Figure 1

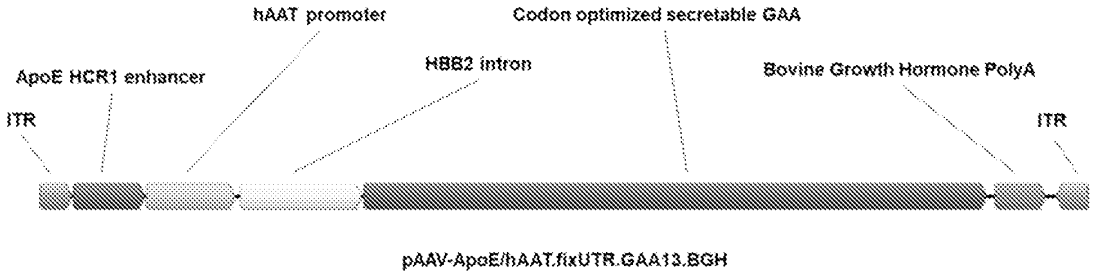


Figure 2

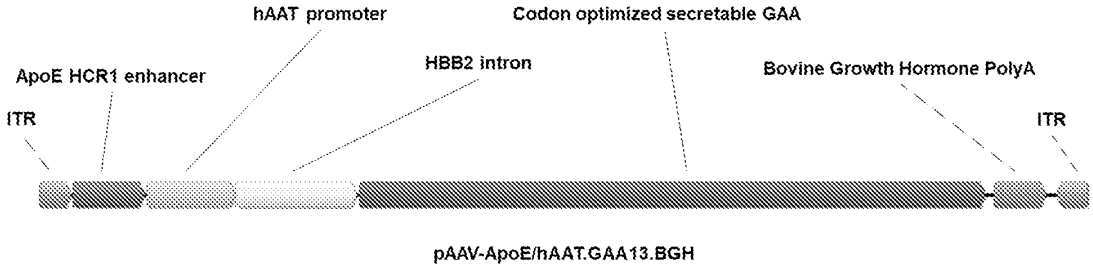


Figure 3

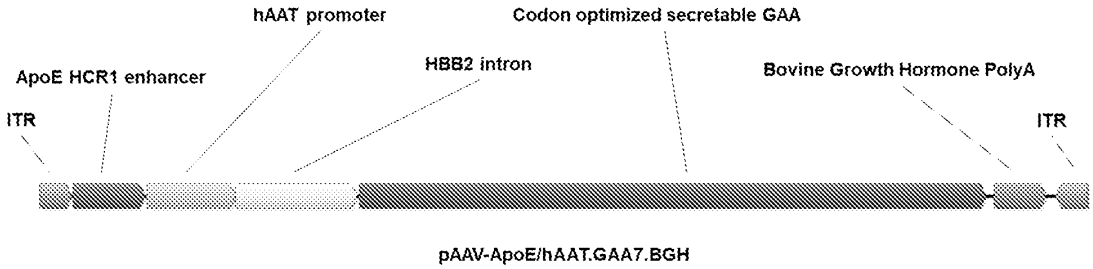
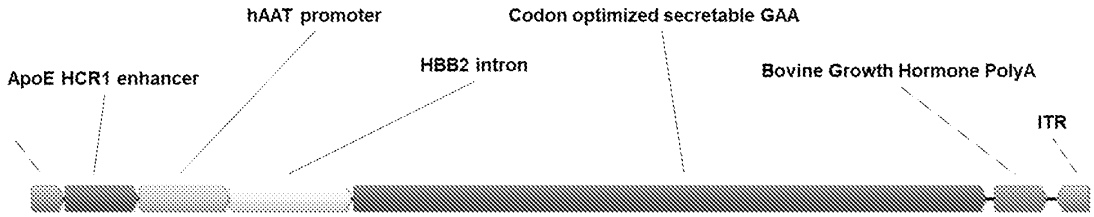
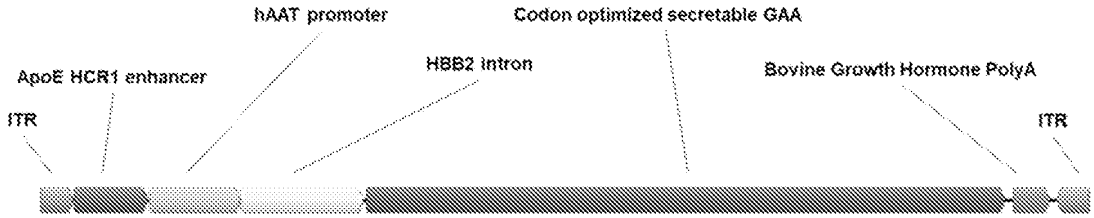


