FIGURE 1A

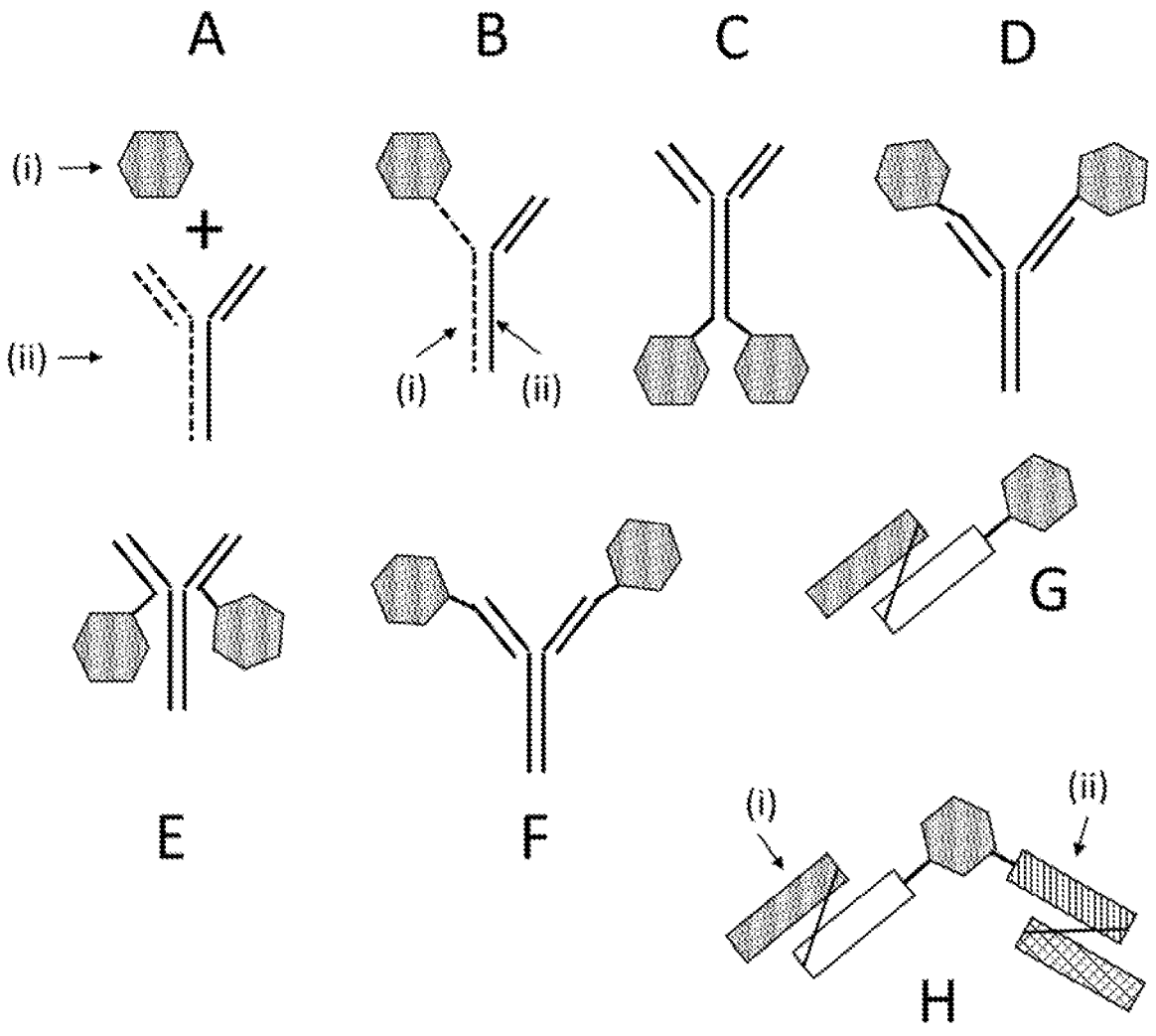


FIGURE 1B

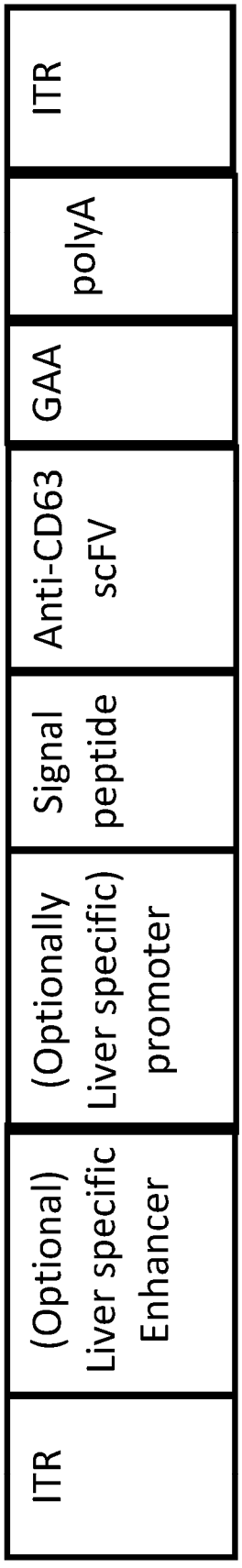

ITR
(Optional) Liver specific Enhancer
(Optionally Liver specific) promoter
Signal peptide
Anti-CD63 scFV
GAA
polyA
ITR

