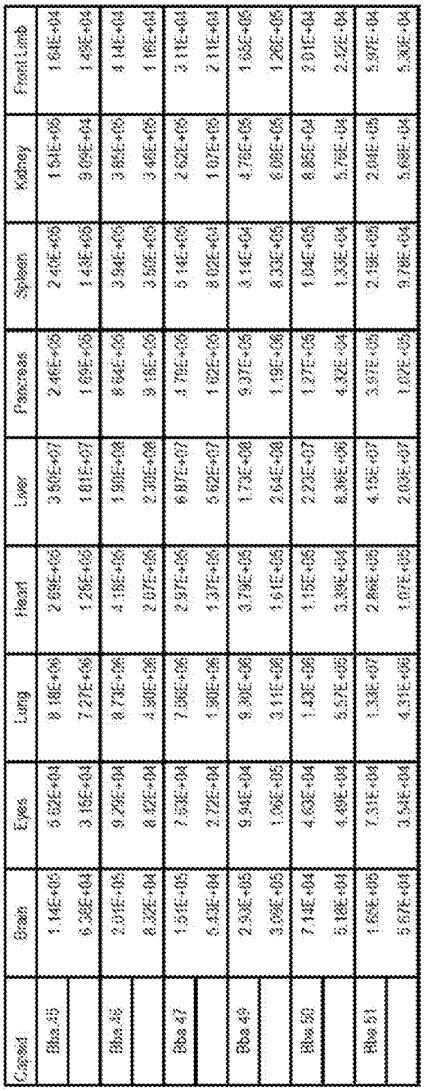
Figure 1



Caprod	Brain	Eyes	Lung	Heart	Liver	Pancreas	Spleen	Kidney	Front Limb
Bba.45	1.14E+05	5.52E+04	9.18E+04	2.69E+05	3.68E+07	2.46E+05	2.40E+05	1.54E+05	1.64E+04
	6.36E+04	3.18E+04	7.27E+04	1.28E+05	1.01E+07	1.69E+05	1.43E+05	9.09E+04	1.49E+04
Bba.46	2.01E+05	9.20E+04	8.73E+04	4.18E+05	1.90E+08	8.64E+05	3.94E+05	3.85E+05	4.14E+04
	8.32E+04	8.42E+04	4.90E+04	2.07E+05	2.30E+08	9.19E+05	3.68E+05	3.46E+05	1.16E+04
Bba.47	1.54E+05	7.35E+04	7.36E+04	2.92E+05	6.87E+07	4.79E+05	5.14E+05	2.62E+05	3.11E+04
	5.43E+04	2.72E+04	1.90E+04	1.31E+05	5.62E+07	1.92E+05	8.02E+04	1.07E+05	2.11E+04
Bba.48	2.93E+05	9.94E+04	9.30E+04	3.79E+05	1.73E+08	9.37E+05	3.14E+05	4.76E+05	1.65E+05
	3.09E+05	1.06E+05	3.11E+04	1.61E+05	2.64E+08	1.19E+06	8.33E+05	6.08E+05	1.28E+05
Bba.50	7.14E+04	4.60E+04	1.43E+05	1.15E+05	2.23E+07	1.27E+05	1.04E+05	8.85E+04	2.01E+04
	5.16E+04	4.49E+04	9.57E+04	3.39E+04	8.39E+06	4.32E+04	1.33E+04	5.79E+04	2.42E+04
Bba.51	1.65E+05	7.31E+04	1.33E+05	2.86E+05	4.16E+07	3.97E+05	2.19E+05	2.04E+05	5.97E+04
	5.67E+04	3.54E+04	4.31E+04	1.07E+05	2.03E+07	1.02E+05	9.78E+04	5.68E+04	5.30E+04

