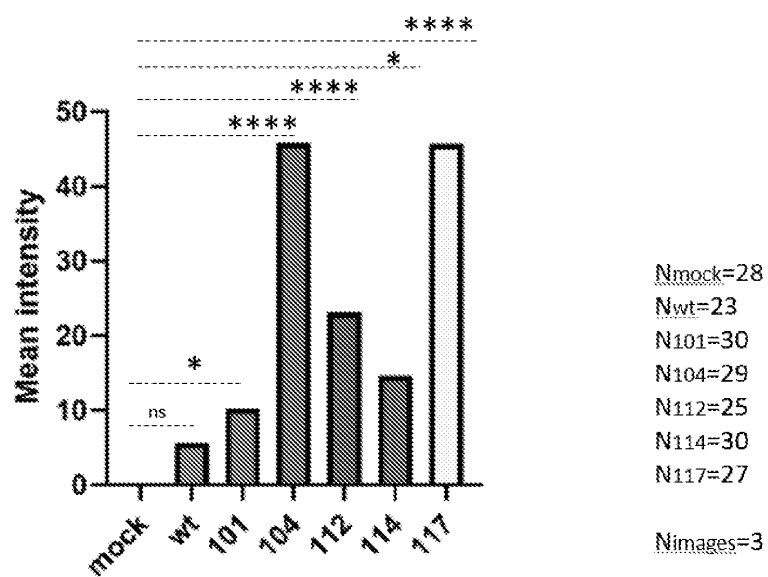


FIG. 65

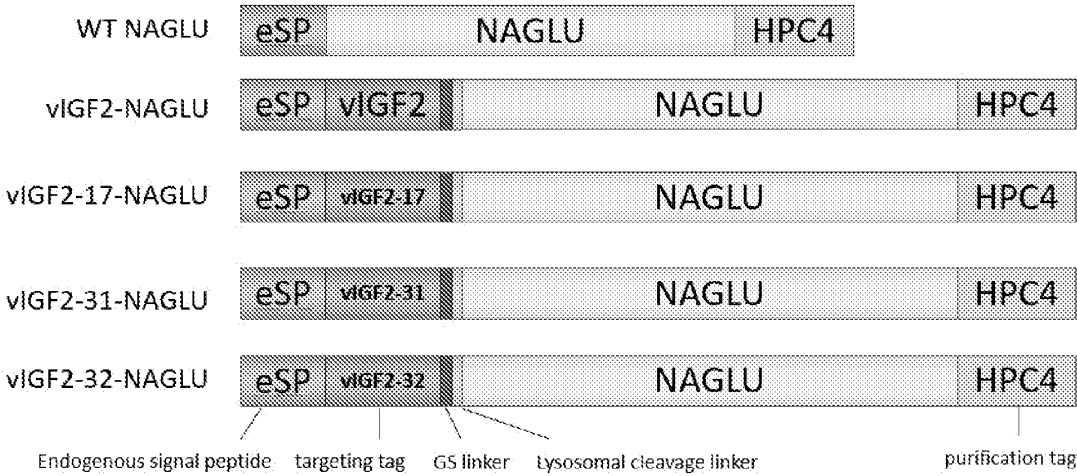


FIG. 66

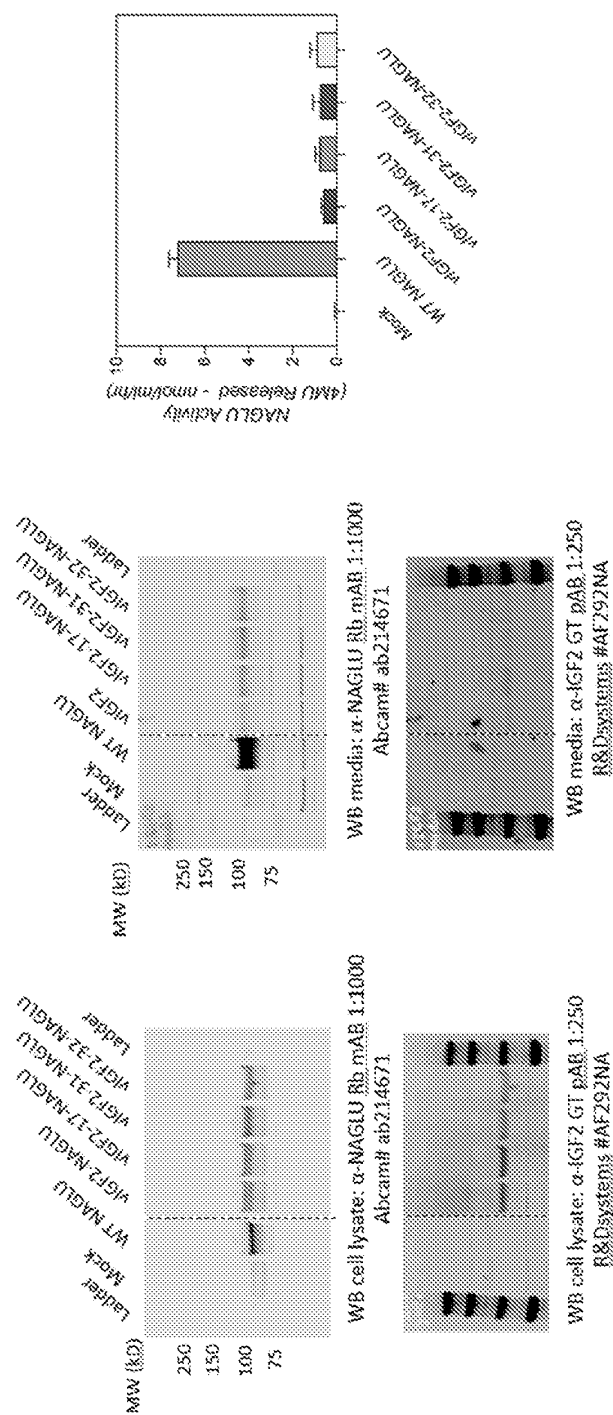
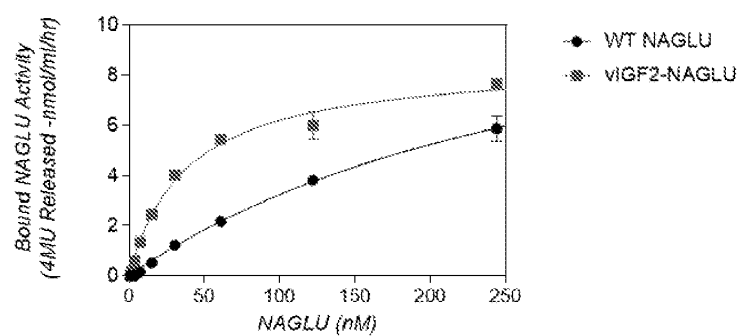


FIG. 67



Sample	Specific activity (nmol/ml/hr)	<i>Bmax</i> (nmol/ml/hr)	<i>Kd</i> (nM)
WT-NAGLU	4613	13.75	325.1
vIGF2-NAGLU	1726	8.558	38.25