FIGURE 2

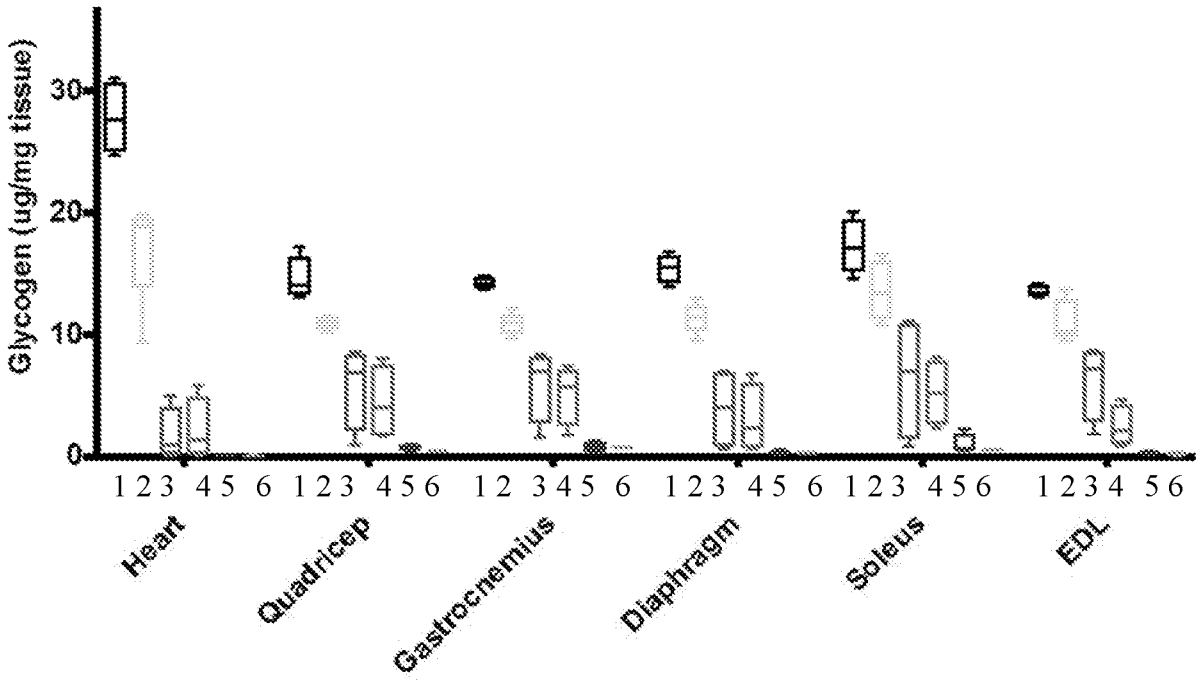

Glycogen (ug/mg tissue)
30
20
10
0
1 2 3 4 5 6 1 2 3 4 5 6 1 2 3 4 5 6 1 2 3 4 5 6 1 2 3 4 5 6 1 2 3 4 5 6
Heart
Quadricep
Gastrocnemius
Diaphragm
Soleus
EDL

FIGURE 3

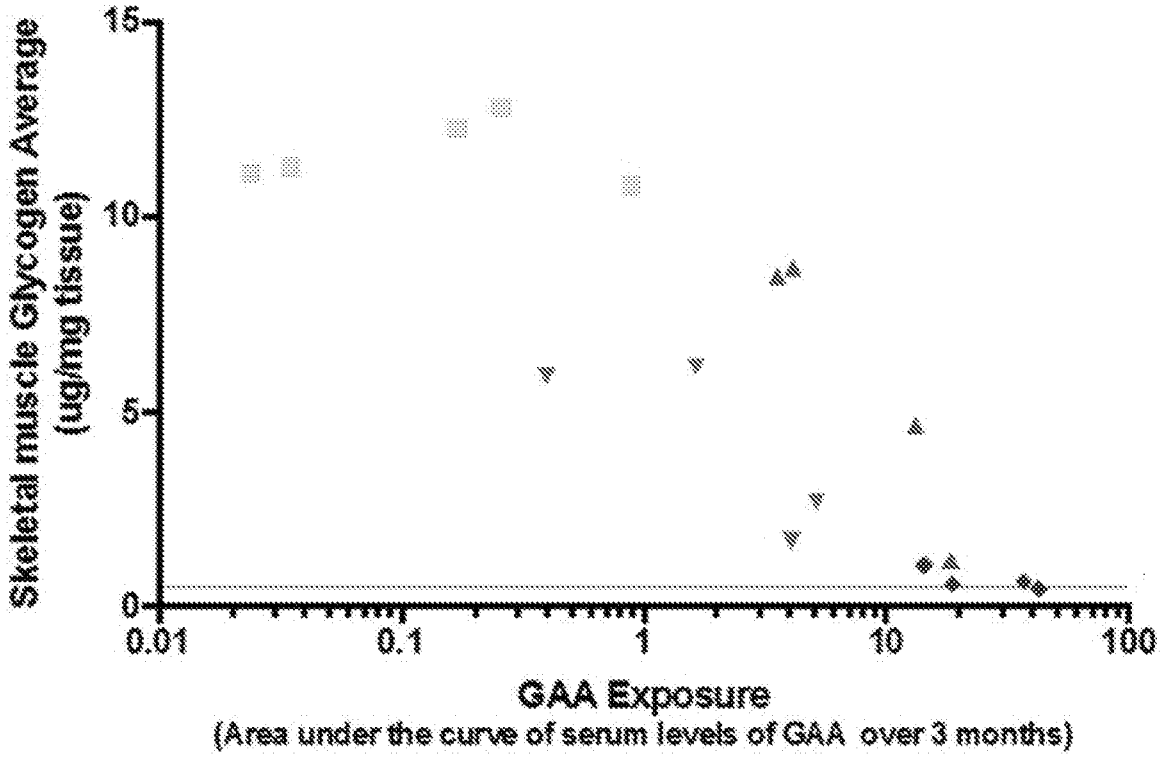

Skeletal muscle Glycogen Average
(ug/mg tissue)
15
10
5
0
0.01
0.1
1
10
100
GAA Exposure
(Area under the curve of serum levels of GAA over 3 months)

FIGURE 4

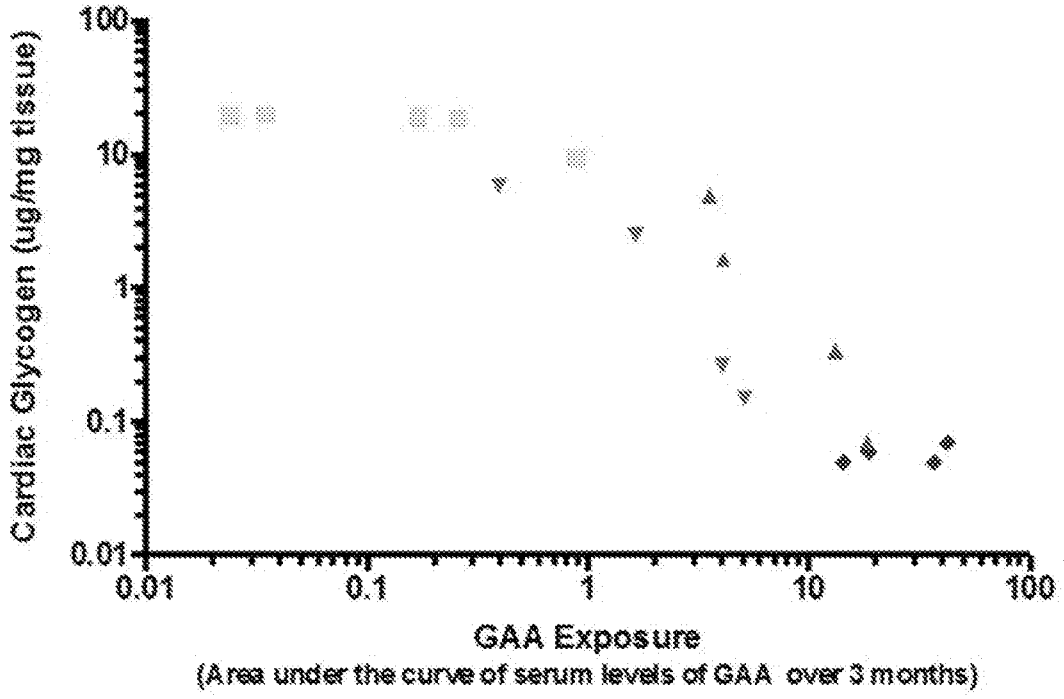

Cardiac Glycogen (ug/mg tissue)
100
10
1
0.1
0.01
0.01
0.1
1
10
100
GAA Exposure
(Area under the curve of serum levels of GAA over 3 months)