Figure 4



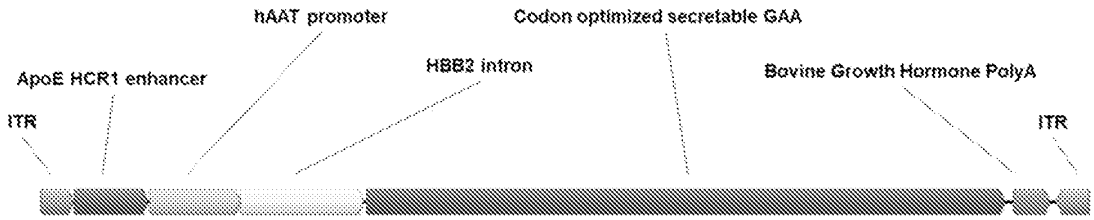
pAAV-ApoE/hAAT.GAA8.BGH

Figure 5



pAAV-ApoE/hAAT.GAA2.wtBGH

Figure 6



pAAV-ApoE/hAAT.GAA5.wtBGH

Figure 7

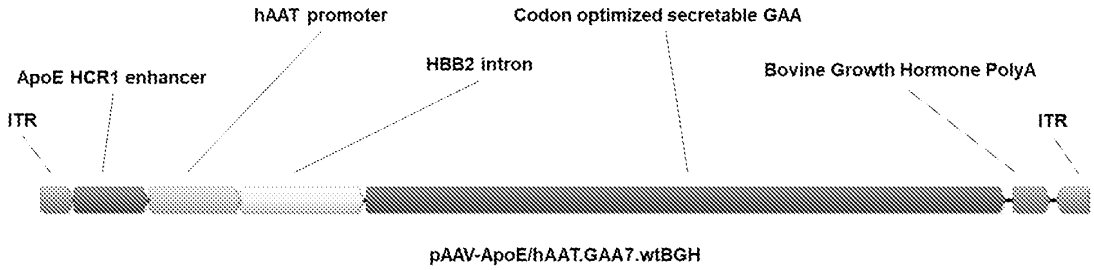


Figure 8

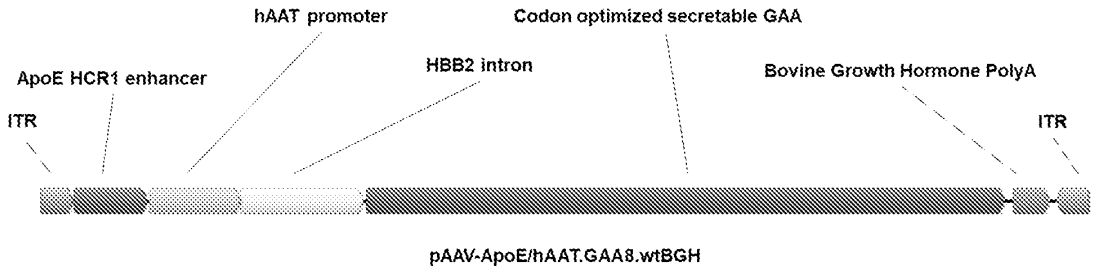


Figure 9

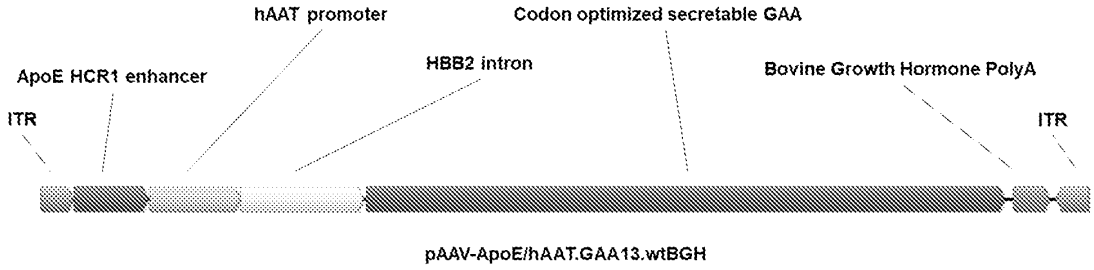


Figure 10

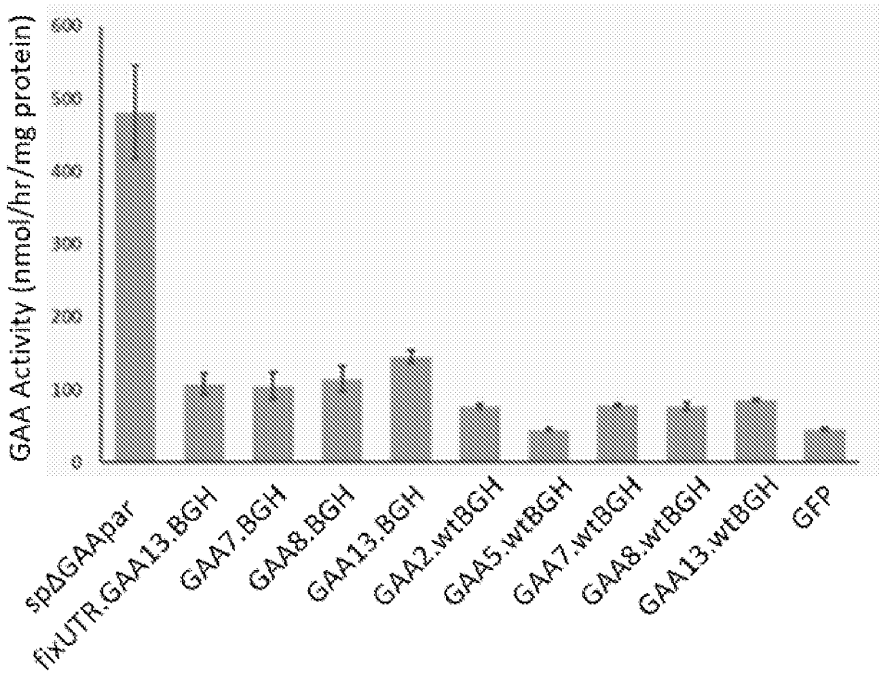

GAA Activity (nmol/hr/mg protein)
0
100
200
300
