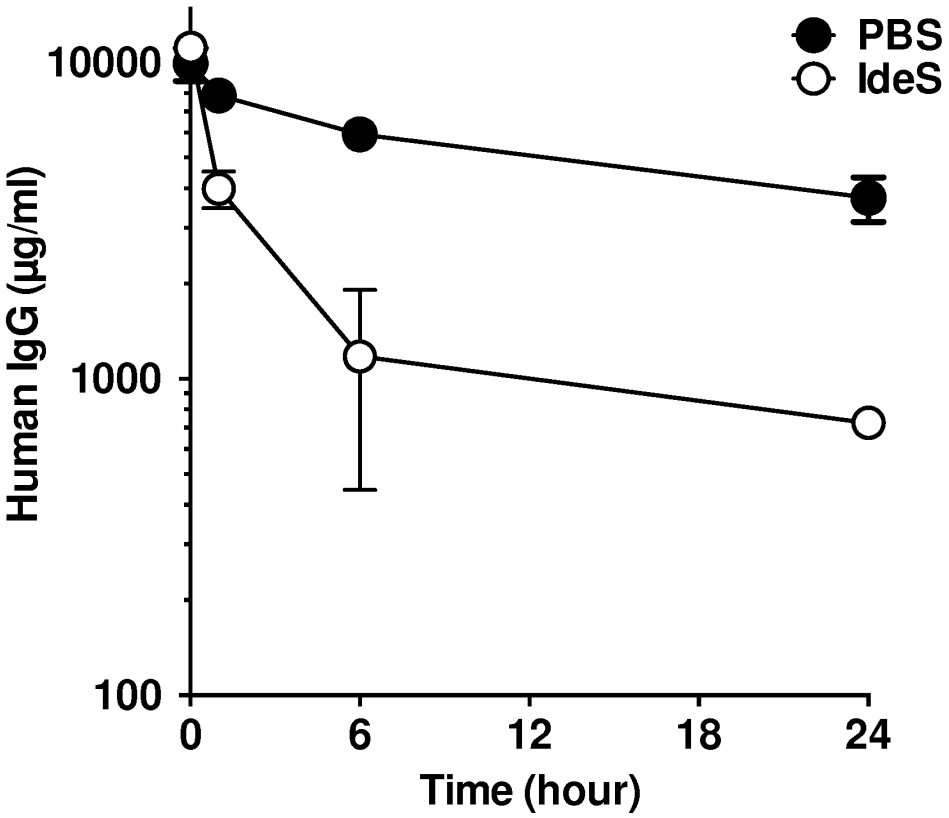


Figure 1

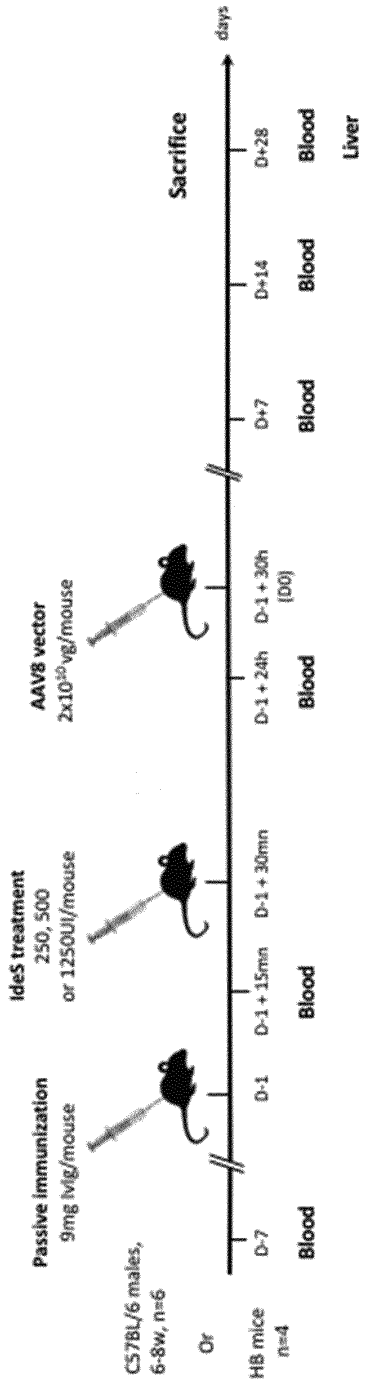

days
Sacrifice
D+28
D+14
D+7
D-1 + 30h (D0)
D-1 + 24h
D-1 + 30mn
D-1 + 15mn
D-1
D-7
Blood
Liver
AAV8 vector
2x10^10 vg/mouse
IdeS treatment
250, 500
or 1250UI/mouse
Passive immunization
9mg IVIg/mouse
C57BL/6 males,
6-8w, n=6
Or
HB mice
n=4