FIG. 68

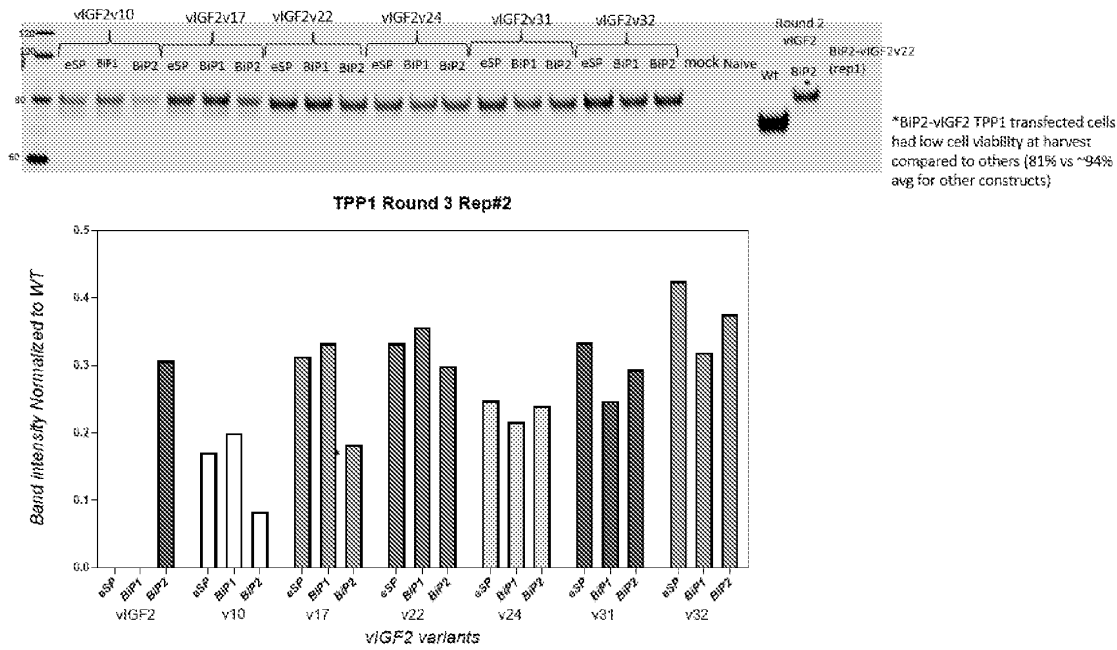
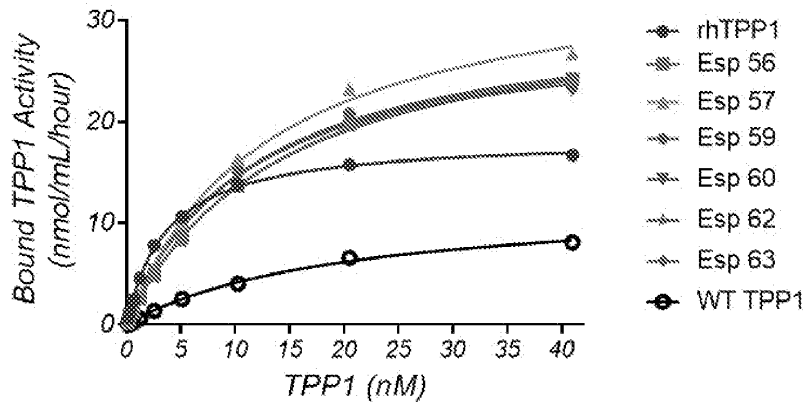


FIG. 69

CIMPR Binding Assay



	rhTPP1	Esp 56	Esp 57	Esp 59	Esp 60	Esp 62	Esp 63	WT TPP1
Bmax	18.48	33.05	35.99	31.21	29.83	32.47	30.92	12.25
Kd	3.704	14.52	12.83	11.41	10.55	14.10	11.36	19.72