400
500
spΔGAApar
fixUTR.GAA13.BGH
GAA7.BGH
GAA8.BGH
GAA13.BGH
GAA2.wtBGH
GAA5.wtBGH
GAA7.wtBGH
GAA8.wtBGH
GAA13.wtBGH
GFP

Figure 11

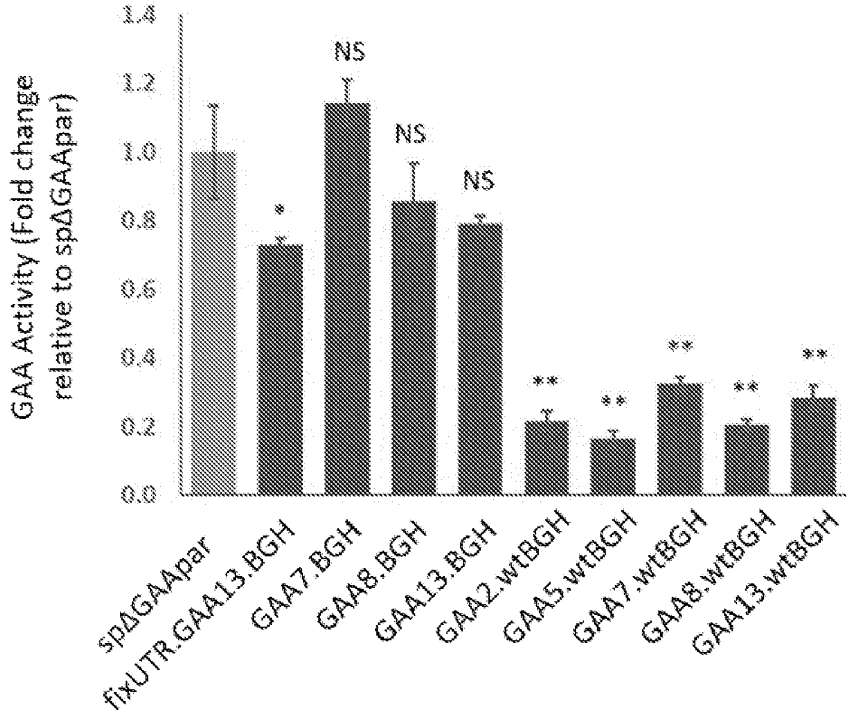

GAA Activity (Fold change relative to spΔGAApar)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
NS
NS
NS
*
**
**
**
**
spΔGAApar
fixUTR.GAA13.BGH
GAA7.BGH
GAA8.BGH
GAA13.BGH
GAA2.wtBGH
GAA5.wtBGH
GAA7.wtBGH
GAA8.wtBGH
GAA13.wtBGH