Figure 2

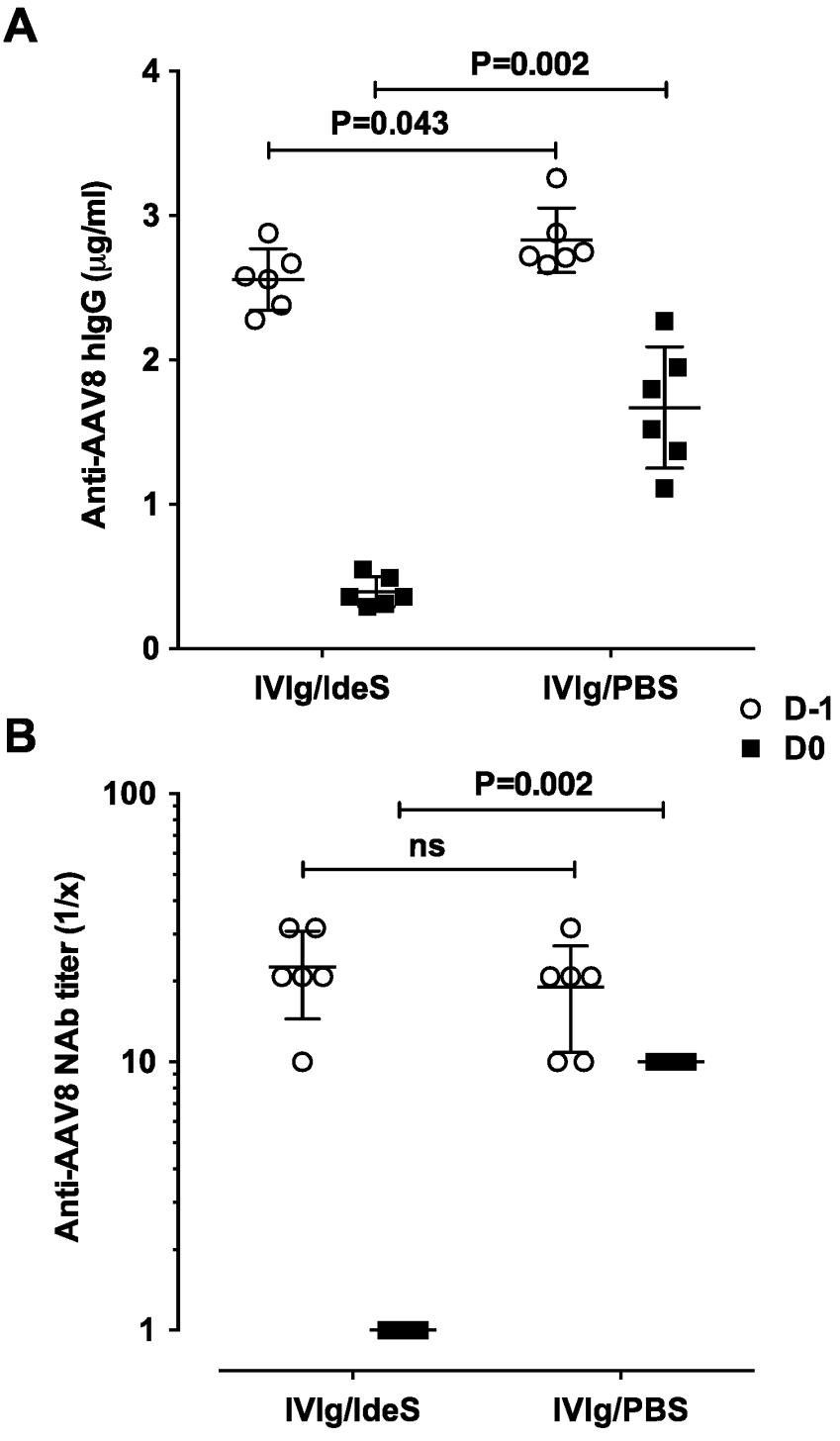


Figure 3 A and B

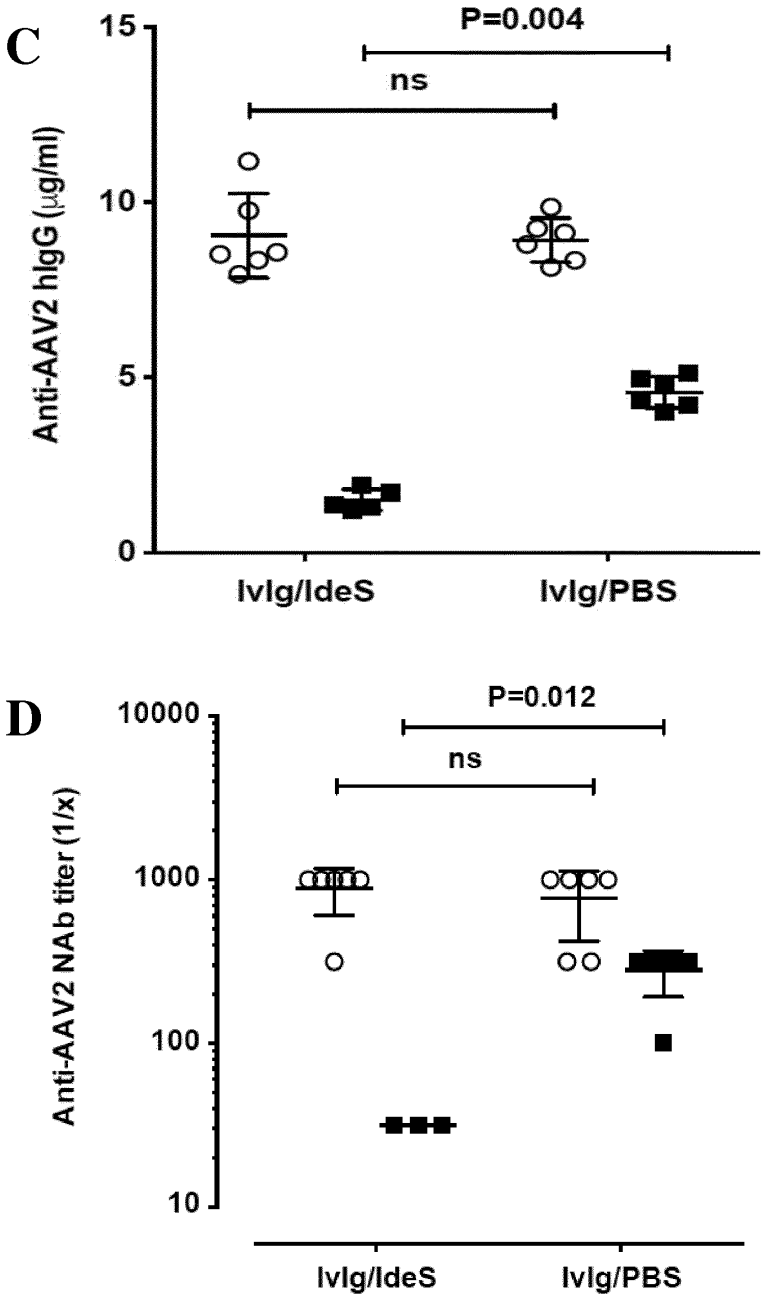
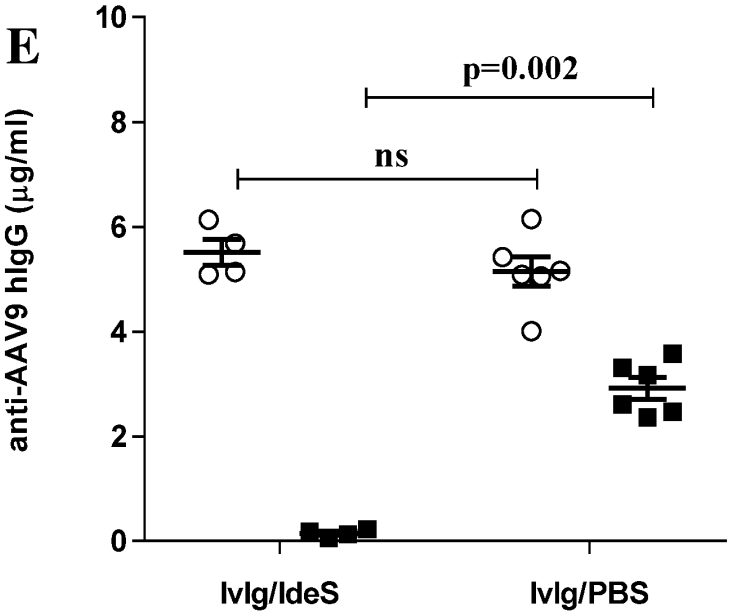


Figure 3 C and D



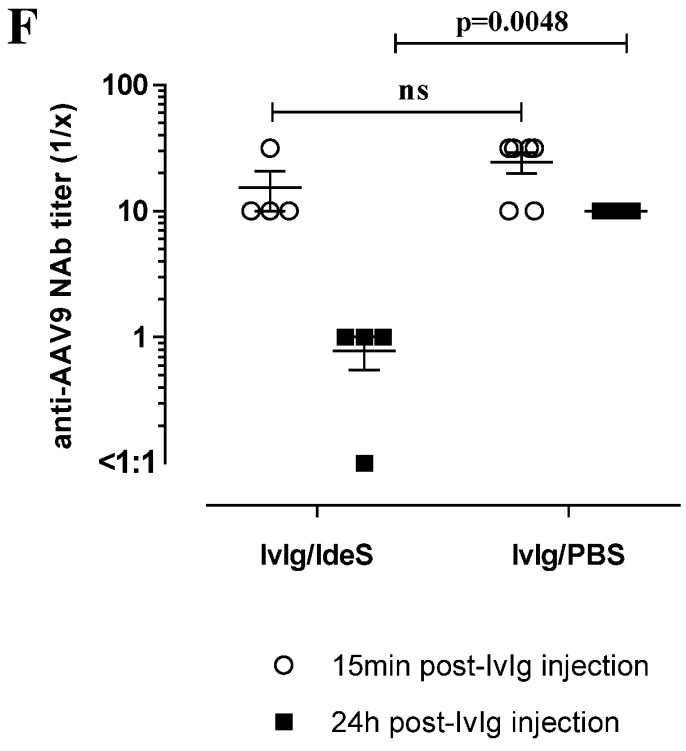


Figure 3 E and F

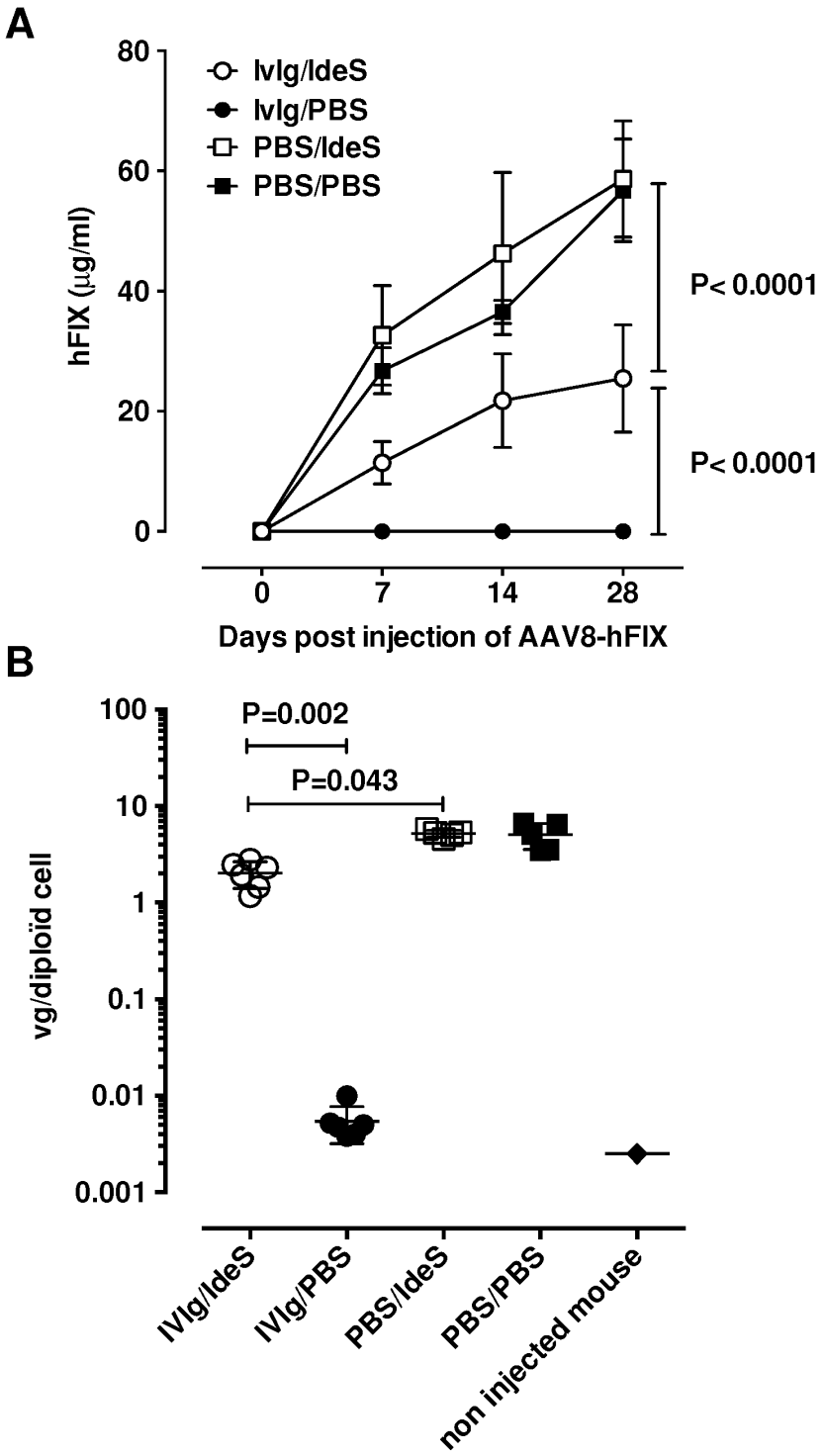
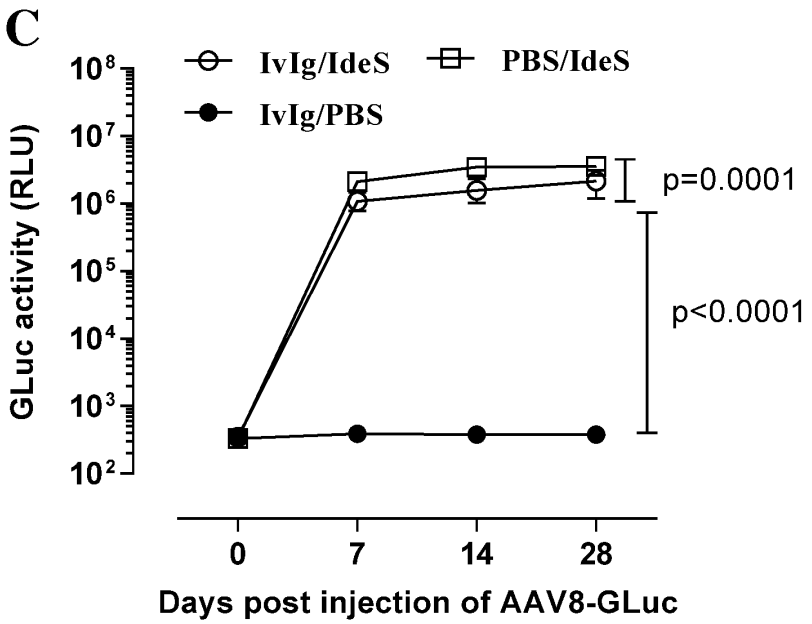


