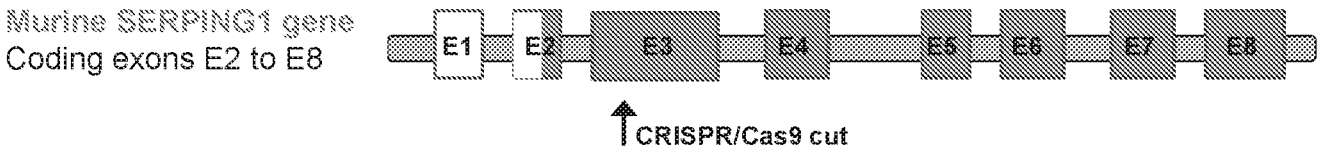
Figure 1



Exon 3 deletion
DNA sequence

Wild-type	AAAAGCAGAGAGAGCTTCCCTGAAAGAGATGACTCCTGGAGTCCCCCAGAGCCTACAGTACT
Mutant S63	AAAAGCAGAGAGAGCTTCCCTGAAAGAGATGACTCCTGGAG----------CCTACAGTACT

Figure 2A

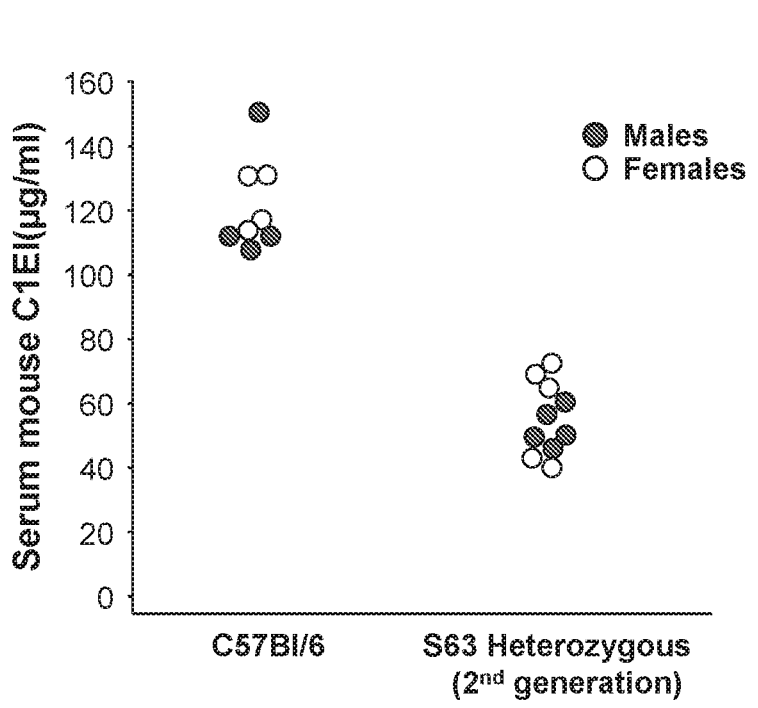

Mouse C1EI (ELISA)
Serum mouse C1EI(µg/ml)
160
140
120
100
80
60
40
20
0
Males
Females
C57Bl/6
S63 Heterozygous
(2nd generation)