Figure 12

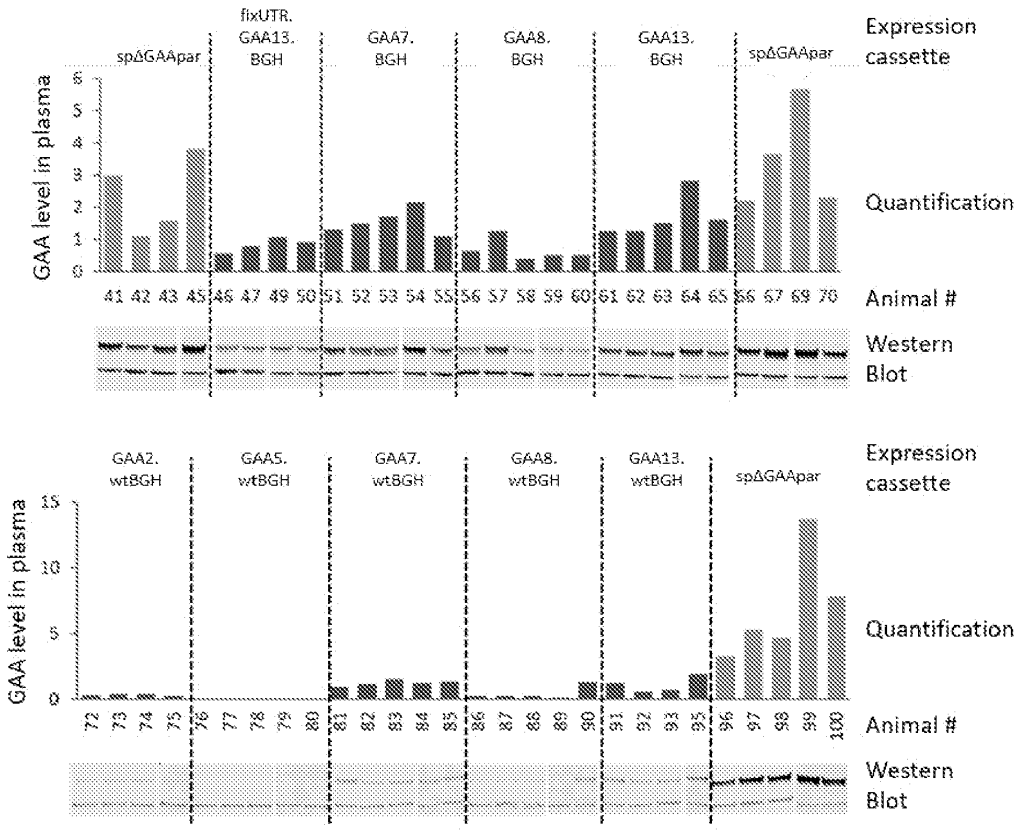

spΔGAApar
fixUTR. GAA13. BGH
GAA7. BGH
GAA8. BGH
GAA13. BGH
spΔGAApar
Expression cassette
GAA level in plasma
Quantification
41 42 43 45 46 47 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 69 70
Animal #
Western Blot
GAA2. wtBGH
GAA5. wtBGH
GAA7. wtBGH
GAA8. wtBGH
GAA13. wtBGH
spΔGAApar
Expression cassette
GAA level in plasma
15
10
5
0
Quantification
72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 95 96 97 98 99 100
Animal #
Western Blot

Figure 13

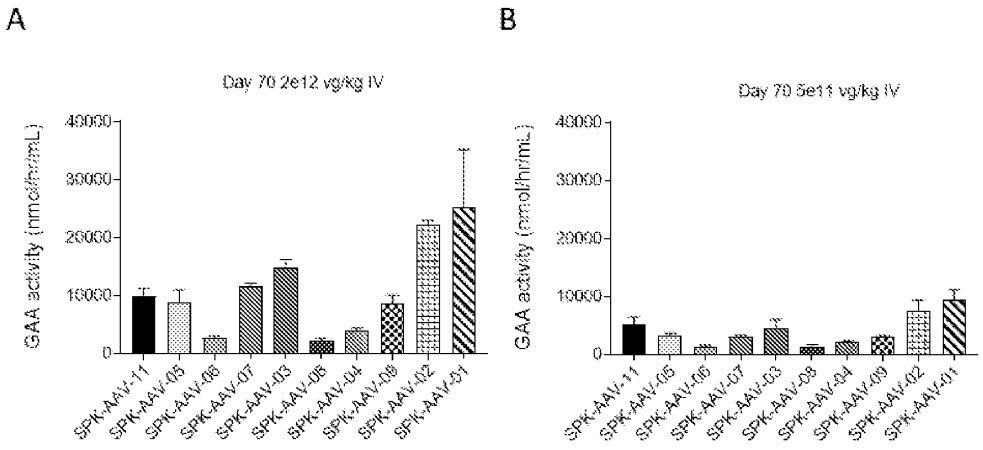

A
Day 70 2e12 vg/kg IV
GAA activity (nmol/hr/mL)
40000
30000
20000
10000
0
SPK-AAV-11
SPK-AAV-05
SPK-AAV-06
SPK-AAV-07
SPK-AAV-03
SPK-AAV-08
SPK-AAV-04
SPK-AAV-09
SPK-AAV-02
SPK-AAV-01
B
Day 70 5e11 vg/kg IV
GAA activity (nmol/hr/mL)
40000
30000
20000
10000
0
SPK-AAV-11
SPK-AAV-05
SPK-AAV-06
SPK-AAV-07
SPK-AAV-03
SPK-AAV-08
SPK-AAV-04
SPK-AAV-09
SPK-AAV-02
SPK-AAV-01