FIG. 70

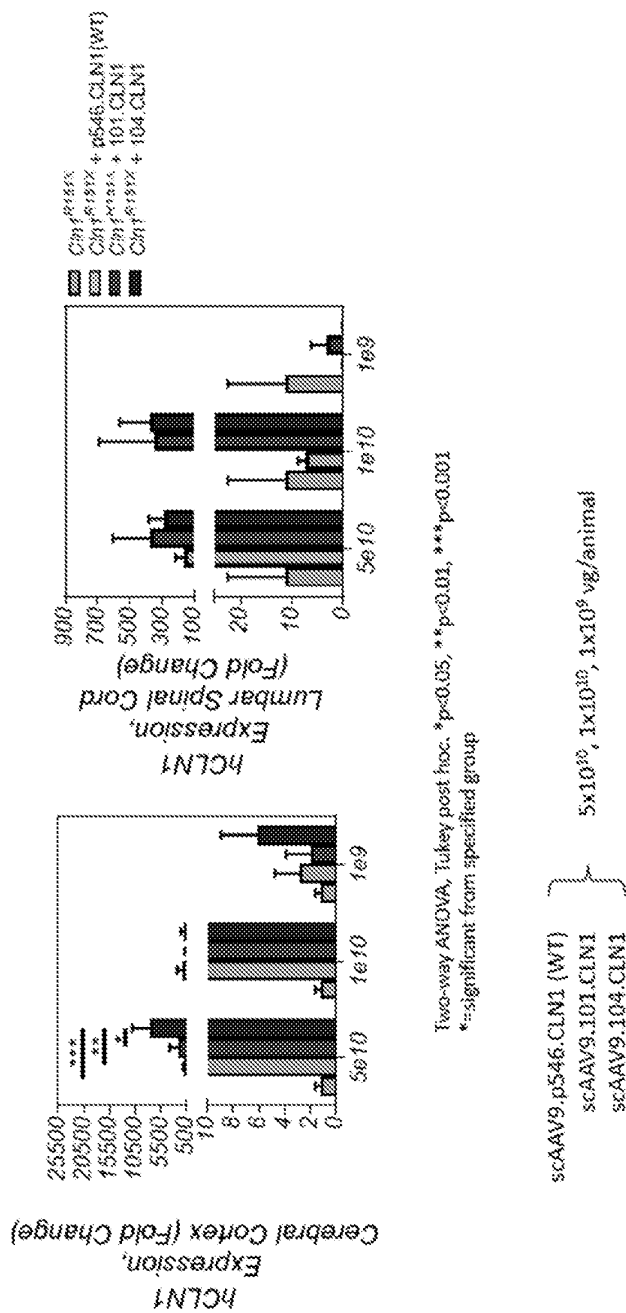
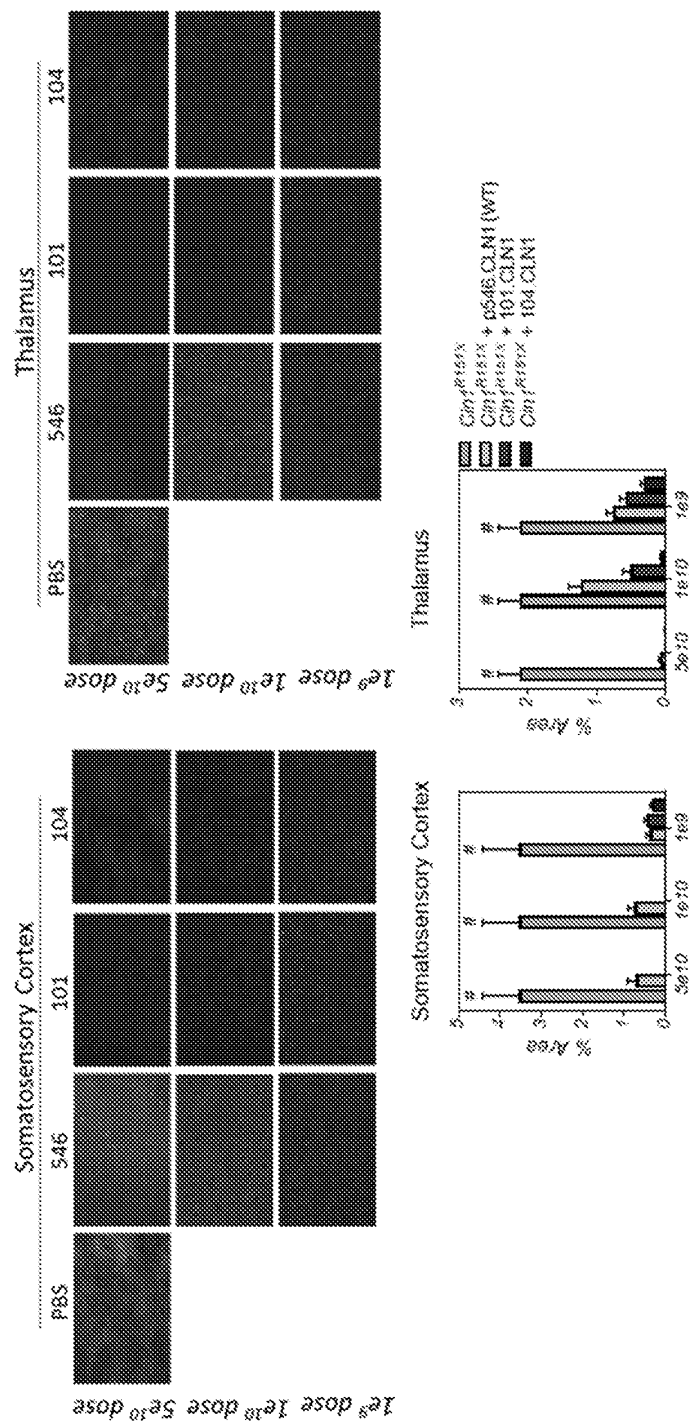