Caprod	Duodenum	Gastrocnemius	Uterus Adenocar	Diaphragm	Tongue	Skin	Mammary MS	Lymph Nodes	Soleus
Bba.45	8.99E+04	2.16E+05	5.43E+04	3.02E+05	8.17E+04	5.34E+04	3.73E+04	5.91E+05	1.91E+04
	5.25E+04	1.53E+05	4.61E+04	1.92E+05	5.69E+04	3.72E+04	2.24E+04	3.63E+05	1.12E+04
Bba.46	2.01E+05	2.30E+05	1.08E+05	5.36E+05	7.97E+04	1.30E+05	4.67E+04	4.88E+05	6.68E+04
	1.53E+05	1.49E+05	1.57E+05	3.35E+05	5.13E+04	9.32E+04	1.73E+04	2.49E+05	6.88E+04
Bba.47	1.49E+05	3.41E+05	1.88E+05	6.09E+05	1.49E+05	1.43E+05	5.88E+04	7.64E+05	8.36E+04
	1.52E+05	3.24E+05	1.90E+05	4.00E+05	1.09E+05	1.14E+05	2.69E+04	2.22E+05	8.91E+04
Bba.48	1.13E+07	6.32E+05	8.79E+05	1.36E+06	1.52E+05	2.43E+05	1.28E+05	1.08E+06	1.56E+05
	6.09E+06	2.70E+05	9.40E+05	7.73E+05	8.83E+04	9.40E+04	4.80E+04	6.46E+05	1.42E+05
Bba.50	1.93E+05	2.44E+05	7.54E+04	1.37E+05	1.88E+05	7.42E+04	2.34E+04	1.19E+05	2.42E+04
	3.09E+05	8.57E+05	6.24E+04	4.96E+04	9.97E+04	1.08E+04	1.66E+04	4.27E+04	1.17E+04
Bba.51	2.72E+05	3.16E+05	1.23E+05	3.85E+05	1.30E+05	1.46E+05	7.66E+04	5.13E+05	5.32E+04
	1.67E+05	3.22E+05	7.77E+04	1.40E+05	5.05E+04	1.00E+05	3.79E+04	2.63E+05	3.70E+04

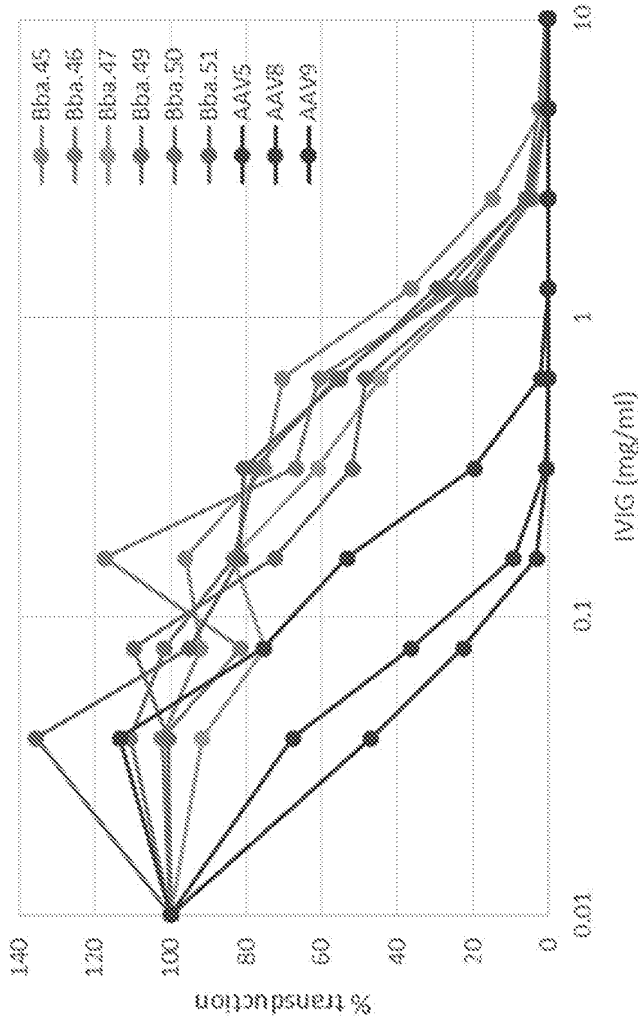

Bba.45
Bba.46
Bba.47
Bba.49
Bba.50
Bba.51
AAV5
AAV8
AAV9
% transduction
140
120
100
80
60
40
20
0
0.01
0.1
1
10
MOI (mg/ml)