Figure 2B

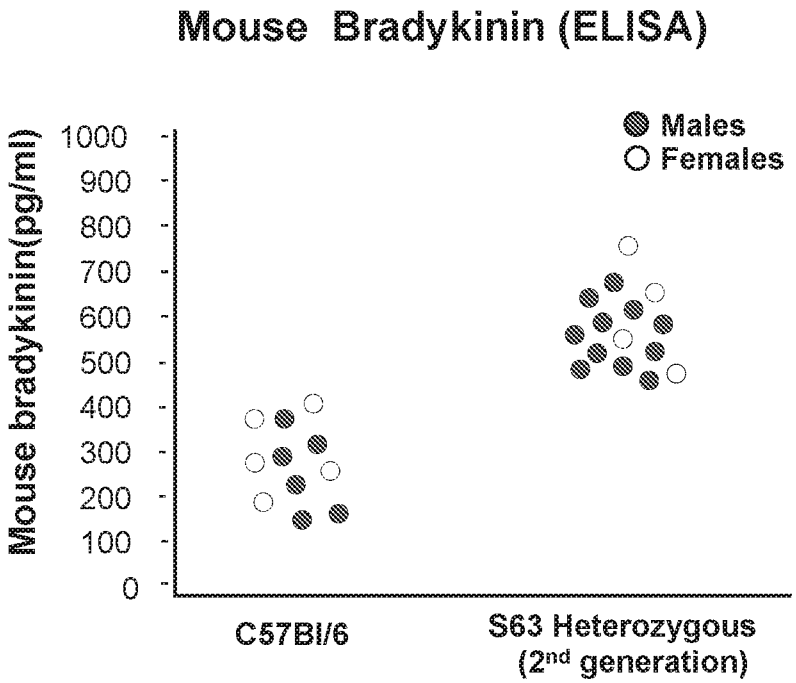

Mouse Bradykinin (ELISA)
Mouse bradykinin(pg/ml)
1000
900
800
700
600
500
400
300
200
100
0
Males
Females
C57Bl/6
S63 Heterozygous
(2nd generation)