FIG. 71



1-way Nested Anova, Fisher's LSD Post Hoc.
= significant from all other groups

FIG. 72

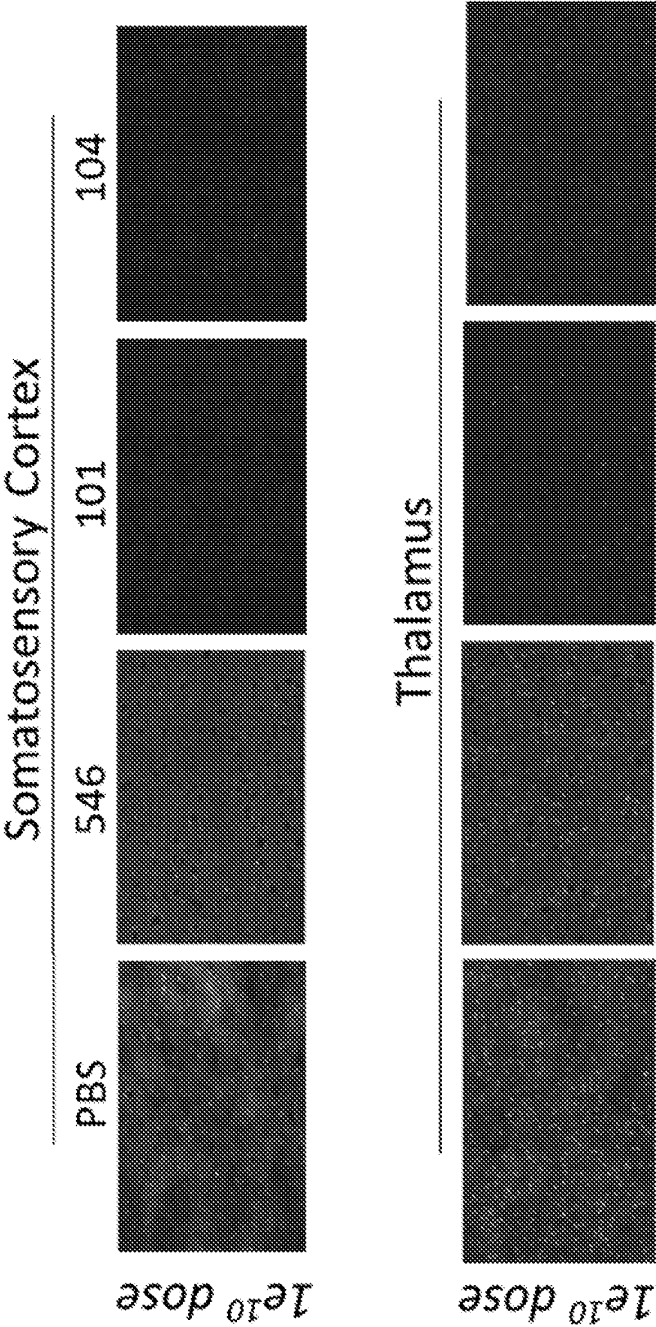


FIG. 73