Figure 2

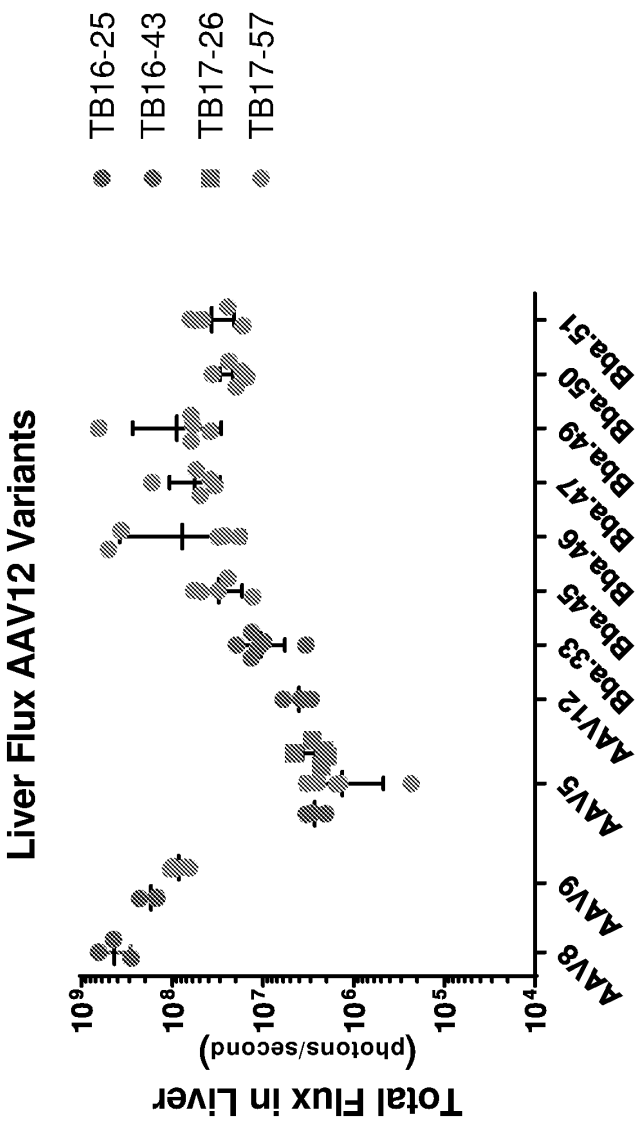
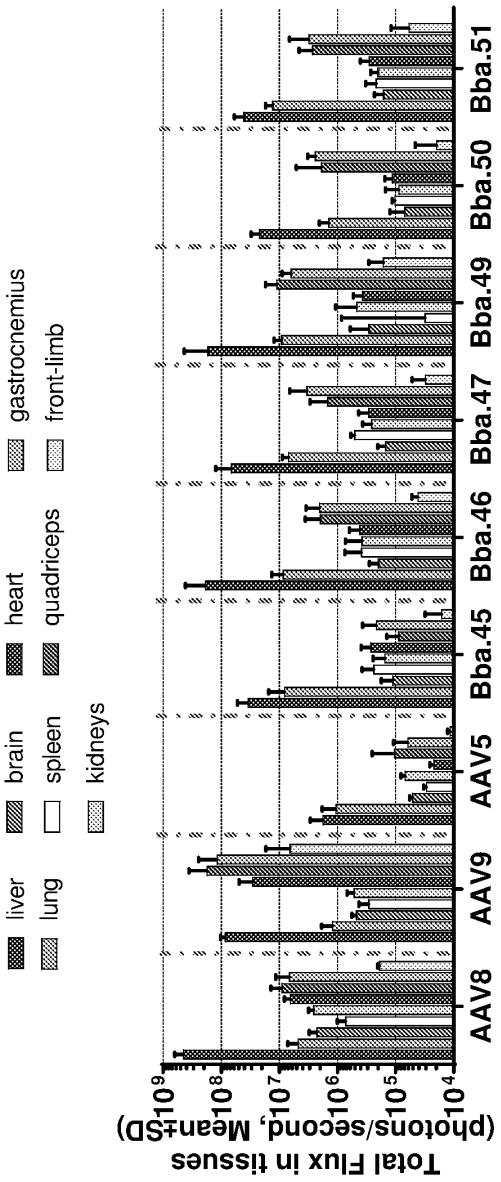

TB16-25
TB16-43
TB17-26
TB17-57
Liver Flux AAV12 Variants
Total Flux in Liver
(photons/second)
10^9
10^8
10^7
10^6
10^5
10^4
AAV8
AAV9
AAV5
AAV12
Bba.33
Bba.45
Bba.46
Bba.47
Bba.49
Bba.50
Bba.51

Figure 3

Figure 4


liver
brain
heart
gastrocnemius
lung
spleen
quadriceps
front-limb
kidneys
Total Flux in tissues
(photons/second, Mean±SD)
10^9
10^8
10^7
10^6
10^5
10^4
AAV8
AAV9
AAV5
Bba.45
Bba.46
Bba.47
Bba.49
Bba.50
Bba.51