Figure 14

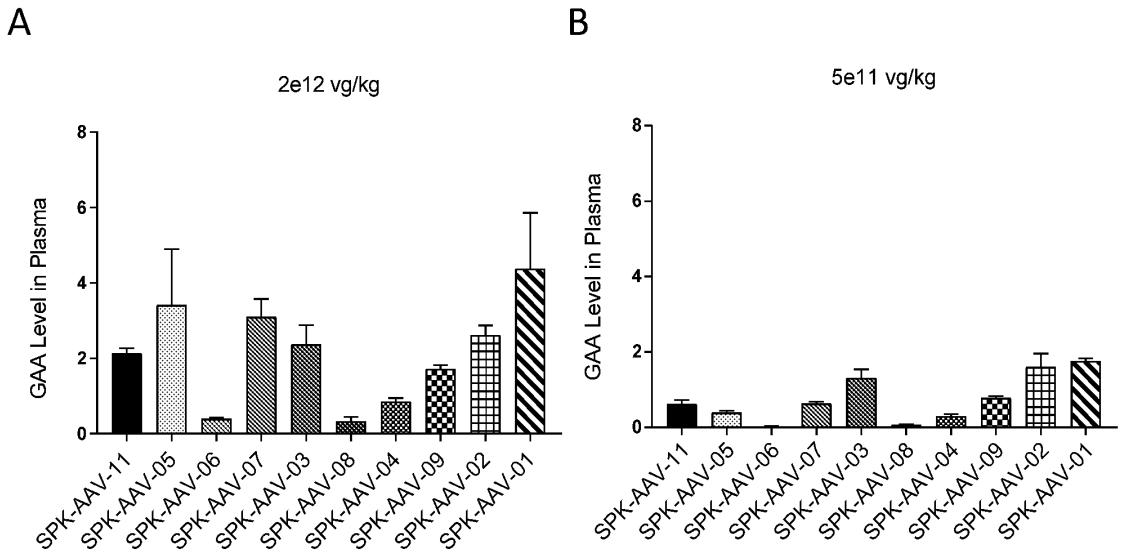

A
2e12 vg/kg
GAA Level in Plasma
0
2
4
6
8
SPK-AAV-11
SPK-AAV-05
SPK-AAV-06
SPK-AAV-07
SPK-AAV-03
SPK-AAV-08
SPK-AAV-04
SPK-AAV-09
SPK-AAV-02
SPK-AAV-01
B
5e11 vg/kg
GAA Level in Plasma
0
2
4
6
8
SPK-AAV-11
SPK-AAV-05
SPK-AAV-06
SPK-AAV-07
SPK-AAV-03
SPK-AAV-08
SPK-AAV-04
SPK-AAV-09
SPK-AAV-02
SPK-AAV-01