FIGURE 5

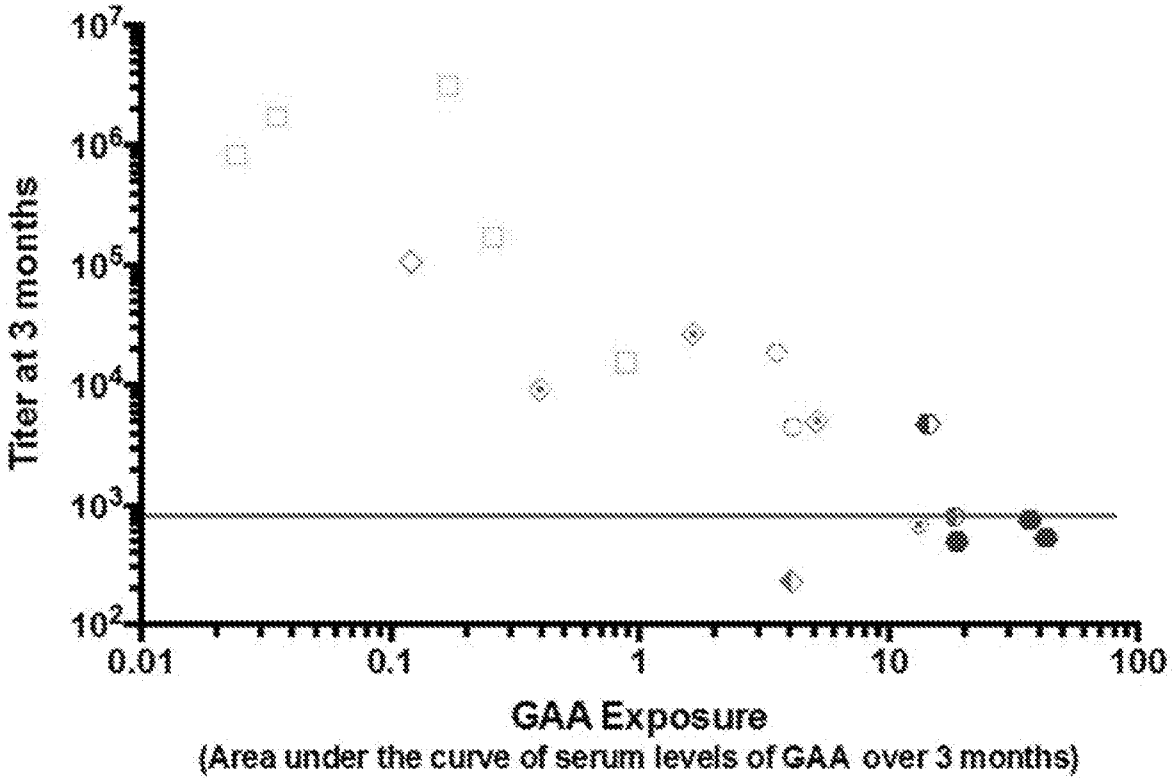

Titer at 3 months
10^7
10^6
10^5
10^4
10^3
10^2
0.01
0.1
1
10
100
GAA Exposure
(Area under the curve of serum levels of GAA over 3 months)

FIGURE 6

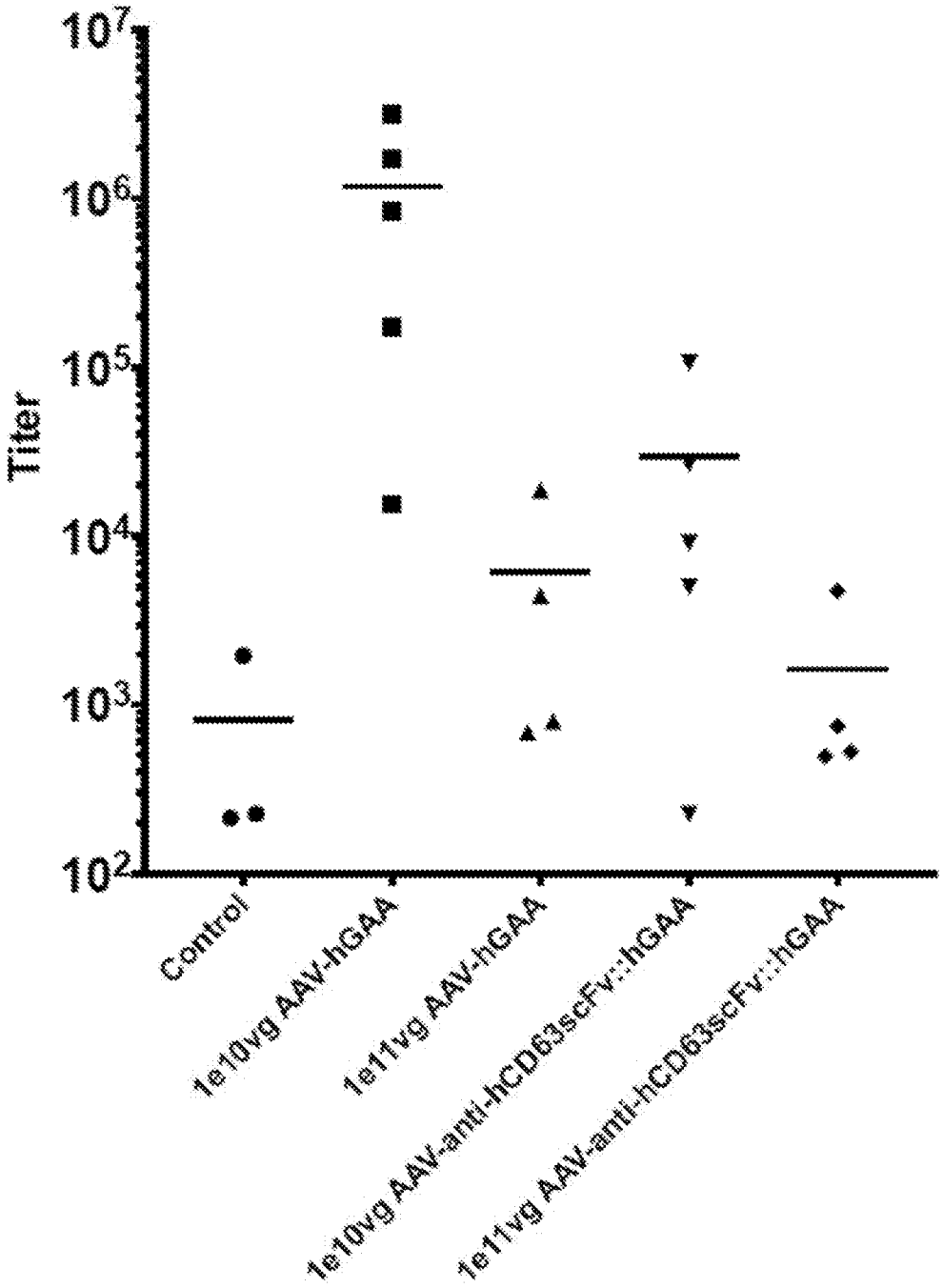

Titer
10^7
10^6
10^5
10^4
10^3
10^2
Control
1e10vg AAV-hGAA
1e11vg AAV-hGAA
1e10vg AAV-anti-hCD63scFv::hGAA
1e11vg AAV-anti-hCD63scFv::hGAA