Figure 4 A and B



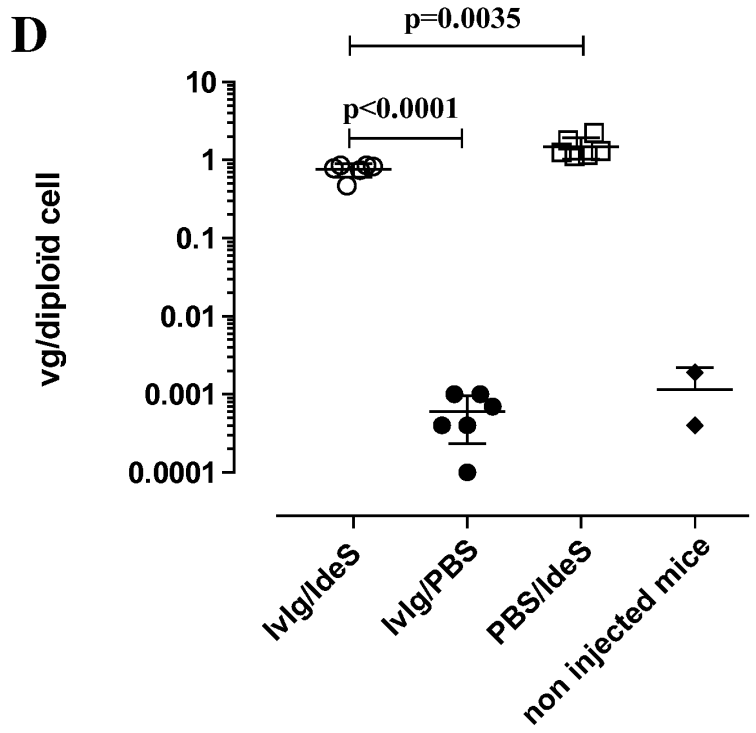
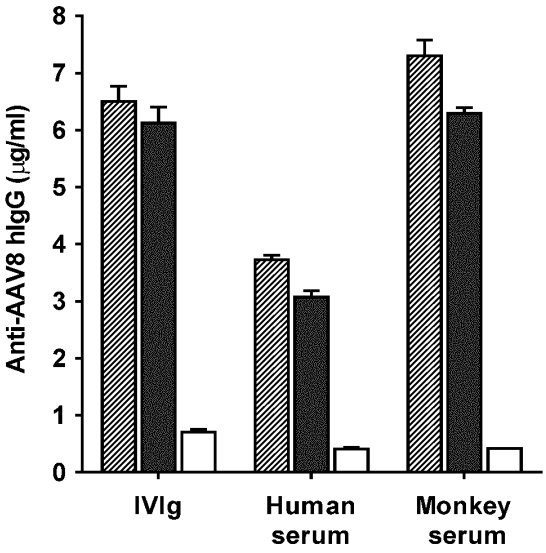