Figure 15

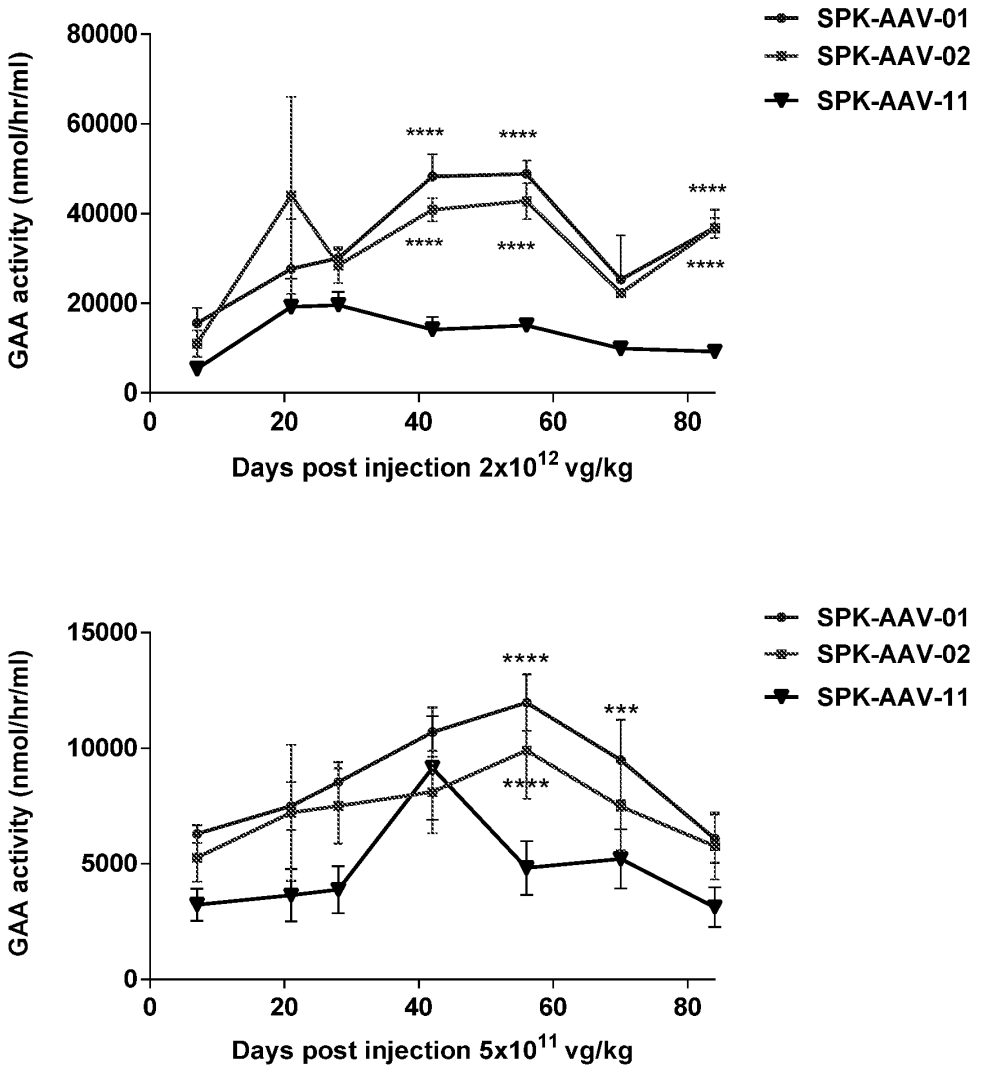

SPK-AAV-01
SPK-AAV-02
SPK-AAV-11
GAA activity (nmol/hr/ml)
80000
60000
40000
20000
0
0
20
40
60
80
Days post injection 2x10^12 vg/kg
****
****
****
****
****
SPK-AAV-01
SPK-AAV-02
SPK-AAV-11
GAA activity (nmol/hr/ml)
15000
10000
5000
0
0
20
40
60
80
Days post injection 5x10^11 vg/kg
****
***
****

Figure 16

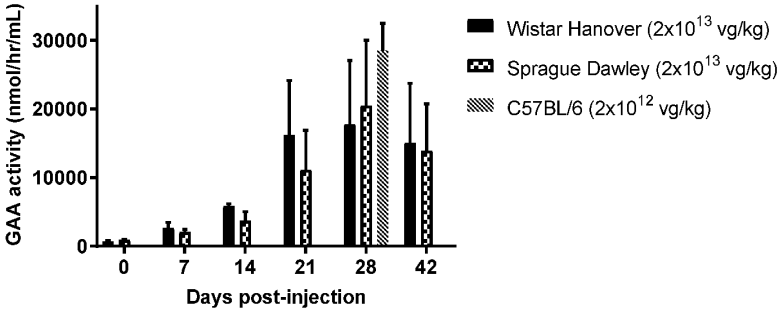

GAA activity (nmol/hr/mL)
30000
20000
10000
0
0
7
14
21
28
42
Days post-injection
Wistar Hanover (2x10^13 vg/kg)
Sprague Dawley (2x10^13 vg/kg)
C57BL/6 (2x10^12 vg/kg)