FIGURE 7A

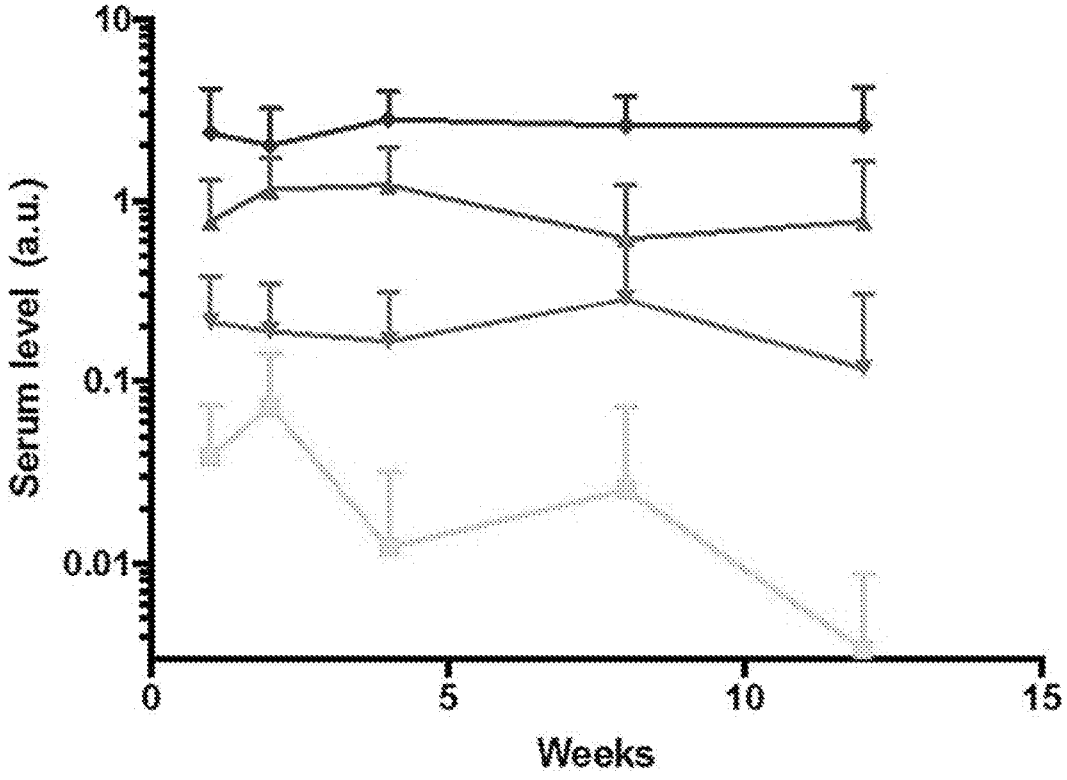


FIGURE 7B

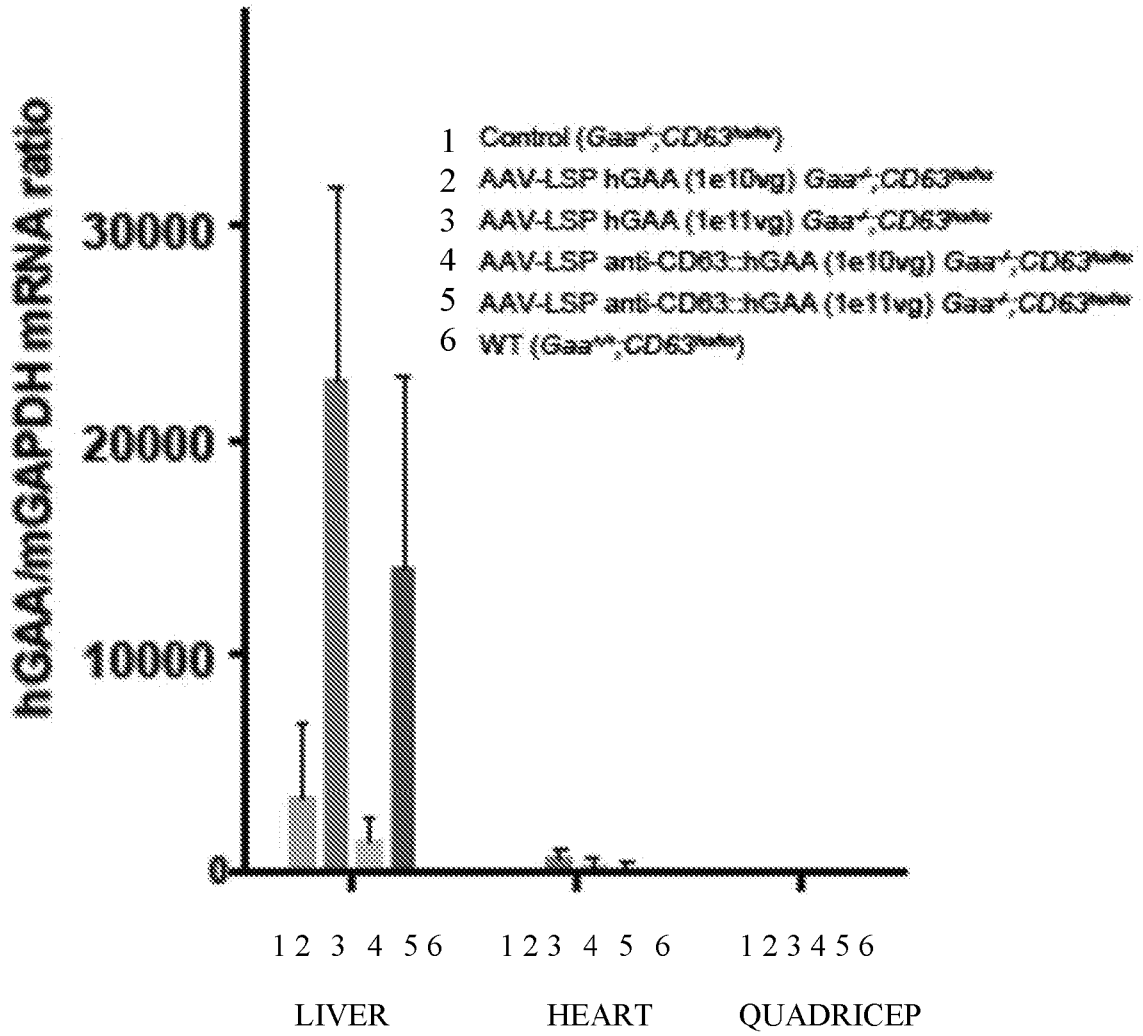

hGAA/mGAPDH mRNA ratio
30000
20000
10000
0
1 Control (Gaa-/-;CD63hGAA/hGAA)
2 AAV-LSP hGAA (1e10vg) Gaa-/-;CD63hGAA/hGAA
3 AAV-LSP hGAA (1e11vg) Gaa-/-;CD63hGAA/hGAA
4 AAV-LSP anti-CD63::hGAA (1e10vg) Gaa-/-;CD63hGAA/hGAA
5 AAV-LSP anti-CD63::hGAA (1e11vg) Gaa-/-;CD63hGAA/hGAA
6 WT (Gaa+/+;CD63hGAA/hGAA)
1 2 3 4 5 6
1 2 3 4 5 6
1 2 3 4 5 6
LIVER
HEART
QUADRICEP