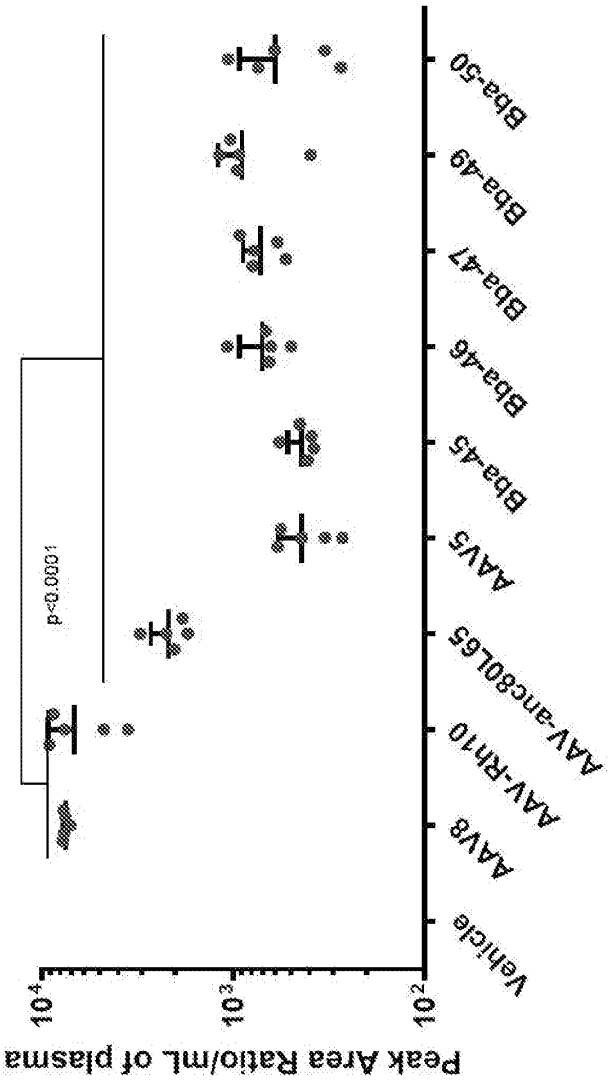

Peak Area Ratio/mL of plasma
10^4
10^3
10^2
p<0.0001
Vehicle
AAV8
AAV-Rh10
AAV-anc80L65
AAV5
Bba-45
Bba-46
Bba-47
Bba-49
Bba-50