Figure 17

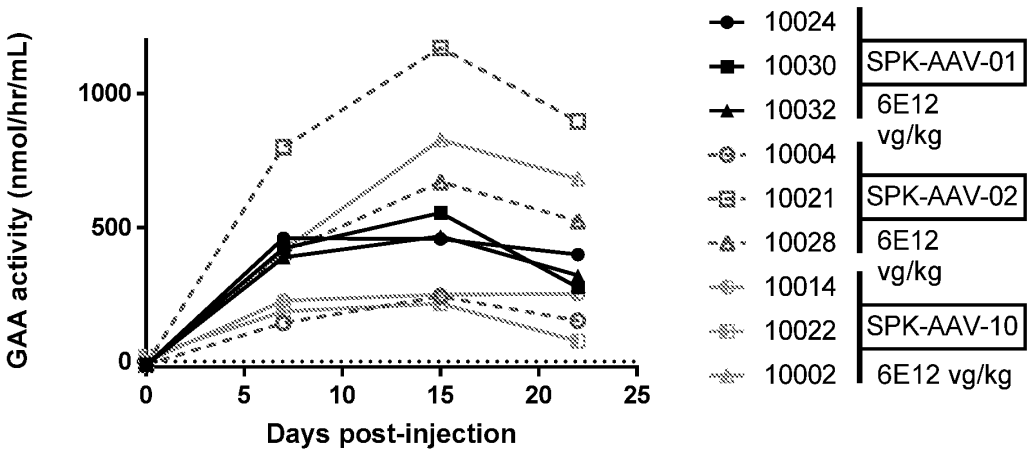

GAA activity (nmol/hr/mL)
1000
500
0
0
5
10
15
20
25
Days post-injection
10024
10030
10032
SPK-AAV-01
6E12 vg/kg
10004
10021
10028
SPK-AAV-02
6E12 vg/kg
10014
10022
10002
SPK-AAV-10
6E12 vg/kg

Figure 18

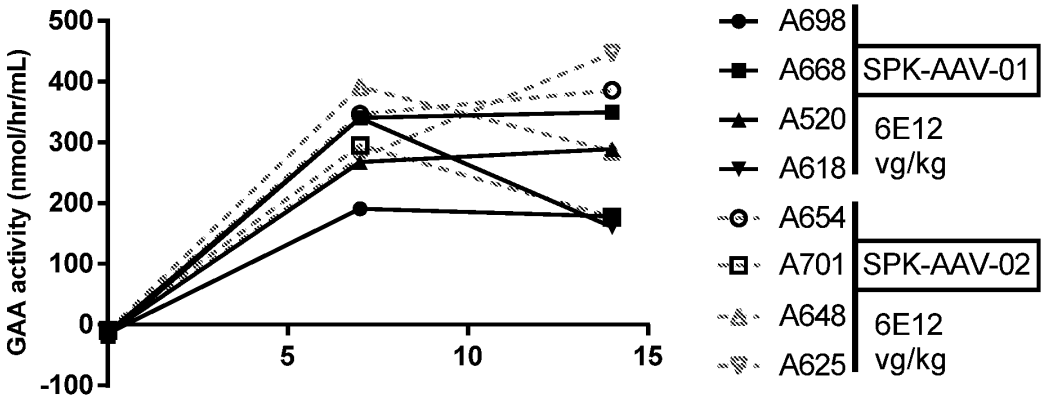
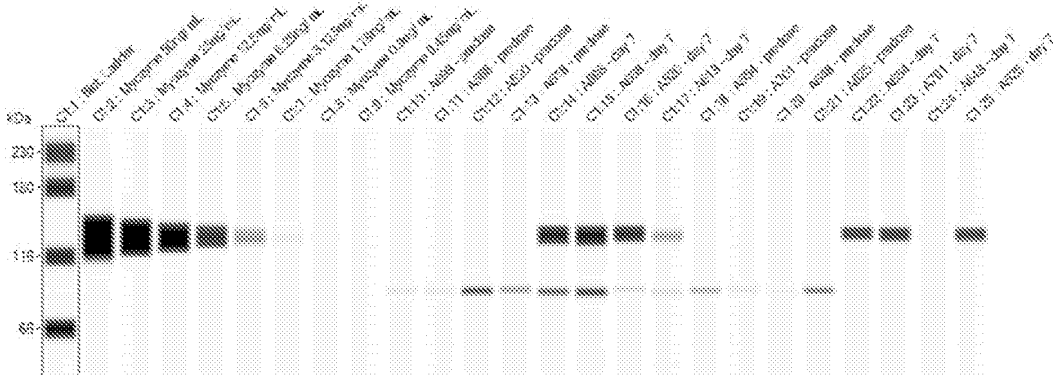

GAA activity (nmol/hr/mL)
500
400
300
200
100
0
-100
5
10
15
A698
A668
A520
A618
SPK-AAV-01
6E12
vg/kg
A654
A701
A648
A625
SPK-AAV-02
6E12
vg/kg