Figure 4 C and D

A



B

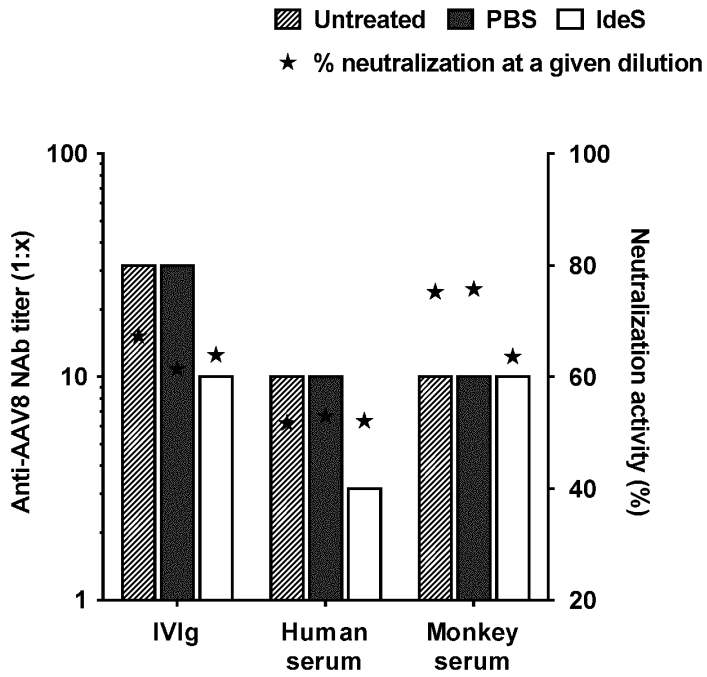


Figure 5 A and B

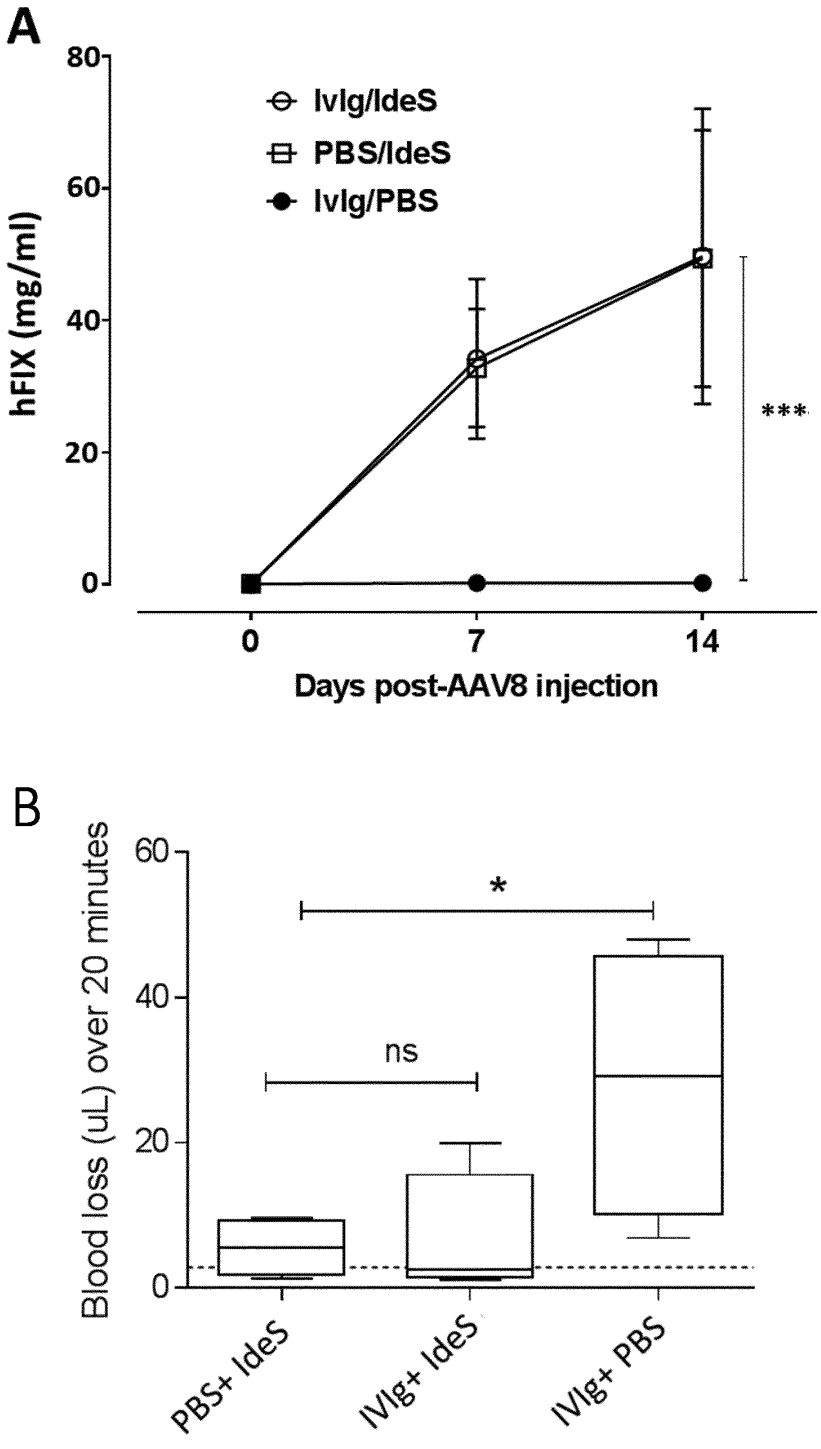


Figure 6 A and B

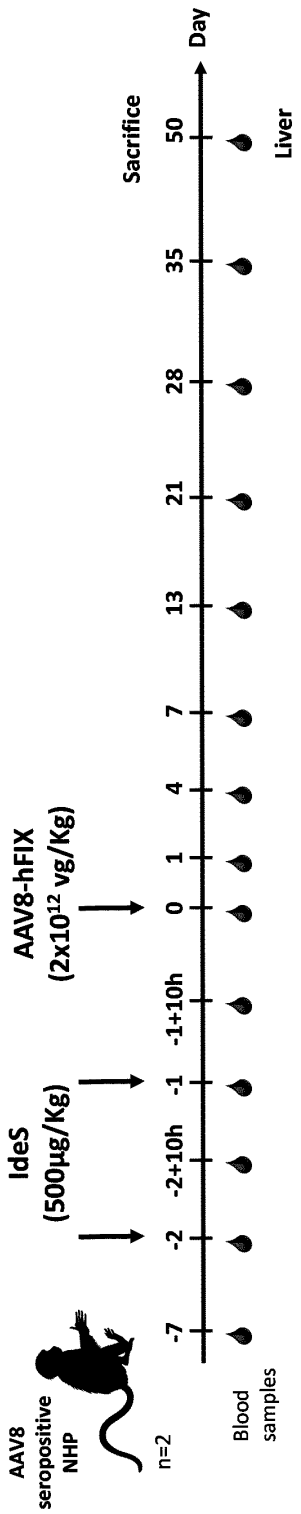

Day
Sacrifice
Liver
50
35
28
21
13
7
4
1
0
-1+10h
-1
-2+10h
-2
-7
AAV8-hFIX
(2x10^12 vg/Kg)
IdeS
(500µg/Kg)
AAV8
seropositive
NHP
n=2
Blood
samples