Figure 3A

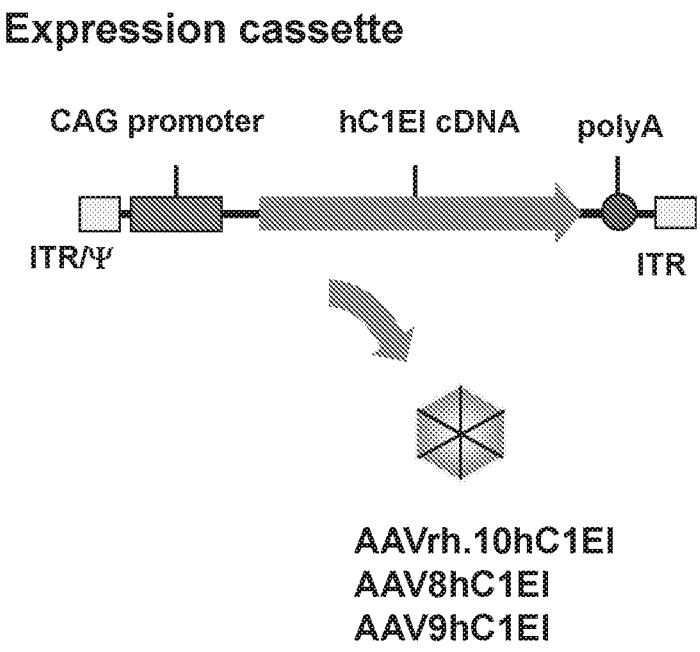


Figure 3B

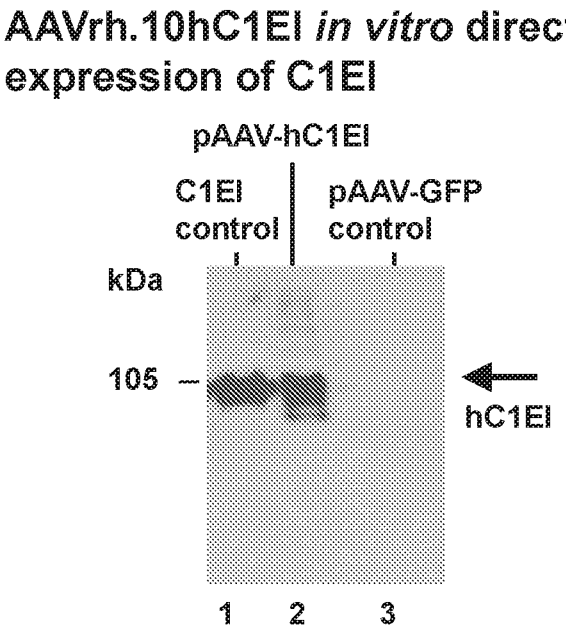


Figure 4A

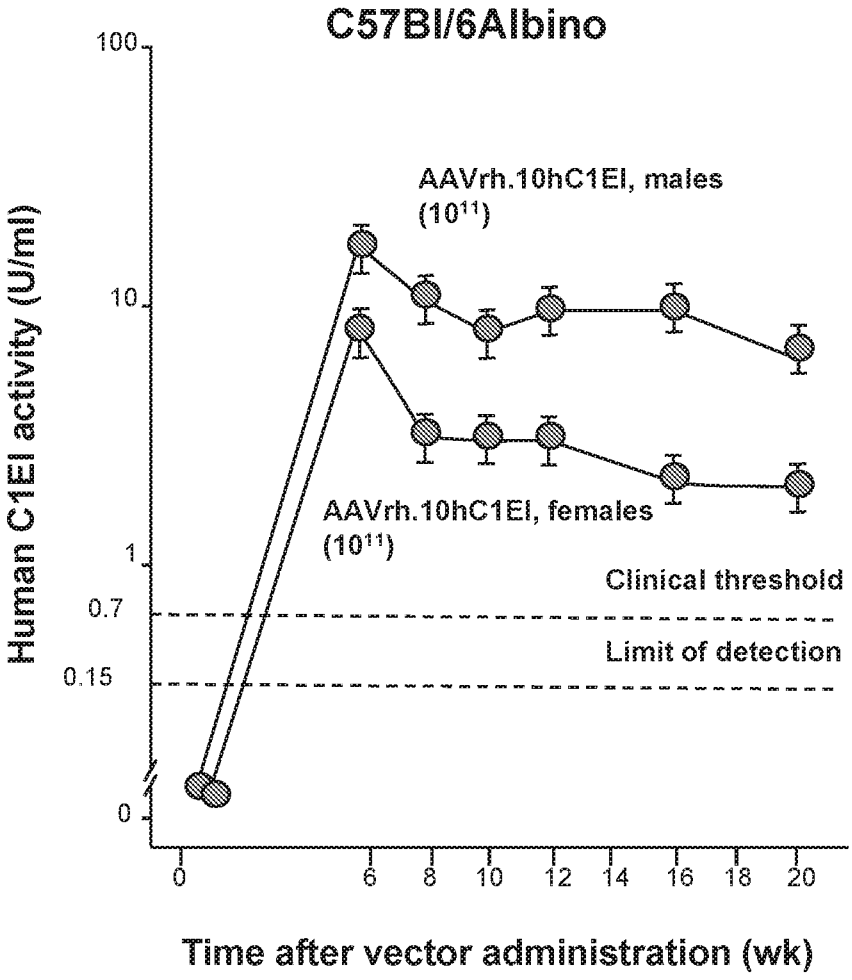

C57Bl/6Albino
100
10
1
0.7
0.15
0
Human C1EI activity (U/ml)
AAVrh.10hC1EI, males
(10^11)
AAVrh.10hC1EI, females
(10^11)
Clinical threshold
Limit of detection
0
6
8
10
12
14
16
18
20
Time after vector administration (wk)