Figure 19



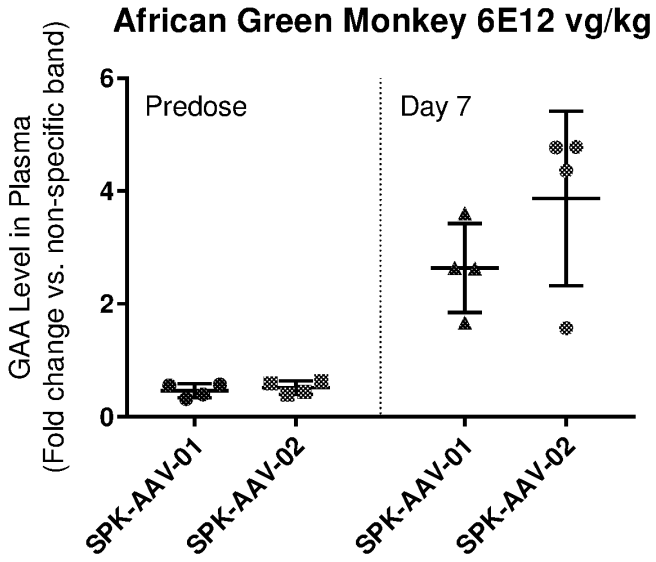

African Green Monkey 6E12 vg/kg
GAA Level in Plasma
(Fold change vs. non-specific band)
6
4
2
0
Predose
Day 7
SPK-AAV-01
SPK-AAV-02
SPK-AAV-01
SPK-AAV-02

Figure 20

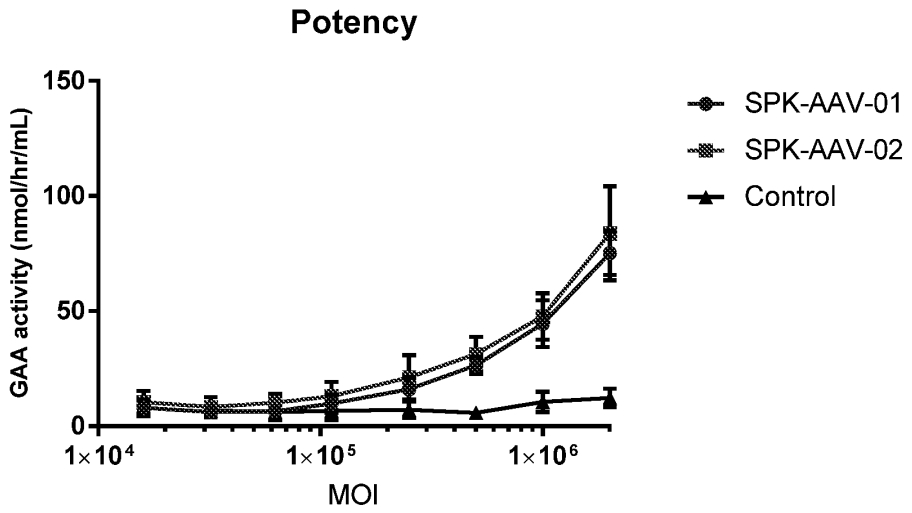
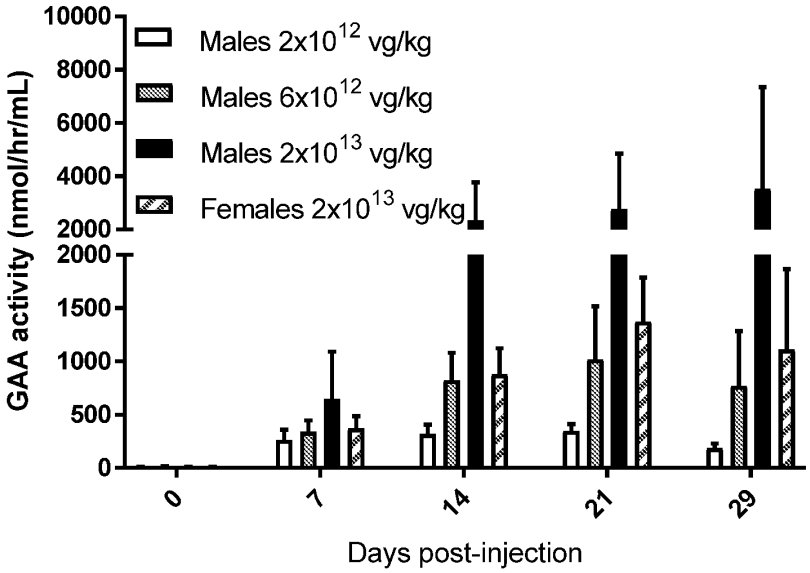

Potency
GAA activity (nmol/hr/mL)
150
100
50
0
1×10⁴
1×10⁵
1×10⁶
MOI
SPK-AAV-01
SPK-AAV-02
Control

Figure 21


GAA activity (nmol/hr/mL)
10000
8000
6000
4000
2000
2000
1500
1000
500
0
Males 2x10^12 vg/kg
Males 6x10^12 vg/kg
Males 2x10^13 vg/kg
Females 2x10^13 vg/kg
0
7
14
21
29
Days post-injection