Figure 5

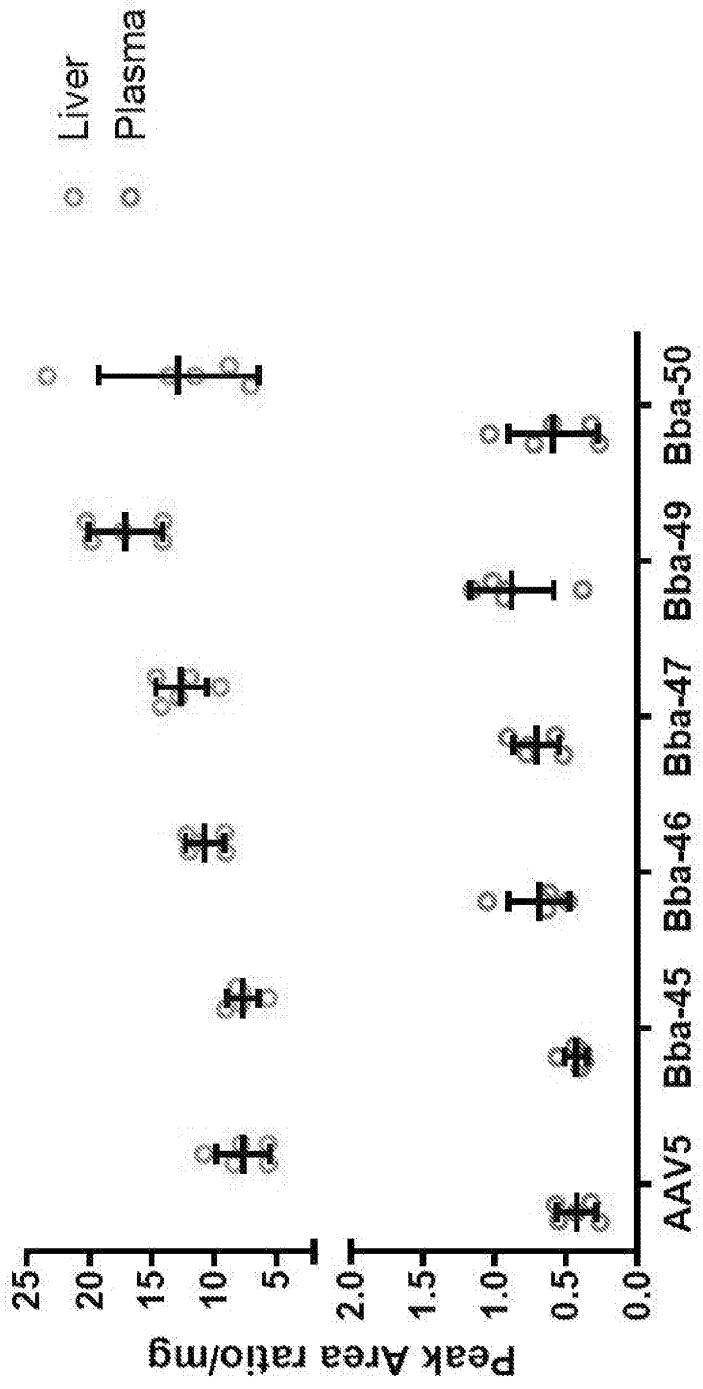

Liver
Plasma
Peak Area ratio/mg
25
20
15
10
5
2.0
1.5
1.0
0.5
0.0
AAV5
Bba-45
Bba-46
Bba-47
Bba-49
Bba-50

Figure 6

Figure 7

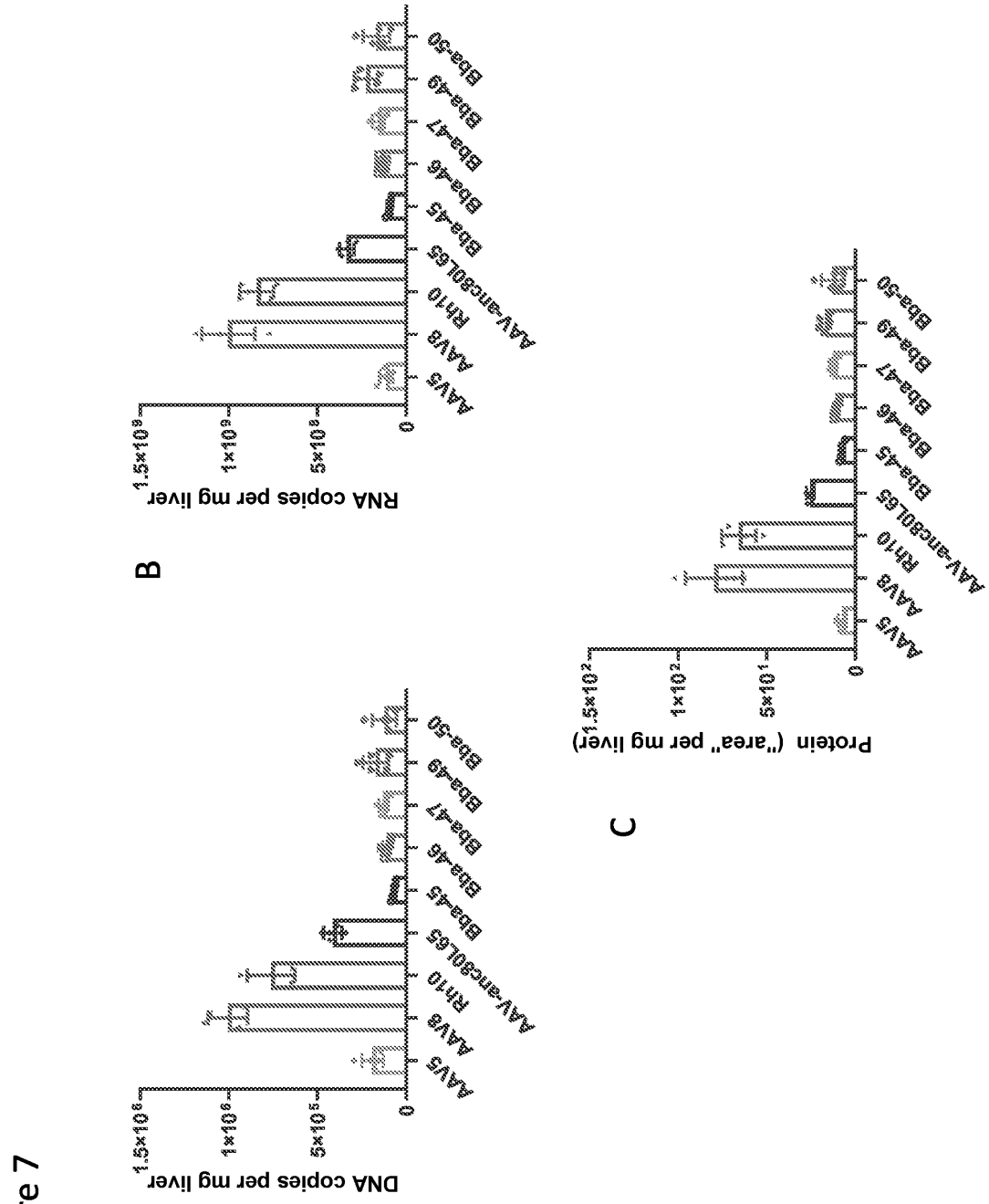
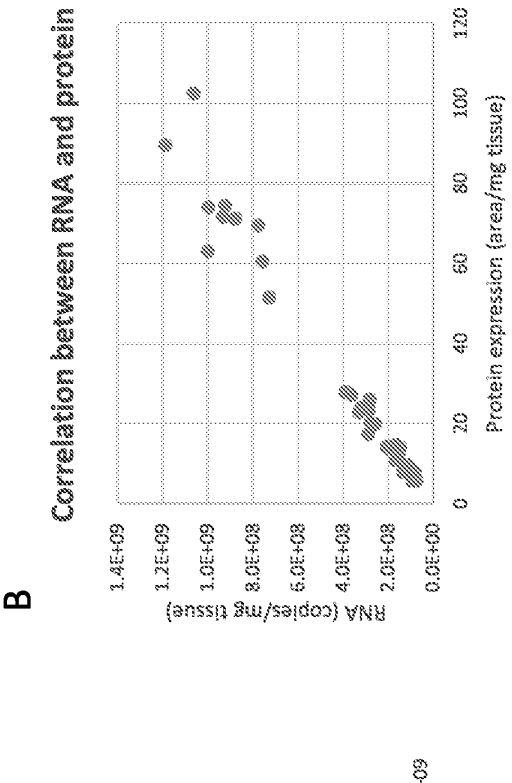