Figure 4B

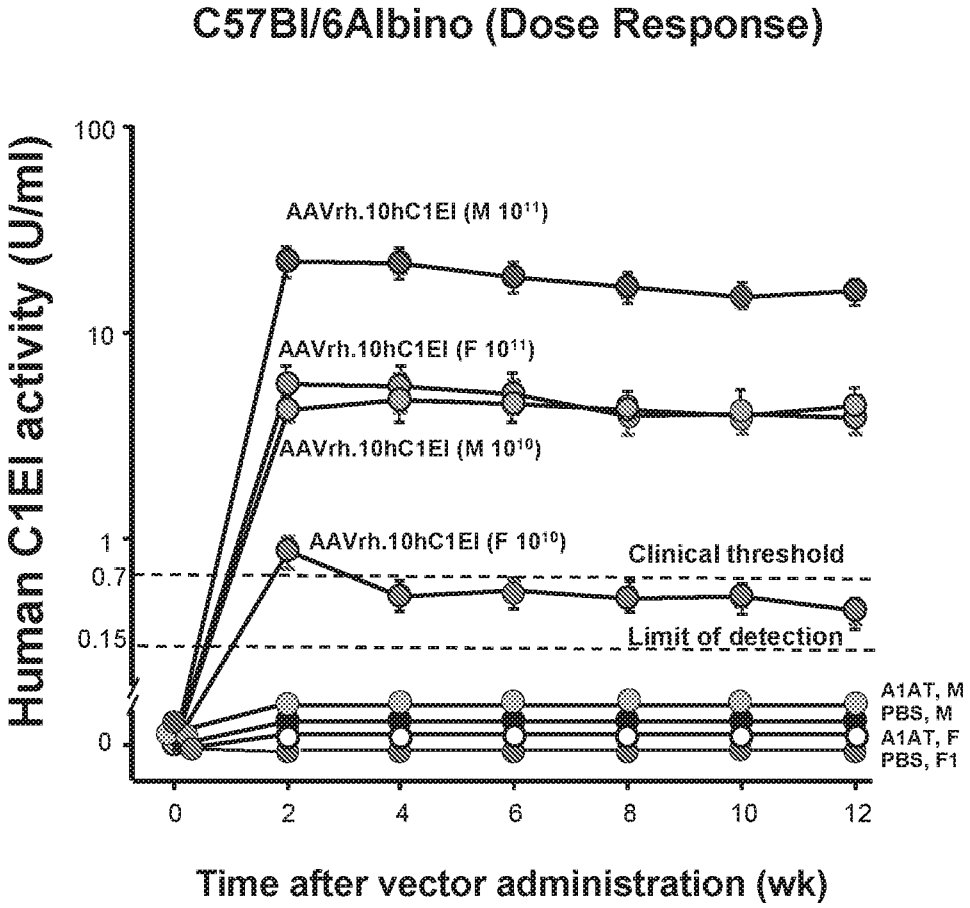

C57Bl/6Albino (Dose Response)
Human C1EI activity (U/ml)
100
10
1
0.7
0.15
0
AAVrh.10hC1EI (M 10^11)
AAVrh.10hC1EI (F 10^11)
AAVrh.10hC1EI (M 10^10)
AAVrh.10hC1EI (F 10^10)
Clinical threshold
Limit of detection
A1AT, M
PBS, M
A1AT, F
PBS, F1
0
2
4
6
8
10
12
Time after vector administration (wk)