Figure 7

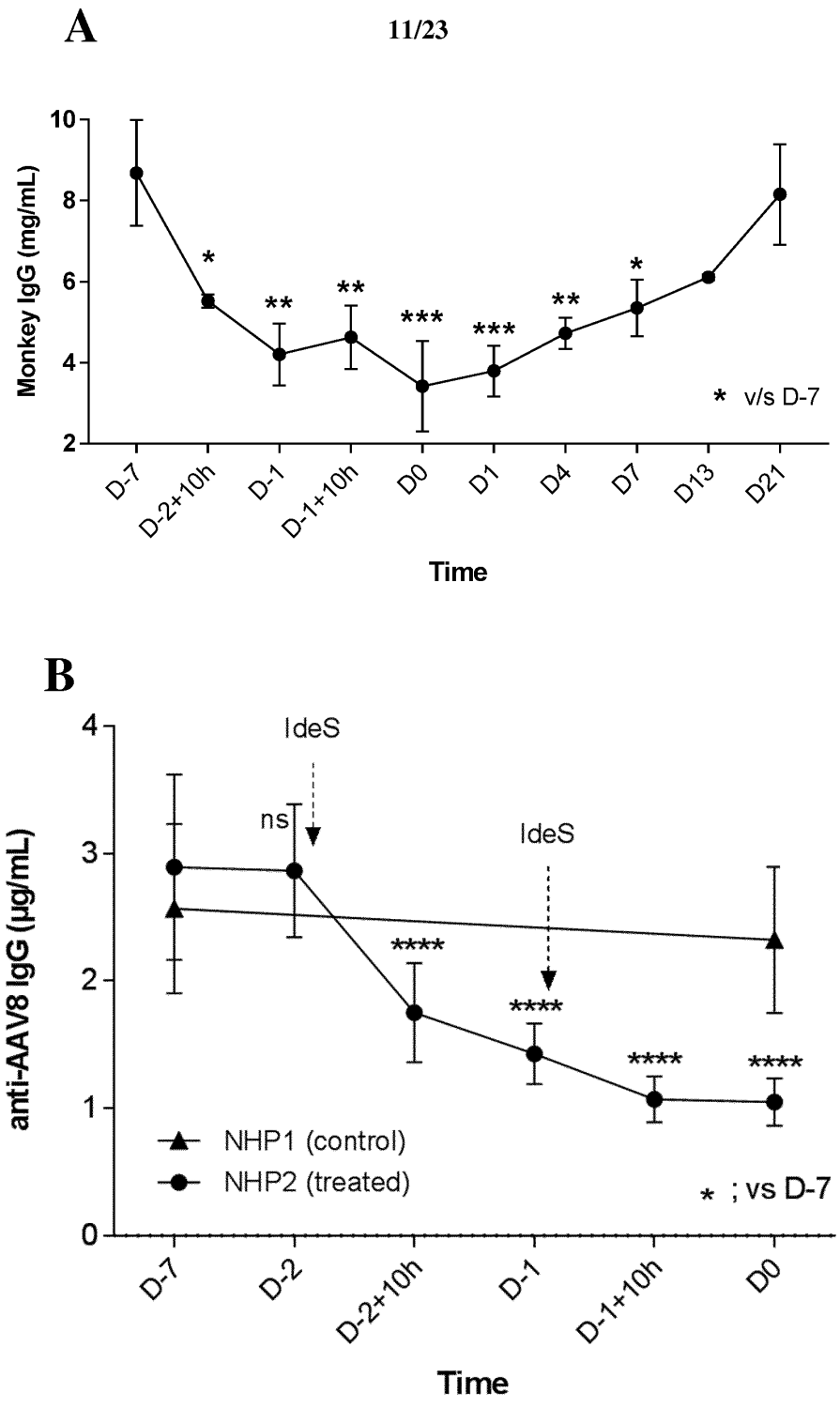


Figure 8 A and B

C

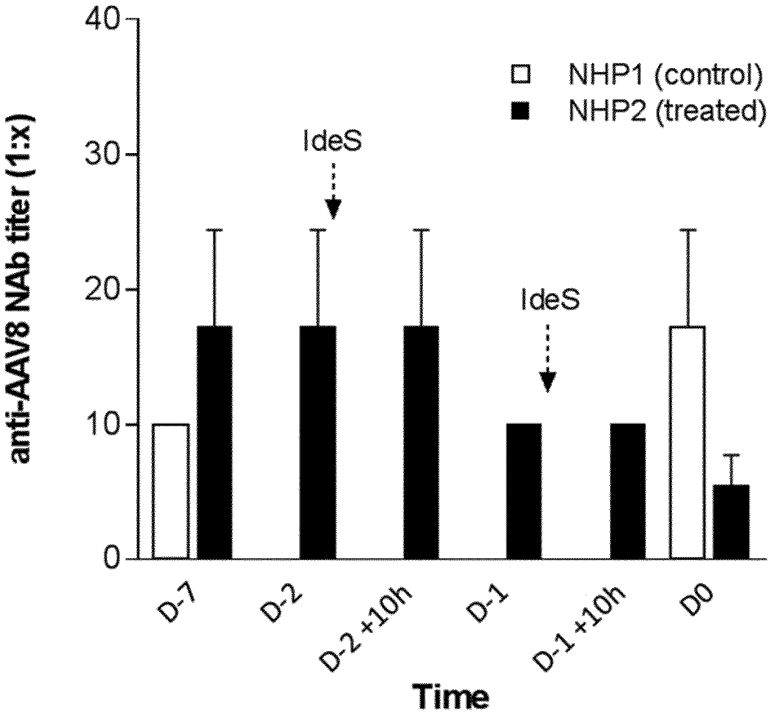


Figure 8 C

A

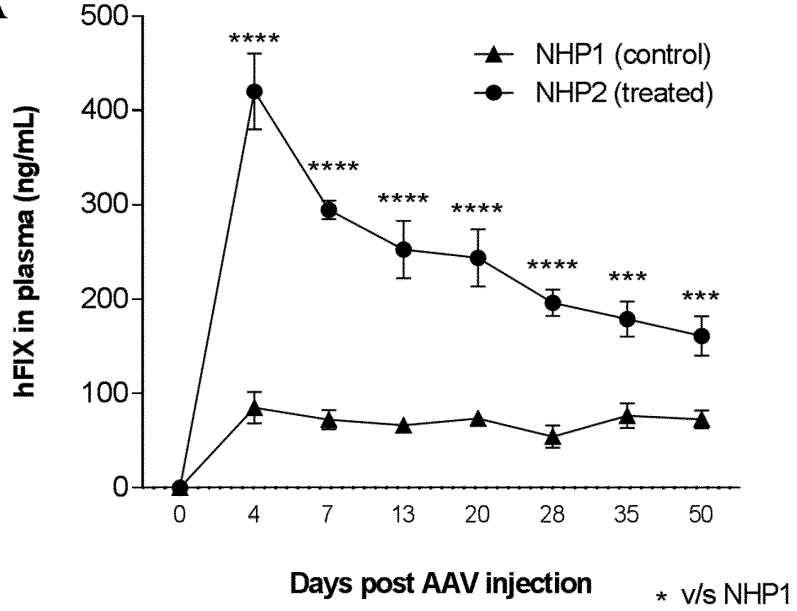


Figure 9A

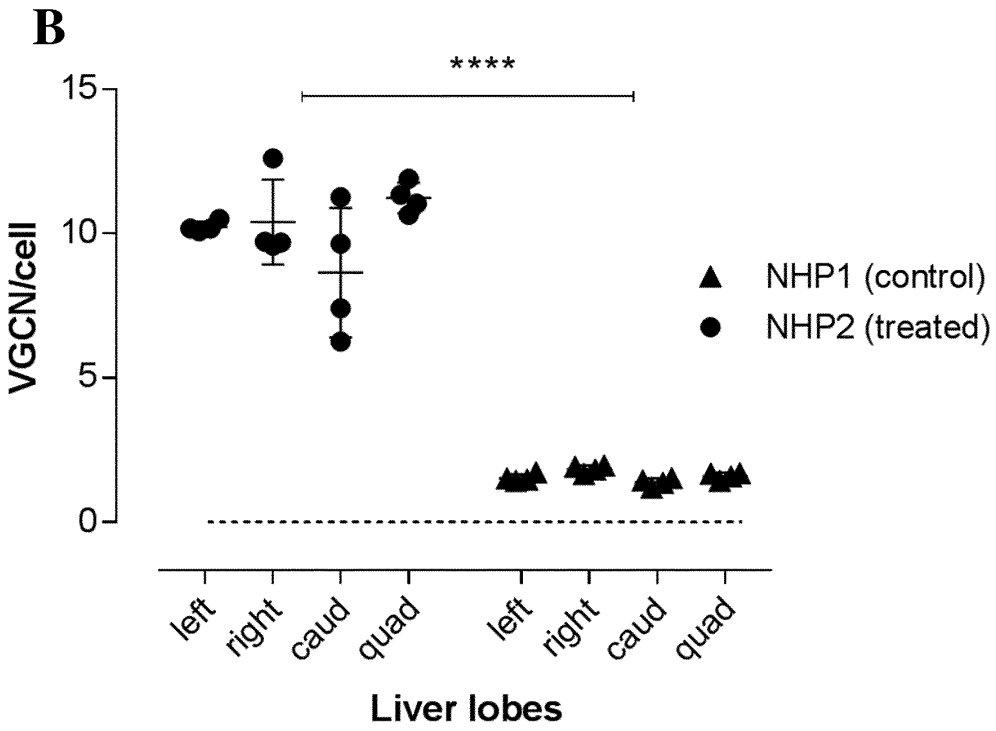


Figure 9 B

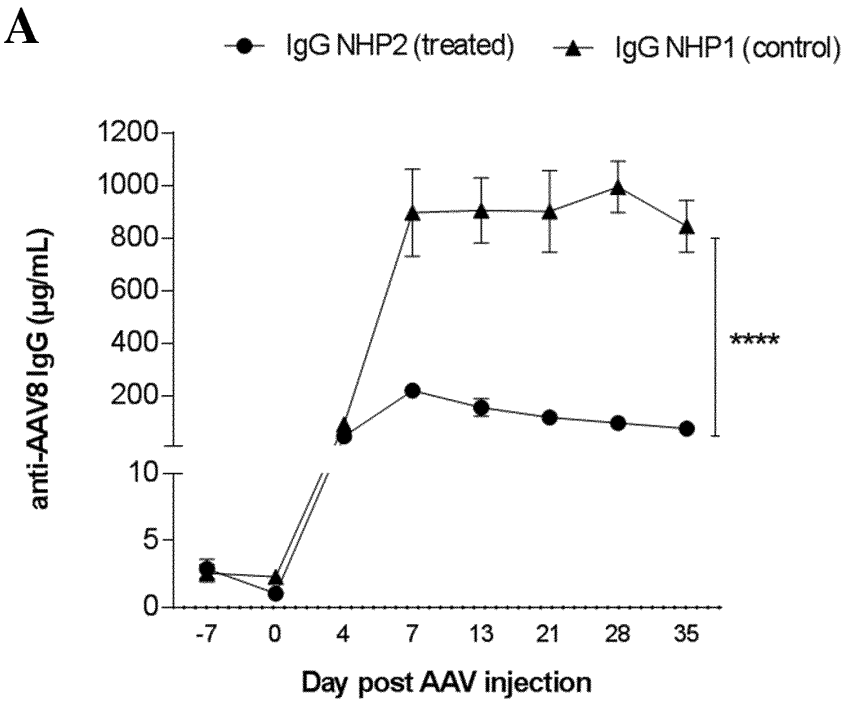