A
DNA copies per mg liver
1.5×10^8
1×10^8
5×10^7
0
AAV5
AAV8
Rh10
AAV-anc80L65
Bba-45
Bba-46
Bba-47
Bba-49
Bba-50
B
RNA copies per mg liver
1.5×10^8
1×10^8
5×10^7
0
AAV5
AAV8
Rh10
AAV-anc80L65
Bba-45
Bba-46
Bba-47
Bba-49
Bba-50
C
Protein ("area" per mg liver)
1.5×10^2
1×10^2
5×10^1
0
AAV5
AAV8
Rh10
AAV-anc80L65
Bba-45
Bba-46
Bba-47
Bba-49
Bba-50

Figure 8


A
Correlation between DNA and RNA
DNA (copies per mg tissue)
1.2E+06
1.0E+06
8.0E+05
6.0E+05
4.0E+05
2.0E+05
0.0E+00
0.0E+00
5.0E+08
1.0E+09
1.5E+09
RNA (copies per mg tissue)
B
Correlation between RNA and protein
RNA (copies/mg tissue)
1.4E+09
1.2E+09
1.0E+09
8.0E+08
6.0E+08
4.0E+08
2.0E+08
0.0E+00
0
20
40
60
80
100
120
Protein expression (area/mg tissue)