Figure 4C

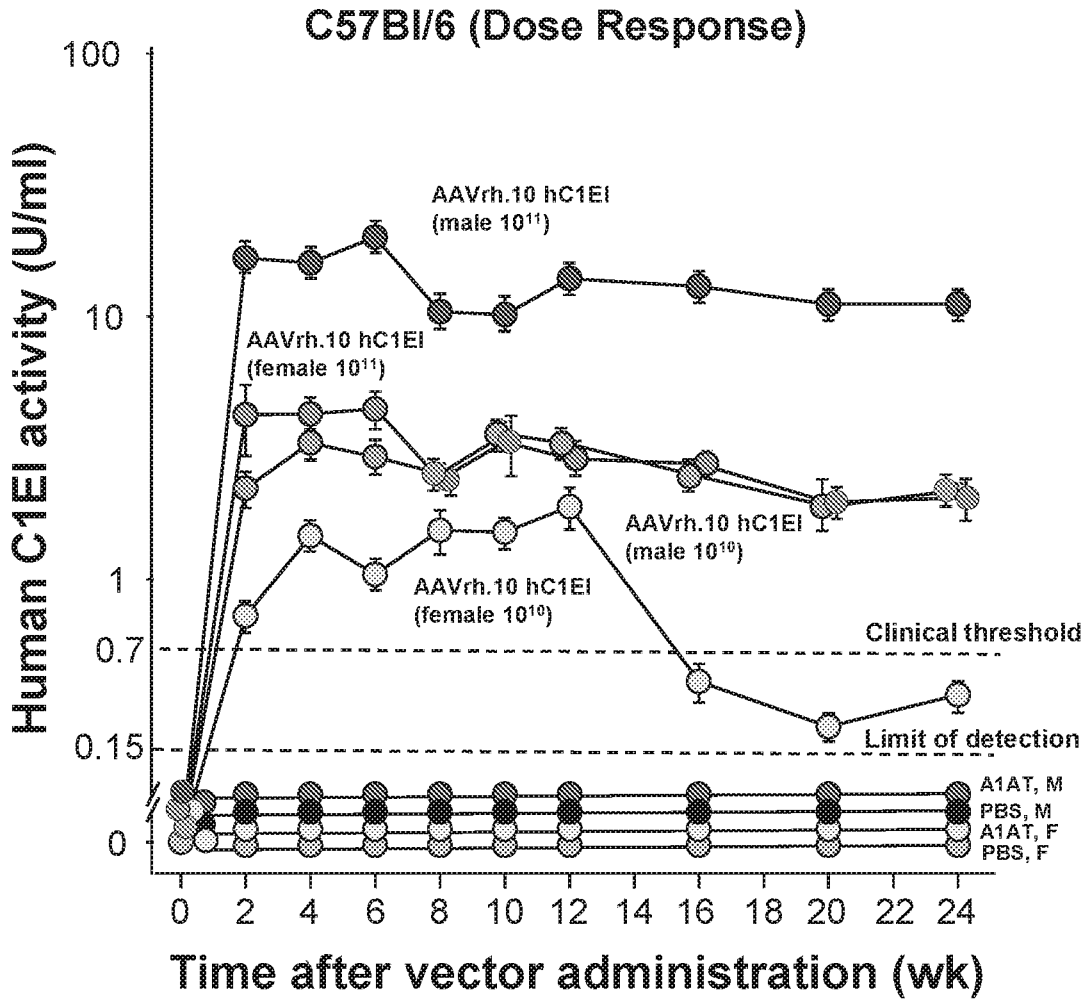