Figure 10 A

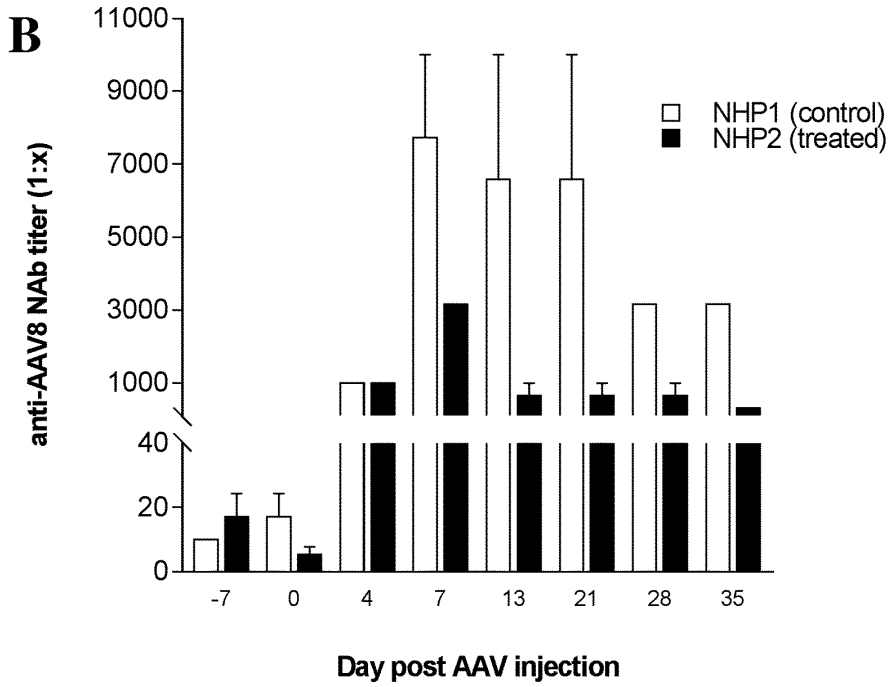

B
11000
9000
7000
5000
3000
1000
40
20
0
anti-AAV8 NAb titer (1:x)
NHP1 (control)
NHP2 (treated)
-7
0
4
7
13
21
28
35
Day post AAV injection

Figure 10 B

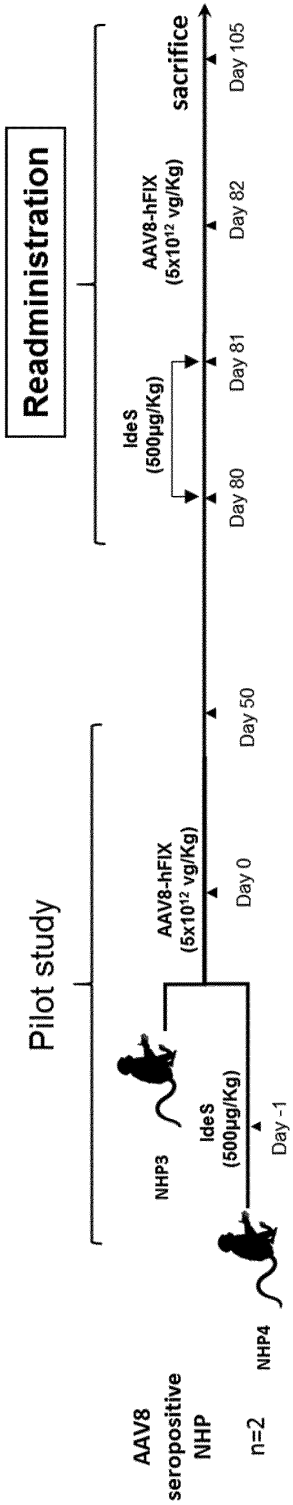
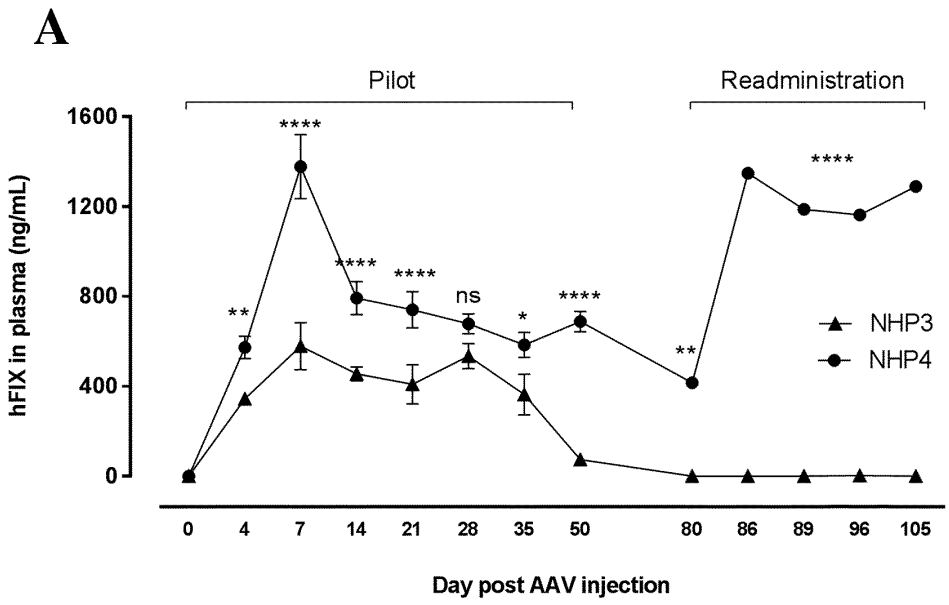