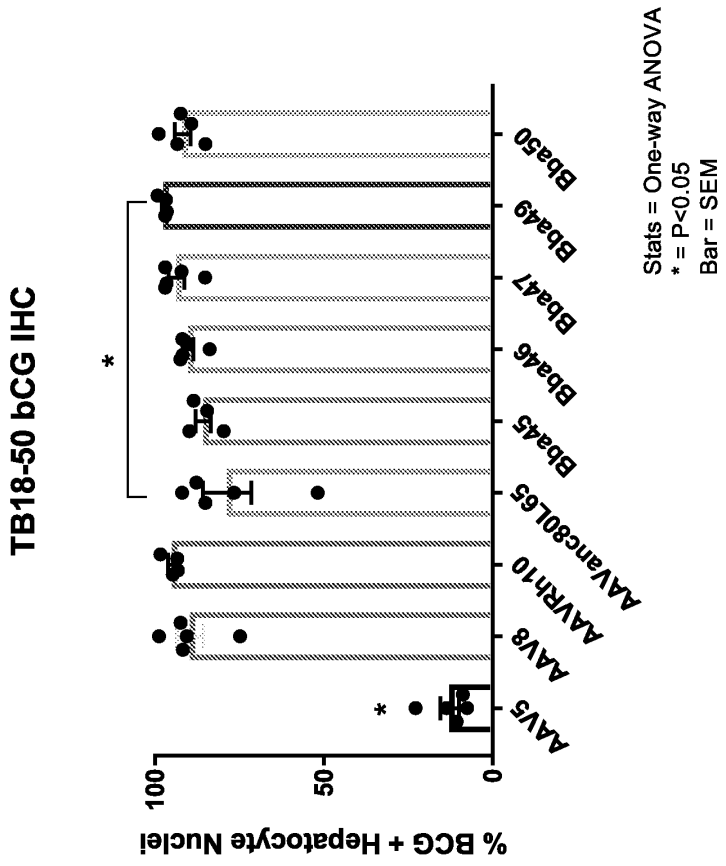

TB18-50 bCG IHC
% BCG + Hepatocyte Nuclei
100
50
0
*
*
AAV5
AAV8
AAVRh10
AAVanc80L65
Bba45
Bba46
Bba47
Bba49
Bba50
Stats = One-way ANOVA
* = P<0.05
Bar = SEM