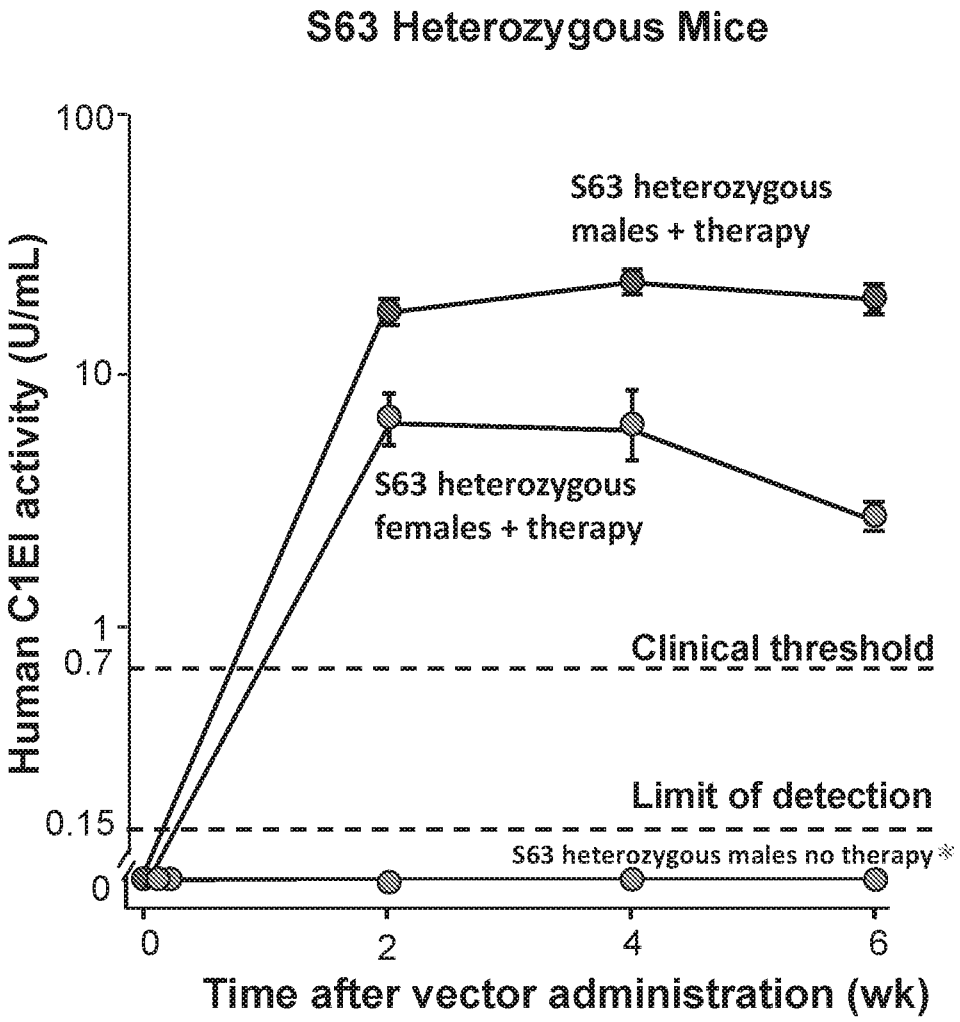