FIGURE 7C

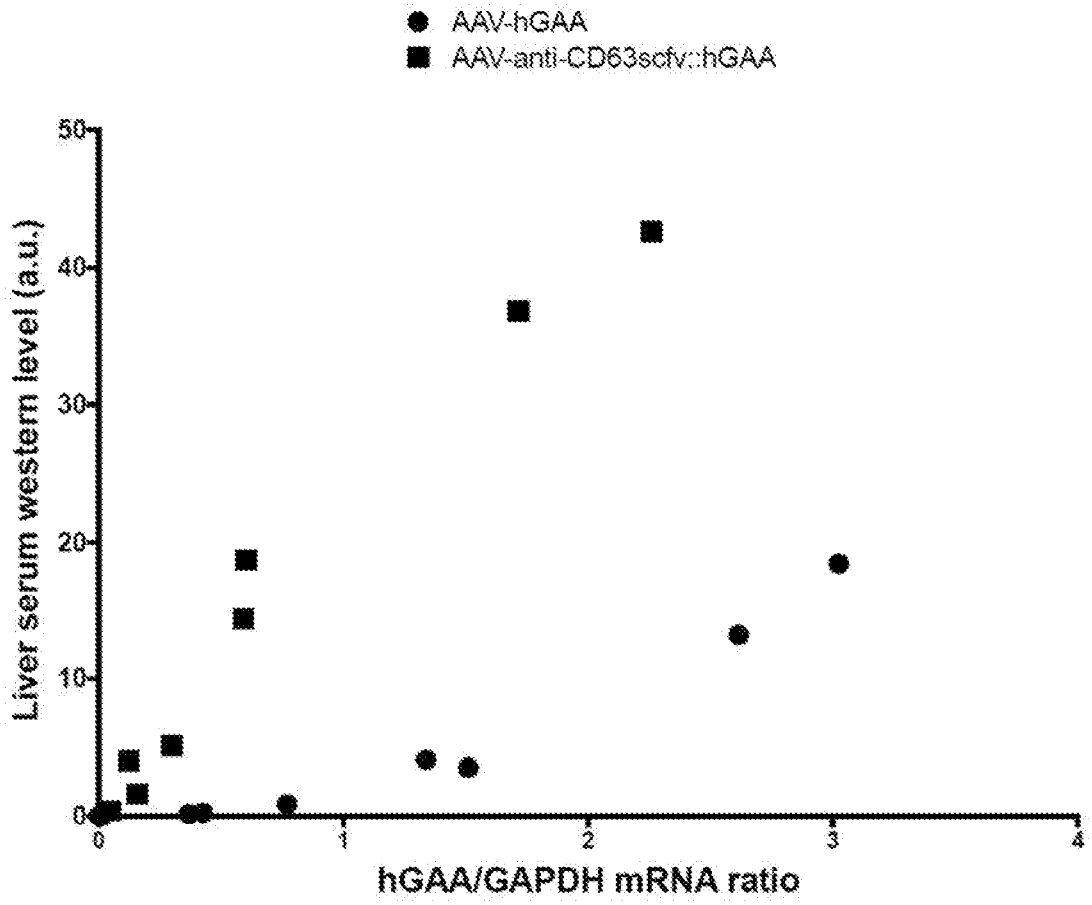

AAV-hGAA
AAV-anti-CD63scfv::hGAA
Liver serum western level (a.u.)
50
40
30
20
10
0
0
1
2
3
4
hGAA/GAPDH mRNA ratio

FIGURE 7D

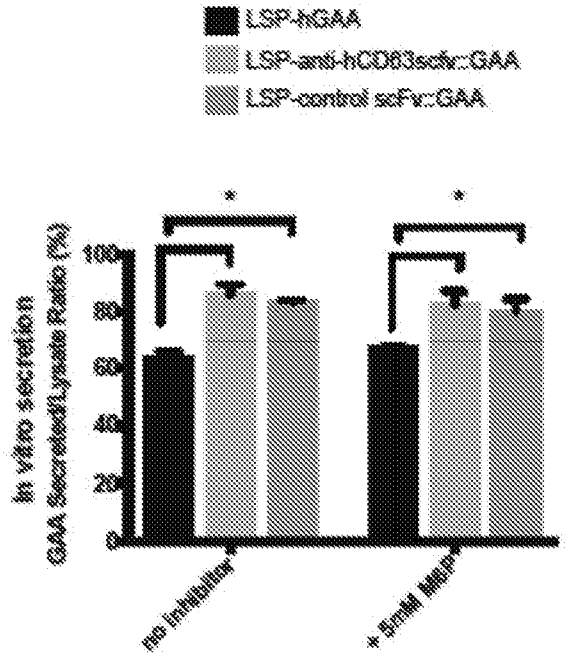

LSP-hGAA
LSP-anti-hCD63scfv::GAA
LSP-control scFv::GAA
In vitro secretion
GAA Secreted/Lysate Ratio (%)
0
2
4
6
8
10
*
*
no inhibition
+ 5mM M6P