Readministration
Pilot study
AAV8 seropositive NHP
n=2
NHP4
NHP3
Day -1
IdeS (500µg/Kg)
Day 0
AAV8-hFIX (5x10¹² vg/Kg)
Day 50
Day 80
IdeS (500µg/Kg)
Day 81
AAV8-hFIX (5x10¹² vg/Kg)
Day 82
sacrifice
Day 105

Figure 11



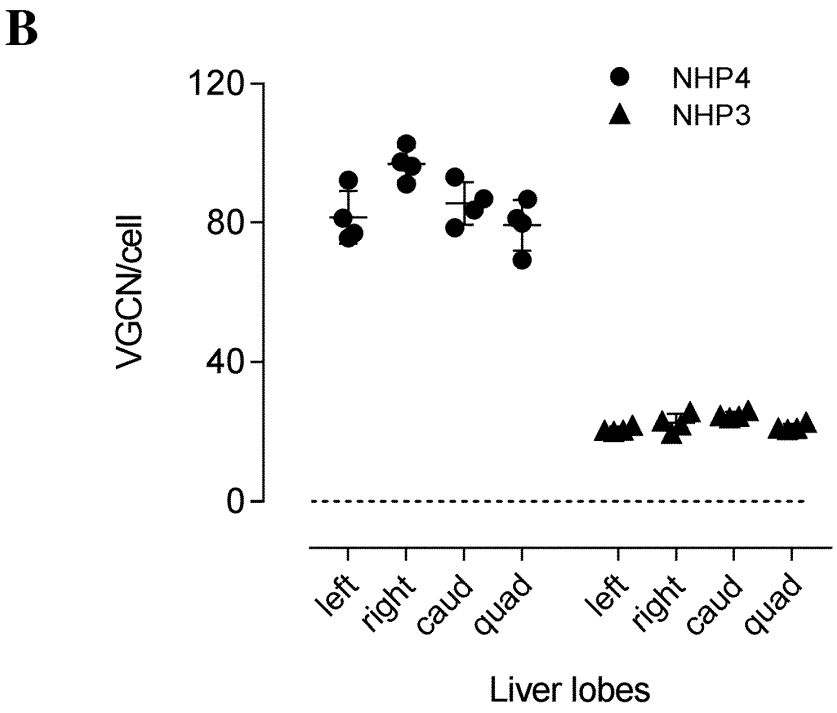


Figure 12 A and B

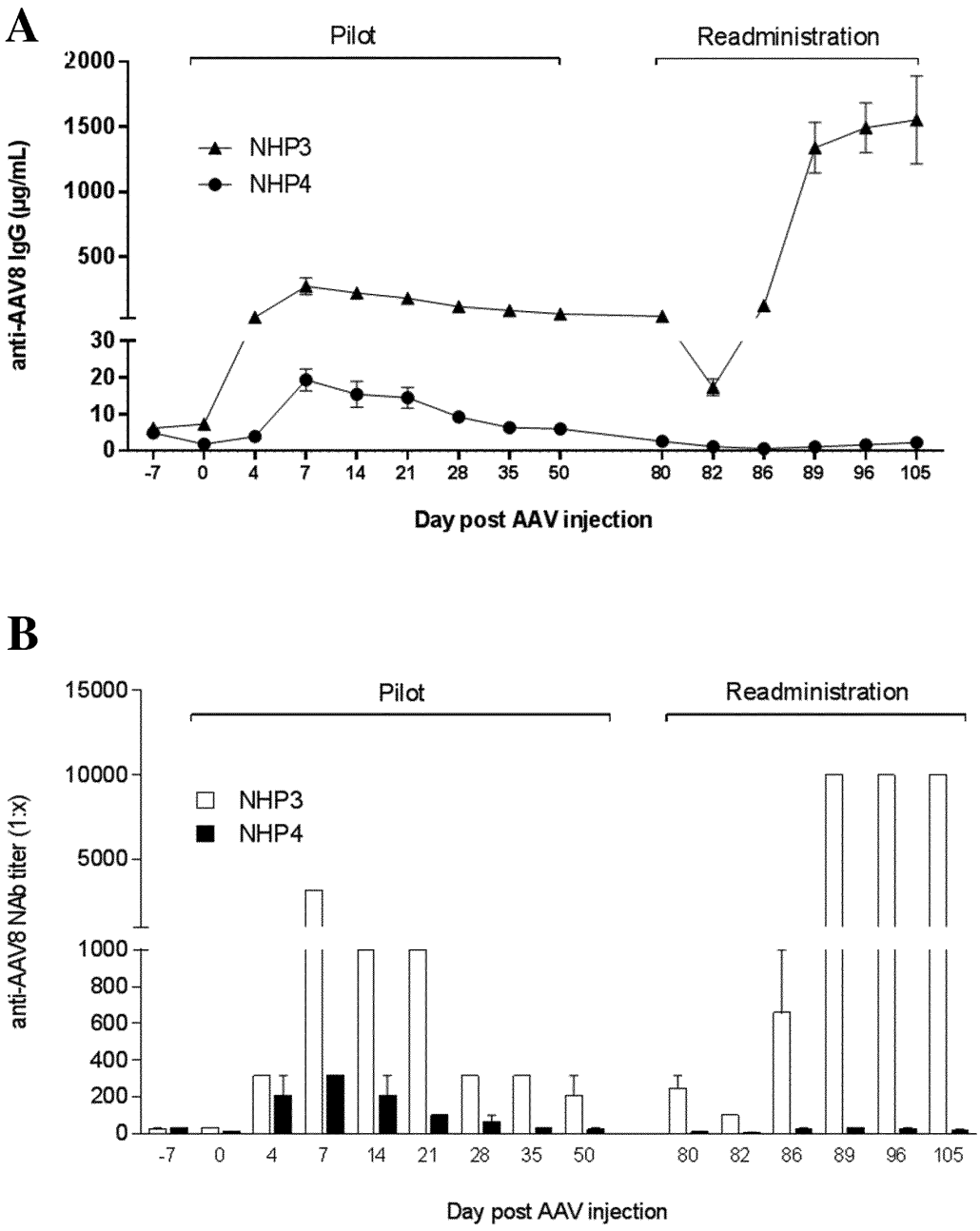


Figure 13 A and B

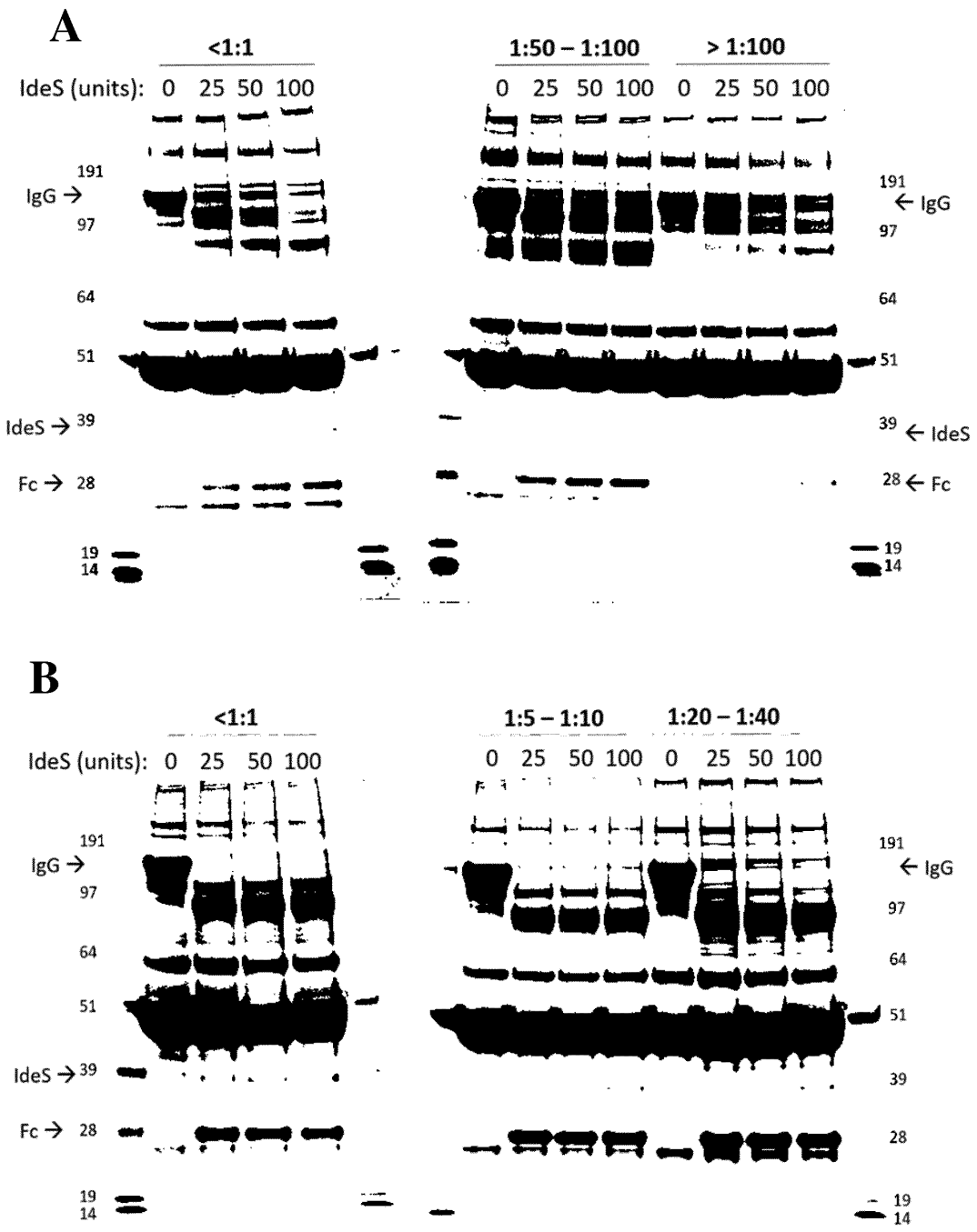


Figure 14 A and B

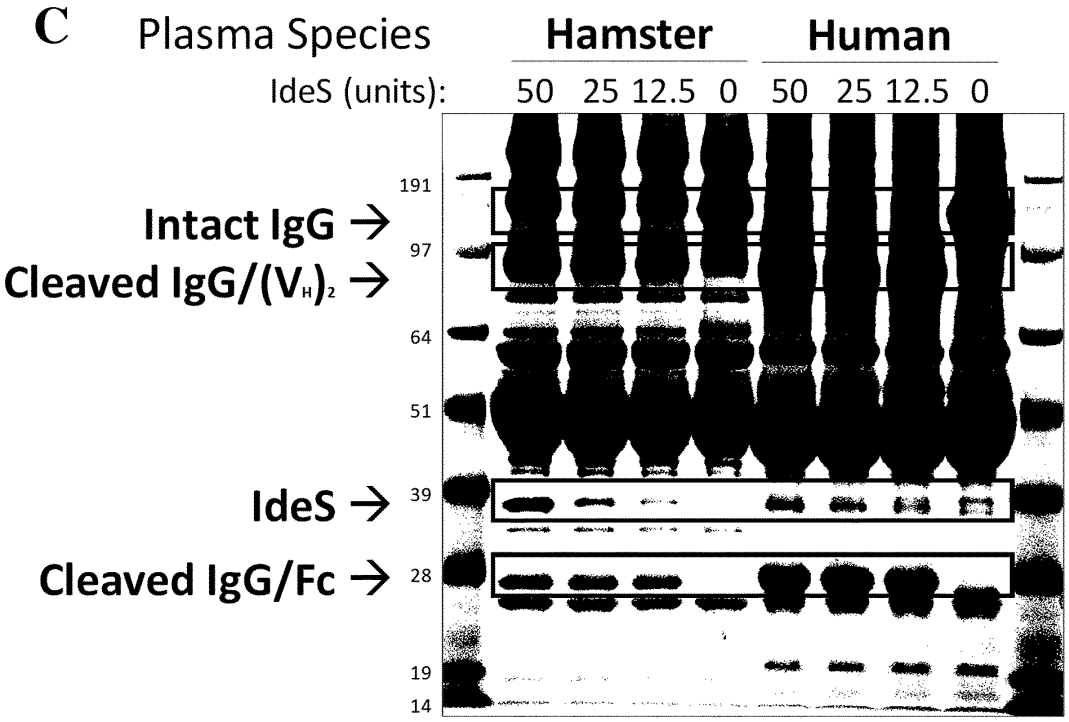


Figure 14 C

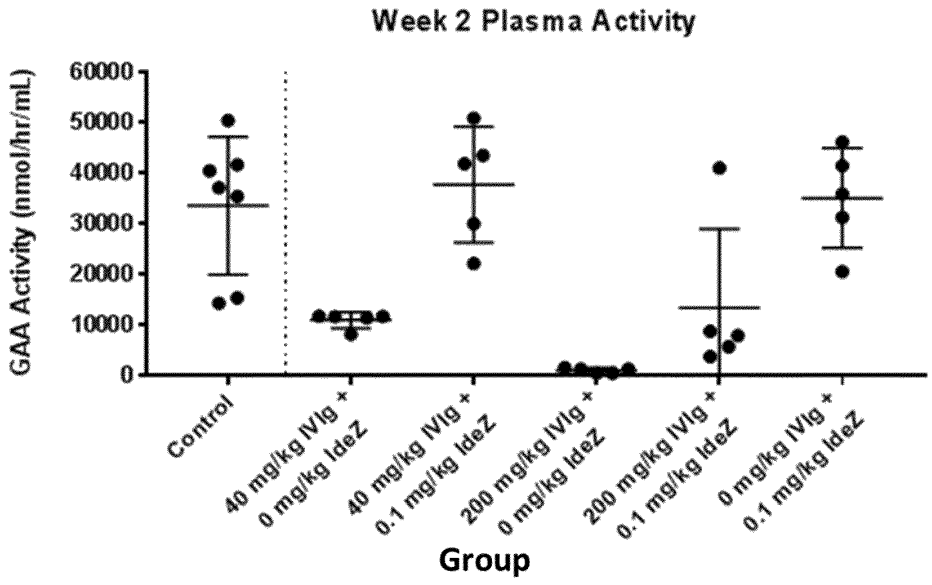


Figure 15

	Pre-IdeS	Post-IdeS
1- Neg Control 0 mg/kg IVIg + 0 mg/kg IdeS	**<1:1**	**<1:1**
	<1:1	**<1:1**
	<1:1	Animal died
	<1:1	**<1:1**
	<1:1	**<1:1**
2- No IdeS 300 mg/kg IVIg + 0 mg/kg IdeS	*1:10-1:20*	*1:20-1:40*
	1:2.5-1:5	*1:5-1:10*
	1:10-1:20	*1:20-1:40*
	1:20-1:40	*1:10-1:20*
	1:20-1:40	*1:10-1:20*
3- IdeS Low 300 mg/kg IVIg + 0.4 mg/kg IdeS	*1:10-1:20*	***1:2.5-1:5***
	1:10-1:20	***1:1-1:2.5***
	1:10-1:20	***1:2.5-1:5***
	1:20-1:40	***1:2.5-1:5***
	1:10-1:20	**1:1-1:2.5**
4- Ides High 300 mg/kg IVIg + 4 mg/kg IdeS	*1:20-1:40*	**<1:1**
	1:20-1:40	**<1:1**
	1:40	**<1:1**
	1:20-1:40	**1:1-1:2.5**
	1:40	**<1:1**