Figure 9

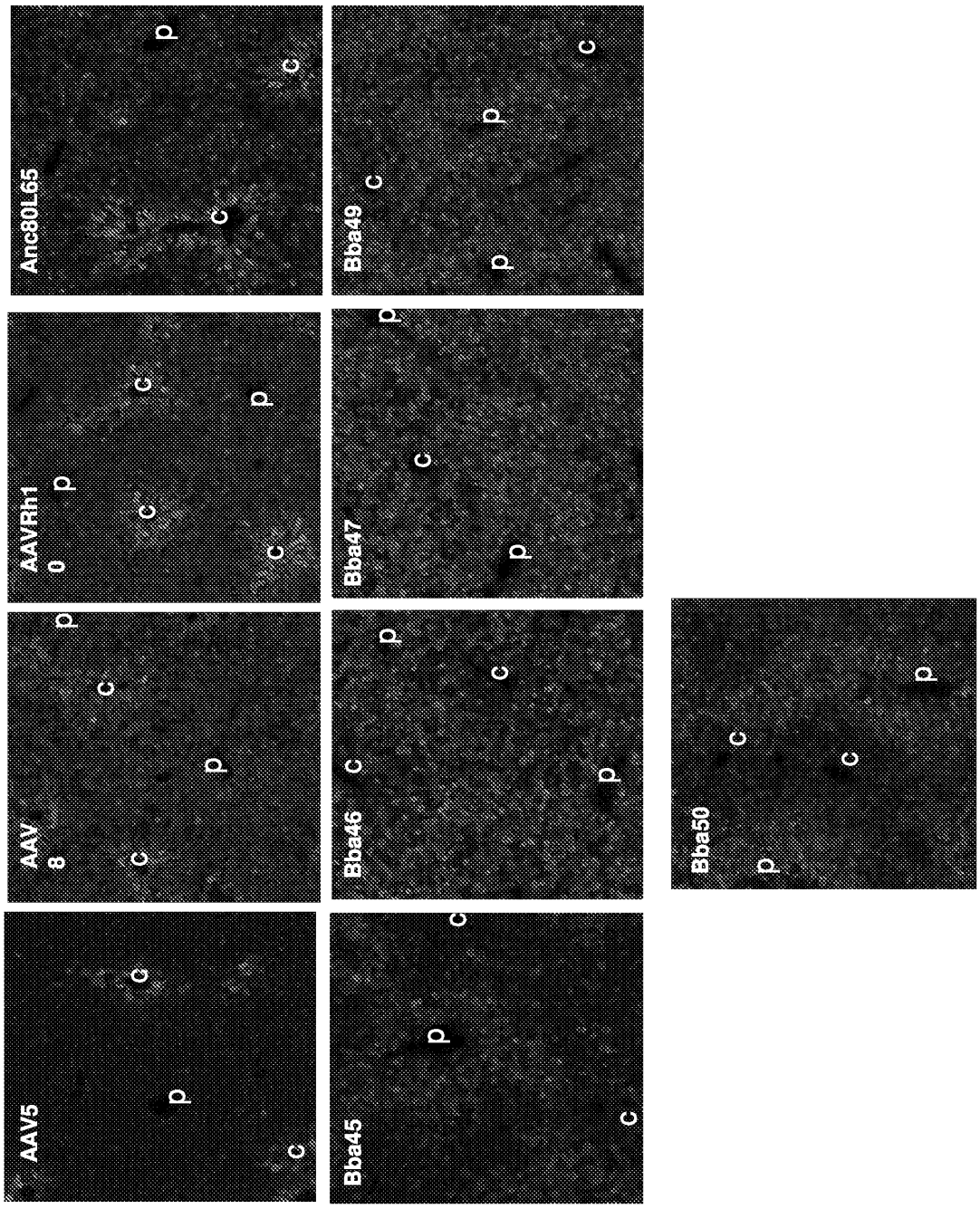
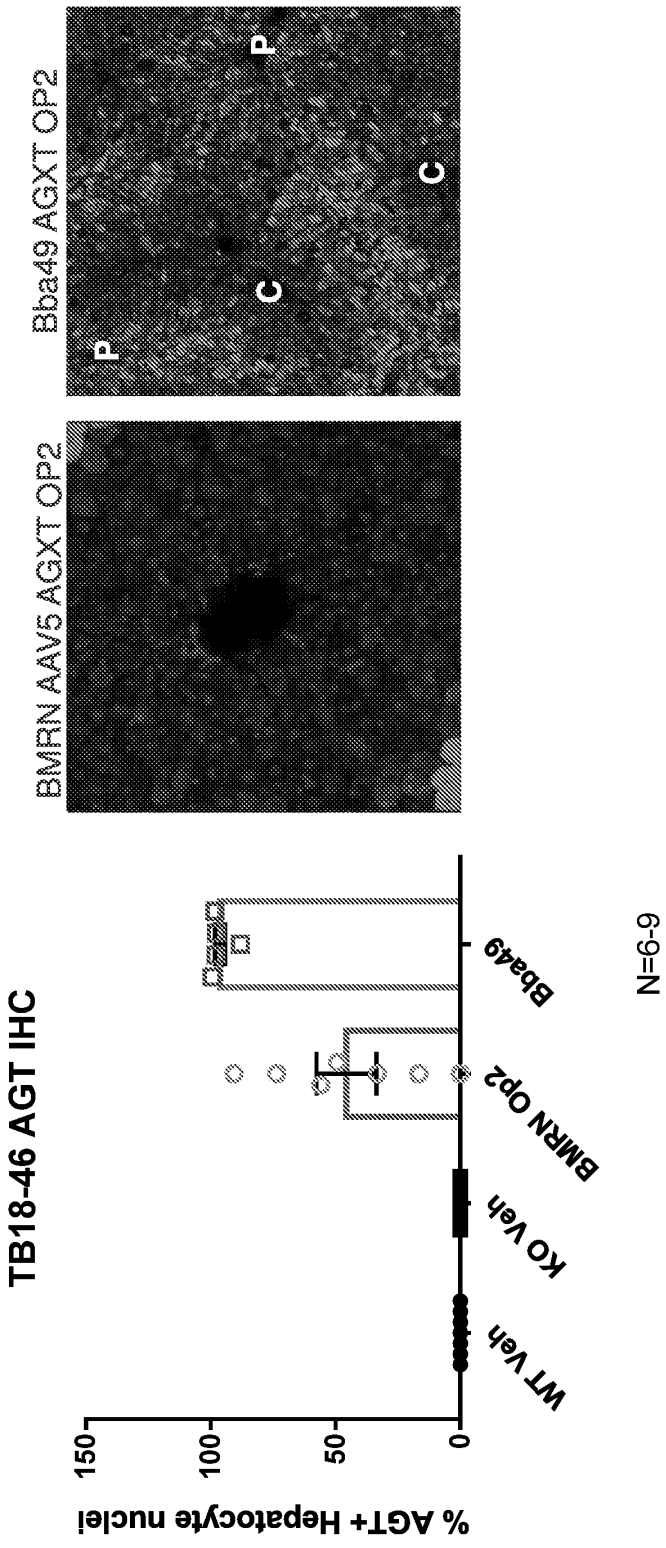


Figure 10

Figure 11


TB18-46 AGT IHC
% AGT+ Hepatocyte nuclei
150
100
50
0
WT Veh
KO Veh
BMRN Op2
Bba49
N=6-9
BMRN AAV5 AGXT OP2
Bba49 AGXT OP2
P
C
P
C