FIGURE 8

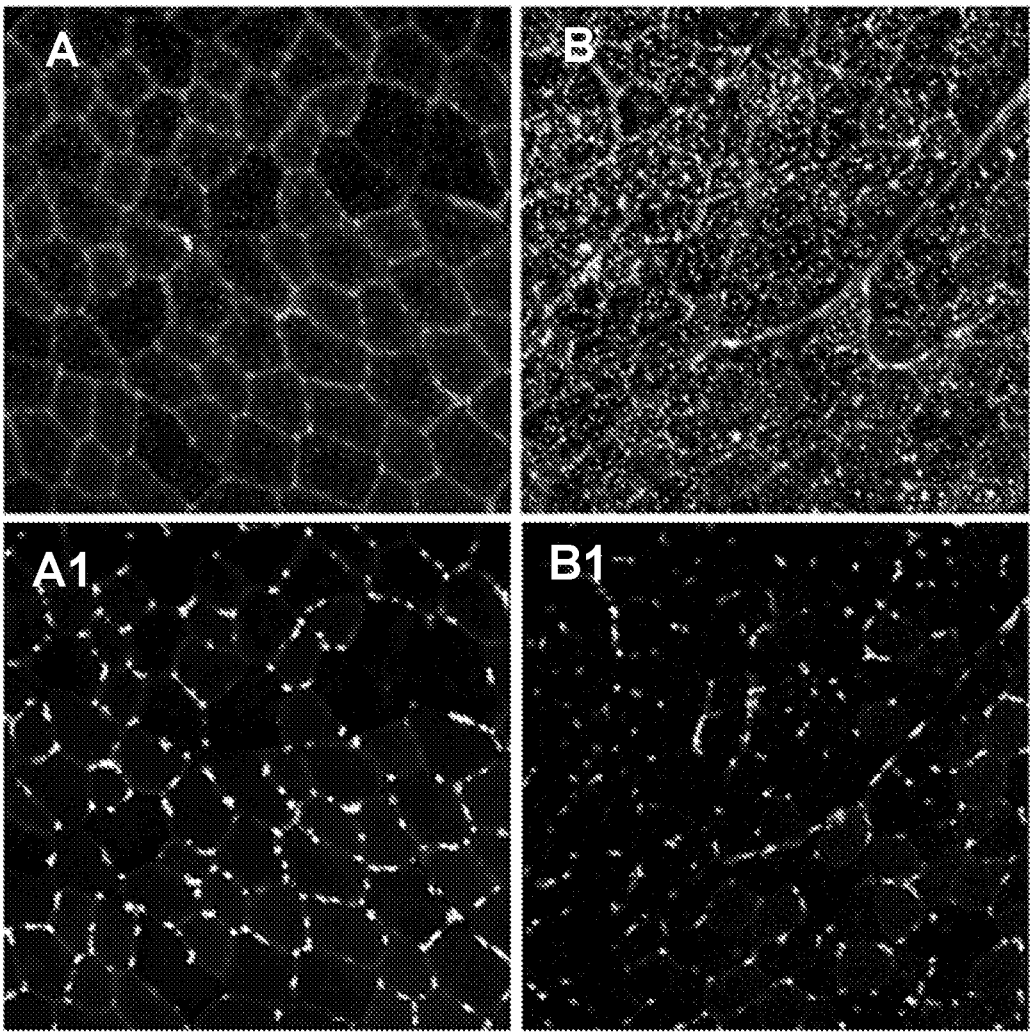


FIGURE 8 (Cont'd)

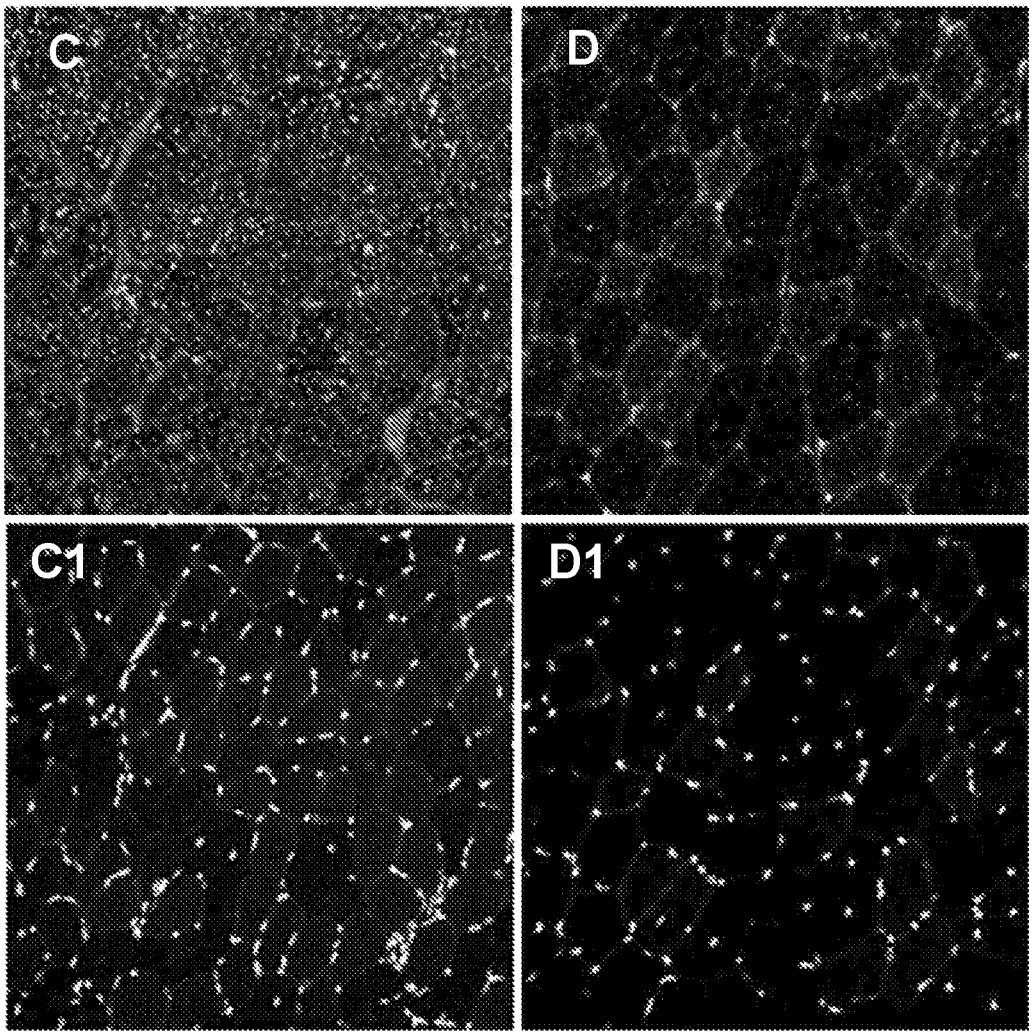
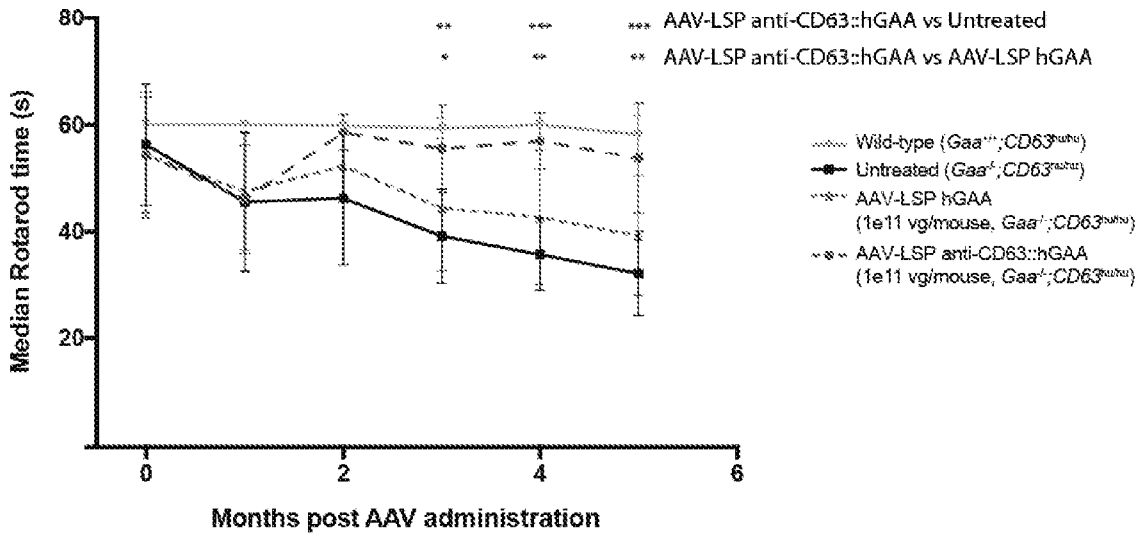