Figure 16

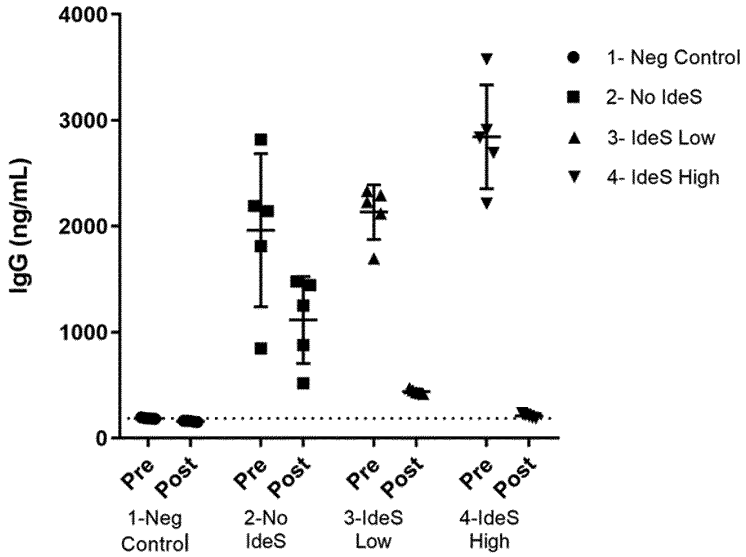


Figure 17

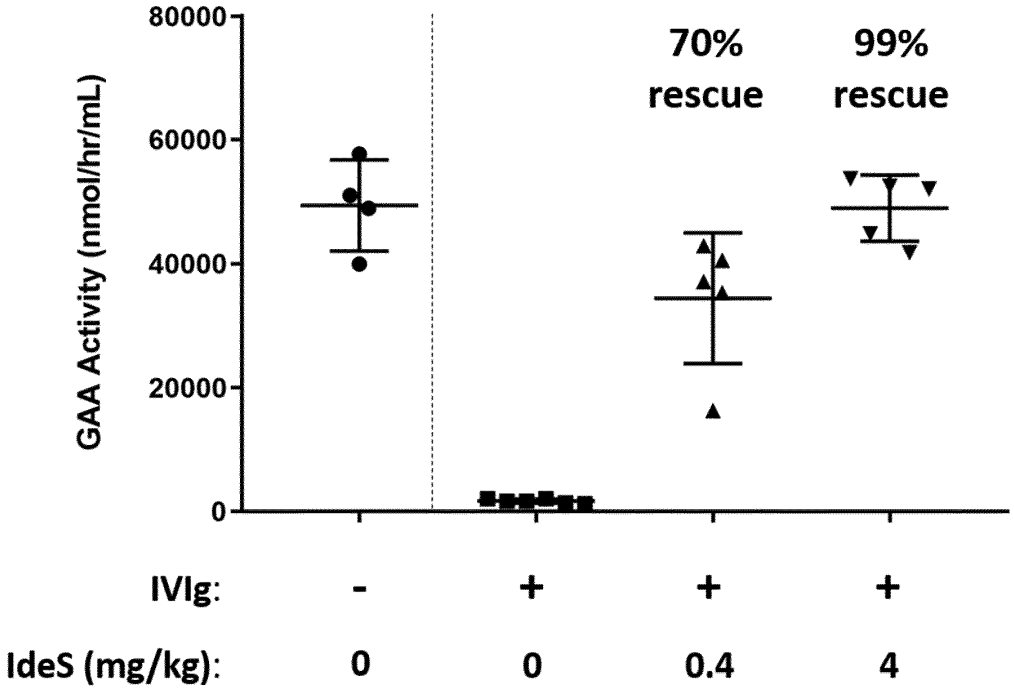
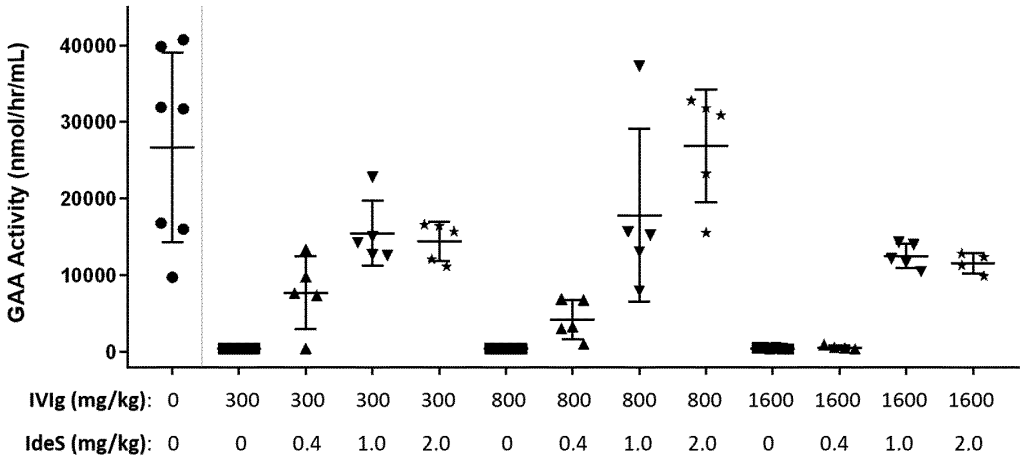


Figure 18



All animals received $2x10^{12}$ vg/kg AAV-Spark100-GAA.

Figure 19

	Pre-IdeS	Post-IdeS
Neg Control 0 mg/kg IVIg + 0 mg/kg IdeS	< 1:2.5	< 1:2.5
	< 1:1	< 1:1
	< 1:1	< 1:1
	< 1:1	< 1:1
	< 1:1	< 1:1
No IdeS 300 mg/kg IVIg + 0 mg/kg IdeS	1:40-1:80	1:20-1:40
	1:40-1:80	1:20-1:40
	1:20-1:40	1:20-1:40
	1:20-1:40	1:20-1:40
	1:40-1:80	1:40-1:80
IdeS (Lot #1) 300mg/kg IVIg + 1 mg/kg IdeS	1:80-1:160	1:1-1:2.5
	1:40-1:80	< 1:1
	1:80-1:160	< 1:1
	1:80-1:160	n.d.
	1:80-1:160	< 1:2.5
IdeS (Lot #2) 300mg/kg IVIg + 1 mg/kg IdeS	1:40-1:80	1:1-1:2.5
	1:20-1:40	< 1:1
	> 1:160	< 1:1
	1:40-1:80	1:20-1:40
	1:40-1:80	1:1-1:2.5

n.d. - no data

Figure 20

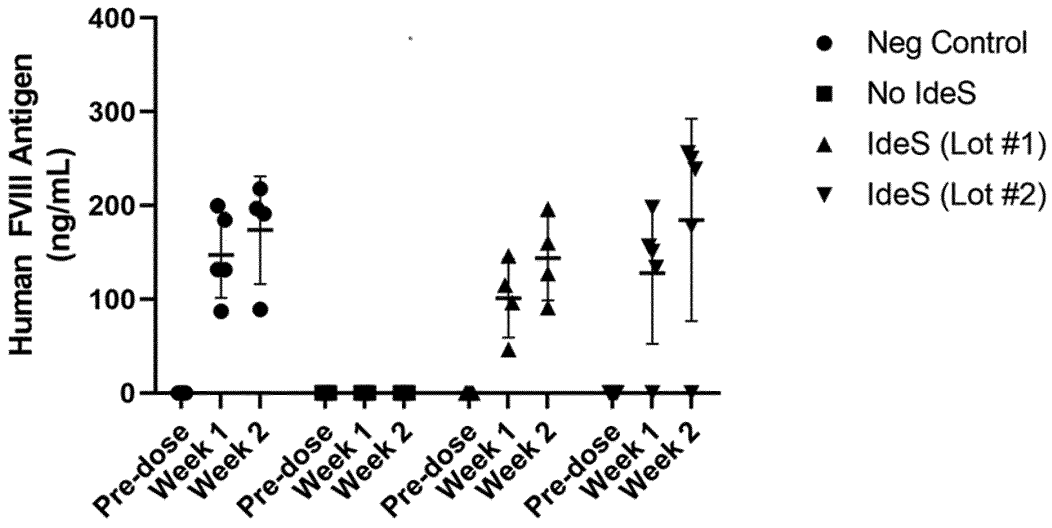


Figure 21

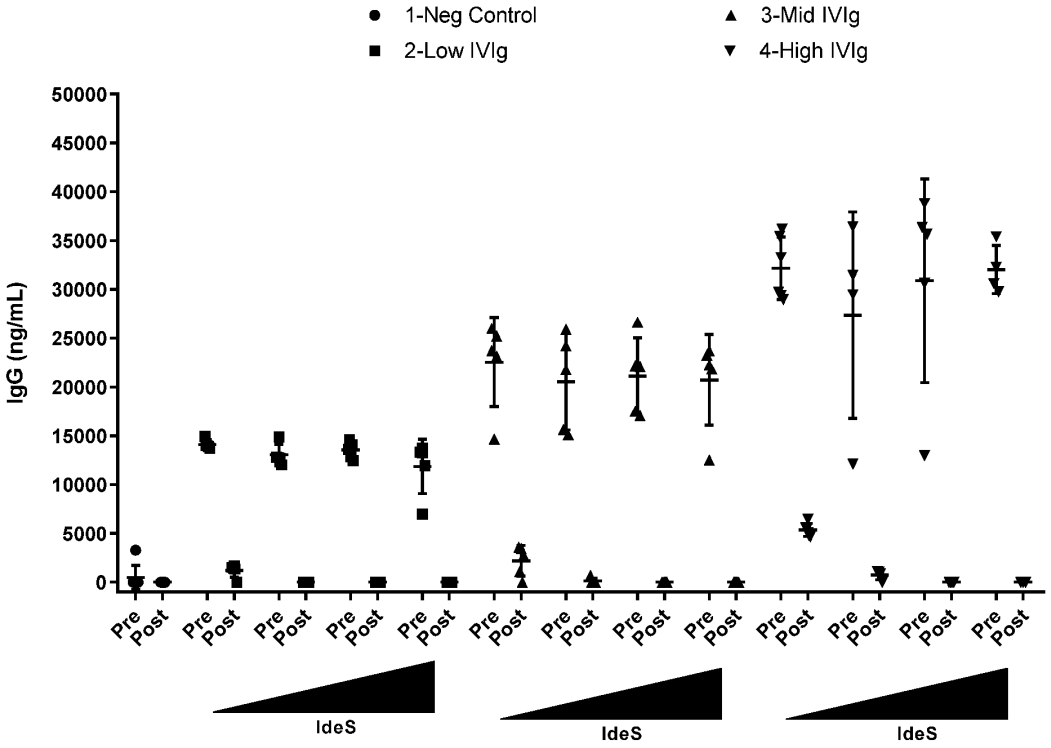

1-Neg Control
2-Low IVIg
3-Mid IVIg
4-High IVIg
IgG (ng/mL)
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
Pre
Post
IdeS
IdeS
IdeS

Figure 22