FIGURE 9

A


Median Rotarod time (s)
80
60
40
20
0
2
4
6
Months post AAV administration
AAV-LSP anti-CD63::hGAA vs Untreated
AAV-LSP anti-CD63::hGAA vs AAV-LSP hGAA
Wild-type (Gaa+/+;CD63hu/hu)
Untreated (Gaa-/-;CD63hu/hu)
AAV-LSP hGAA
(1e11 vg/mouse, Gaa-/-;CD63hu/hu)
AAV-LSP anti-CD63::hGAA
(1e11 vg/mouse, Gaa-/-;CD63hu/hu)

B

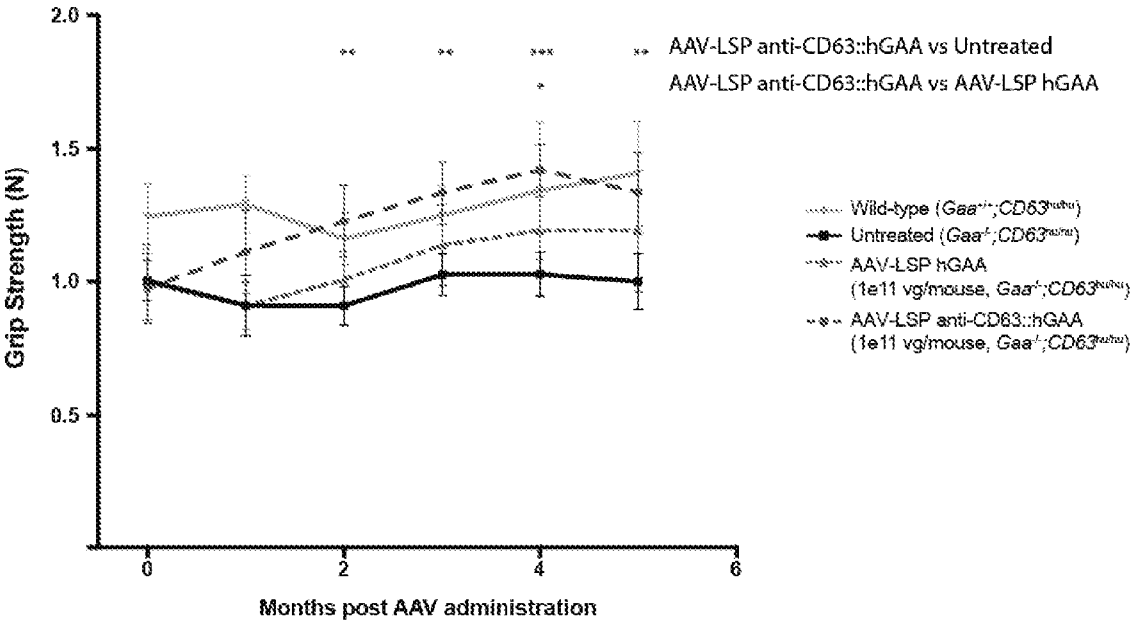

Grip Strength (N)
2.0
1.5
1.0
0.5
0
2
4
6
Months post AAV administration
AAV-LSP anti-CD63::hGAA vs Untreated
AAV-LSP anti-CD63::hGAA vs AAV-LSP hGAA
Wild-type (Gaa+/+;CD63hu/hu)
Untreated (Gaa-/-;CD63hu/hu)
AAV-LSP hGAA
(1e11 vg/mouse, Gaa-/-;CD63hu/hu)
AAV-LSP anti-CD63::hGAA
(1e11 vg/mouse, Gaa-/-;CD63hu/hu)

FIGURE 10A

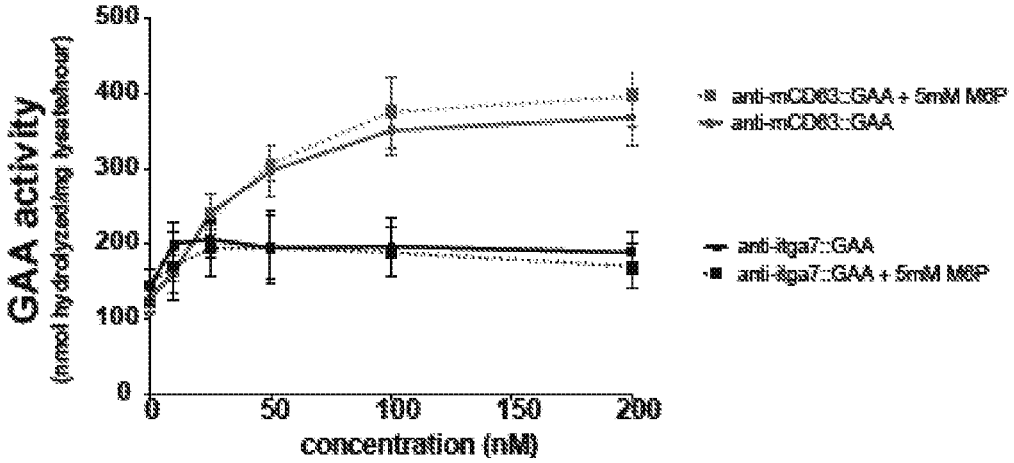
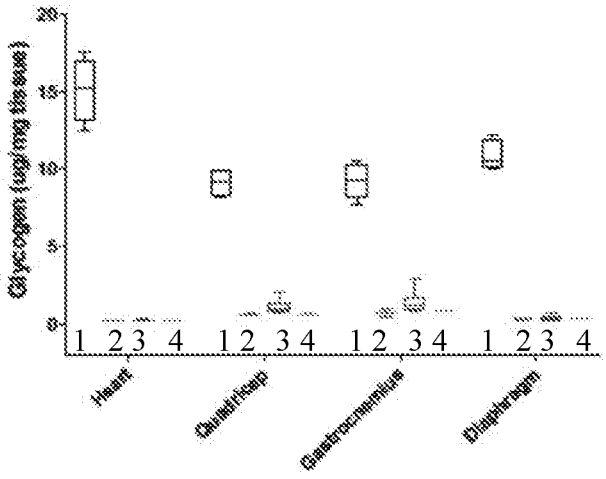

GAA activity
(nmol hydrolyzed/mg lysate/hour)
500
400
300
200
100
0
0
50
100
150
200
concentration (nM)
anti-mCD63::GAA + 5mM M6P
anti-mCD63::GAA
anti-itga7::GAA
anti-itga7::GAA + 5mM M6P

FIGURE 10B



1 Untreated control ($GAA^{-/-}$, $CD63^{hu/hu}$)
2 anti-hCD63scfv::GAA ($GAA^{-/-}$, $CD63^{hu/hu}$)
3 anti-itga7::GAA ($GAA^{-/-}$, $CD63^{hu/hu}$)
4 Untreated wild-type ($GAA^{+/+}$, $CD63^{hu/hu}$)

FIGURE 11

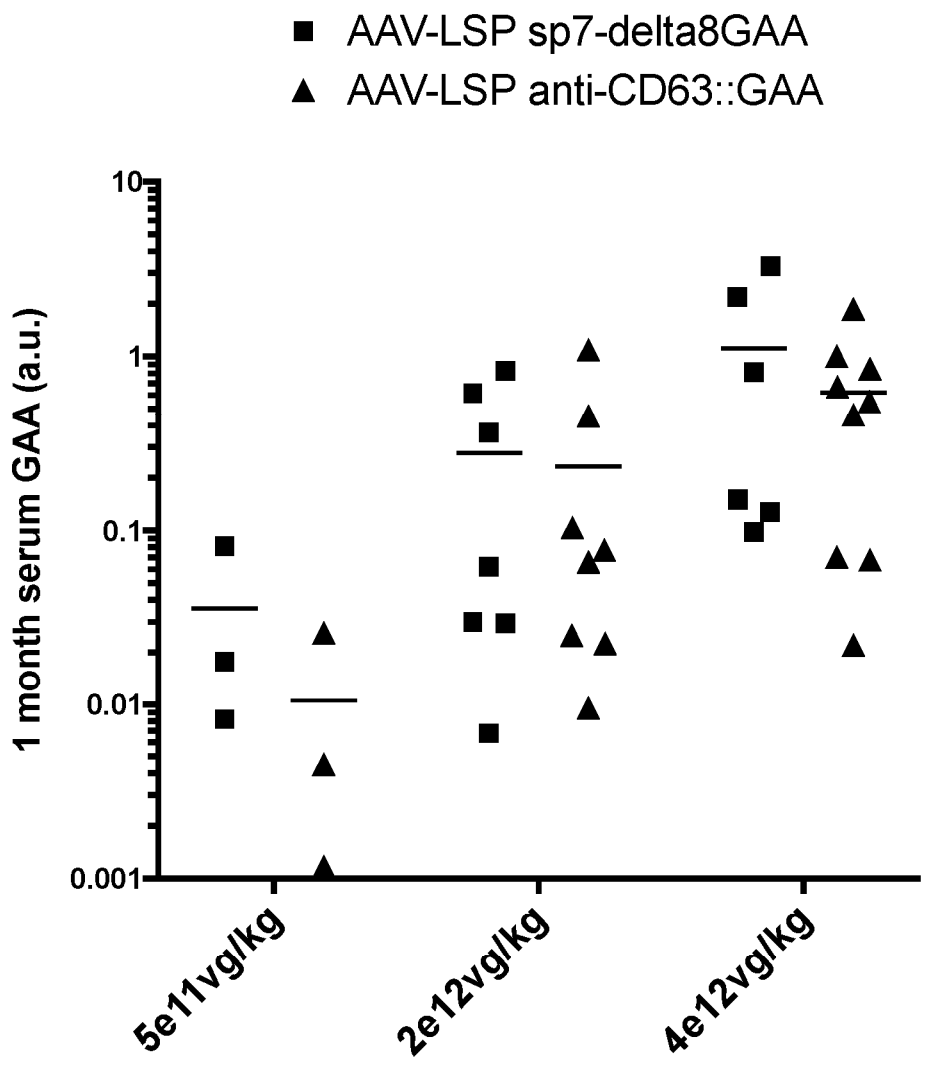
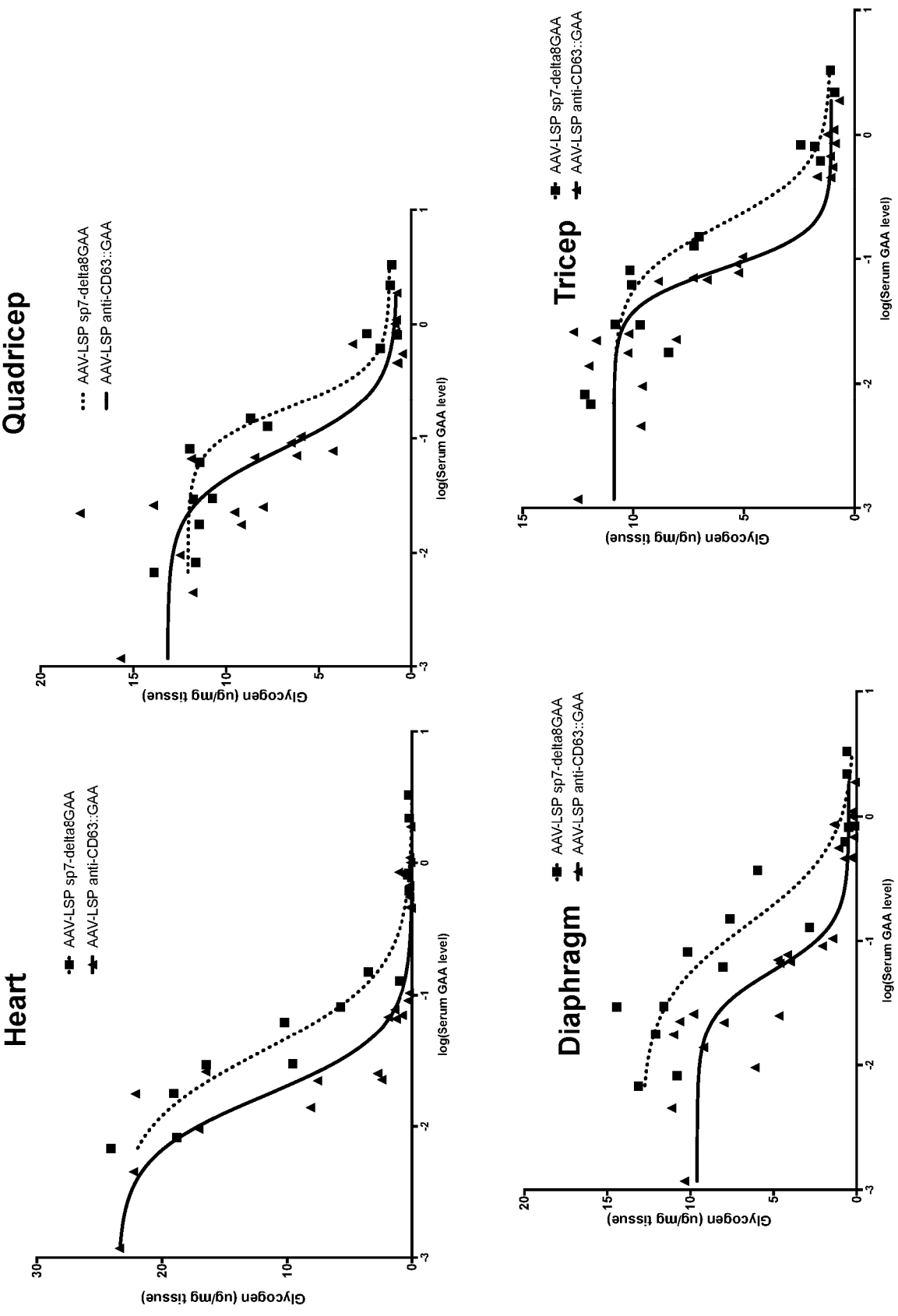

AAV-LSP sp7-delta8GAA
AAV-LSP anti-CD63::GAA
1 month serum GAA (a.u.)
10
1
0.1
0.01
0.001
5e11vg/kg
2e12vg/kg
4e12vg/kg

FIGURE 12


Heart
Quadricep
Tricep
Diaphragm
AAV-LSP sp7-delta8GAA
AAV-LSP anti-CD63::GAA
Glycogen (ug/mg tissue)
log(Serum GAA level)