C57Bl/6 (Dose Response)
Human C1EI activity (U/ml)
100
10
1
0.7
0.15
0
AAVrh.10 hC1EI
(male 10^11)
AAVrh.10 hC1EI
(female 10^11)
AAVrh.10 hC1EI
(male 10^10)
AAVrh.10 hC1EI
(female 10^10)
Clinical threshold
Limit of detection
A1AT, M
PBS, M
A1AT, F
PBS, F
0 2 4 6 8 10 12 14 16 18 20 22 24
Time after vector administration (wk)

Figure 4D



※S63 heterozygous females no therapy n=1, no activity

Figure 5A

AAV8hC1EI Vector

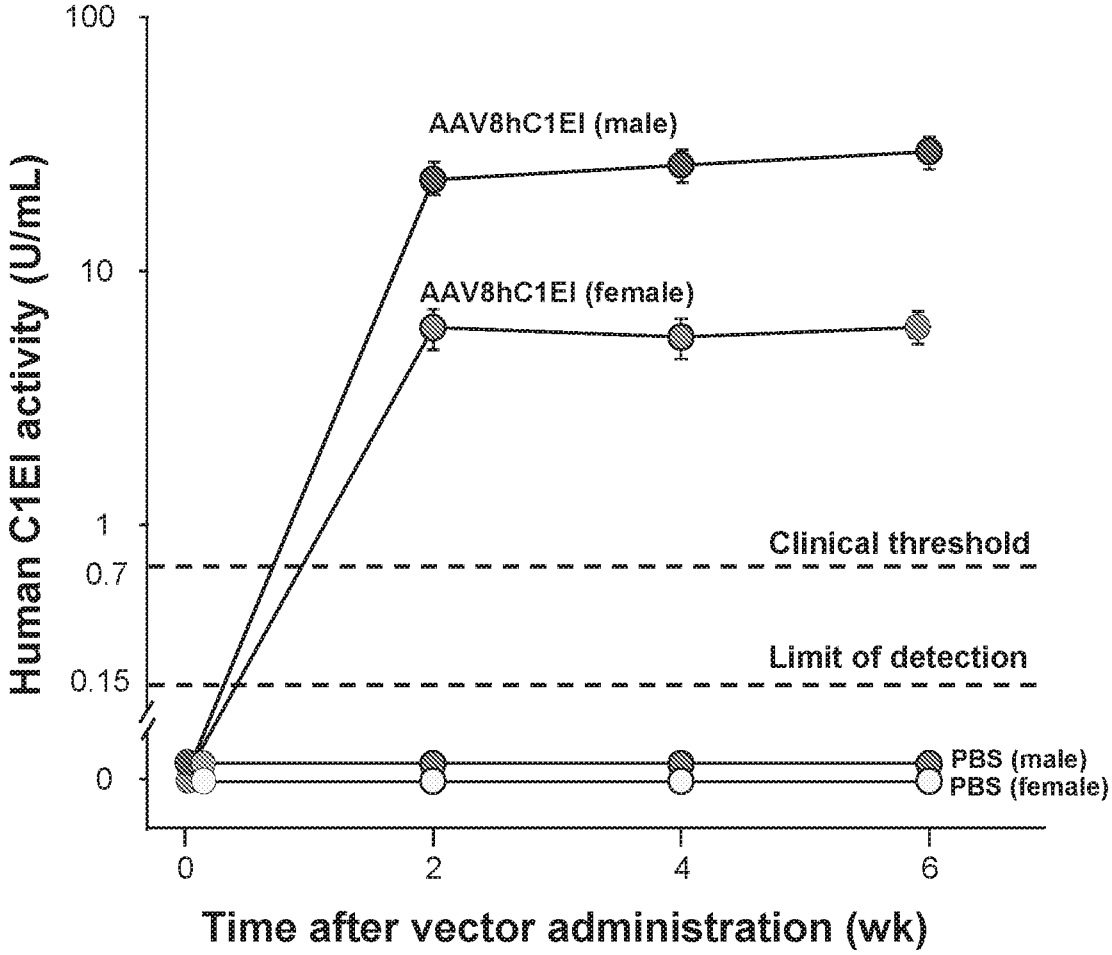


Figure 5B

AAV9hC1EI Vector

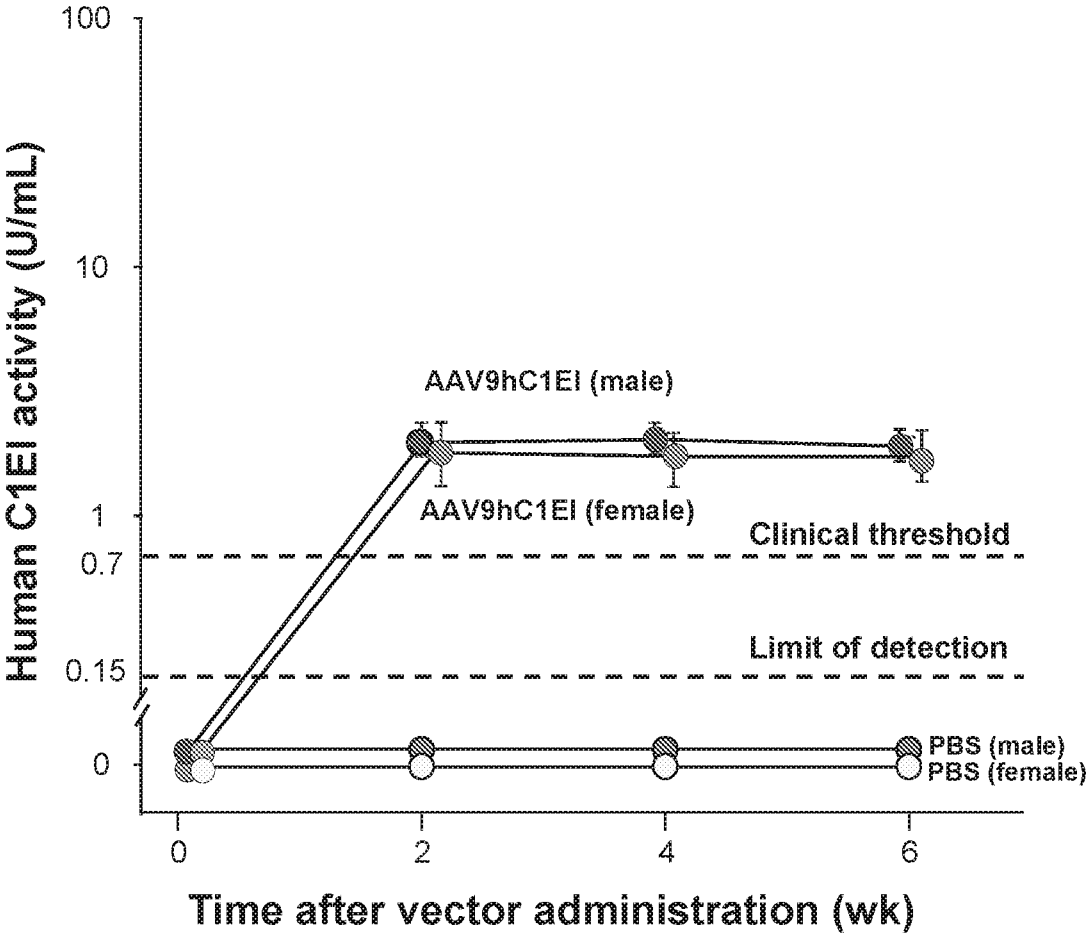


Figure 5C

AAVrh.10hC1EI Vector

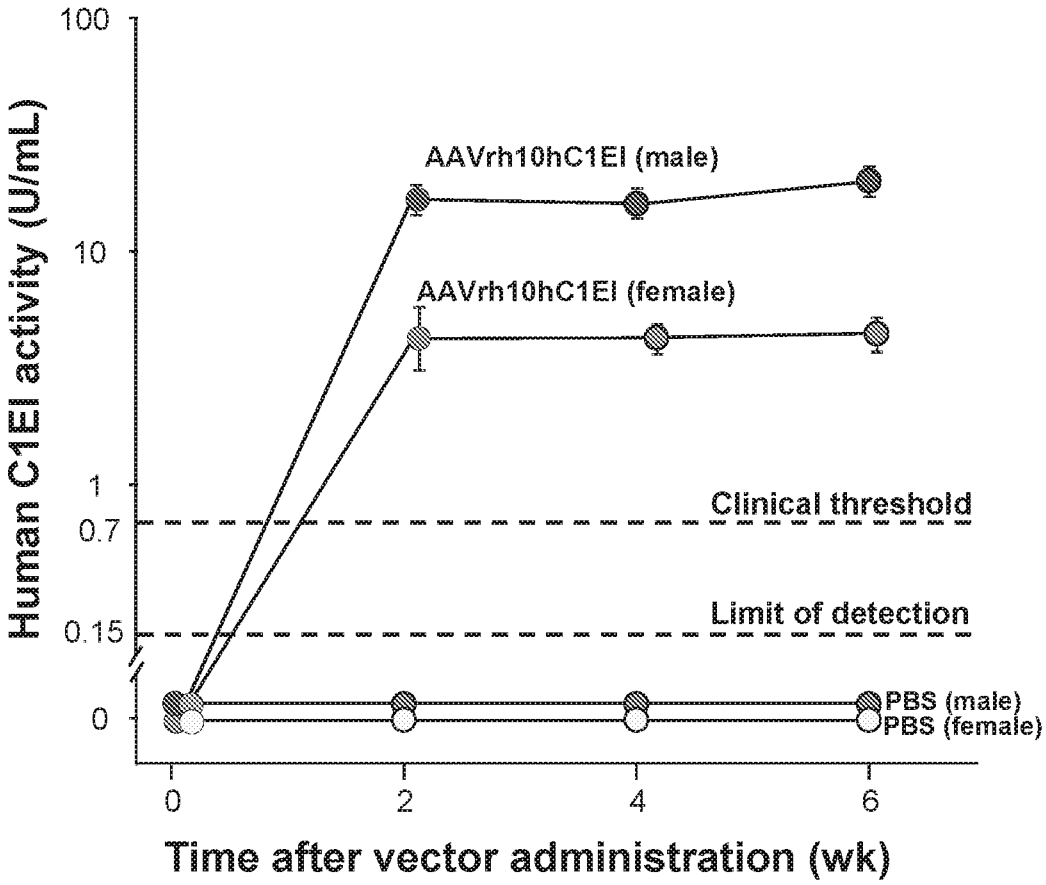


Figure 5D

AAV8hC1EI, AAV9hC1EI, or AAVrh.10hC1EI Vector

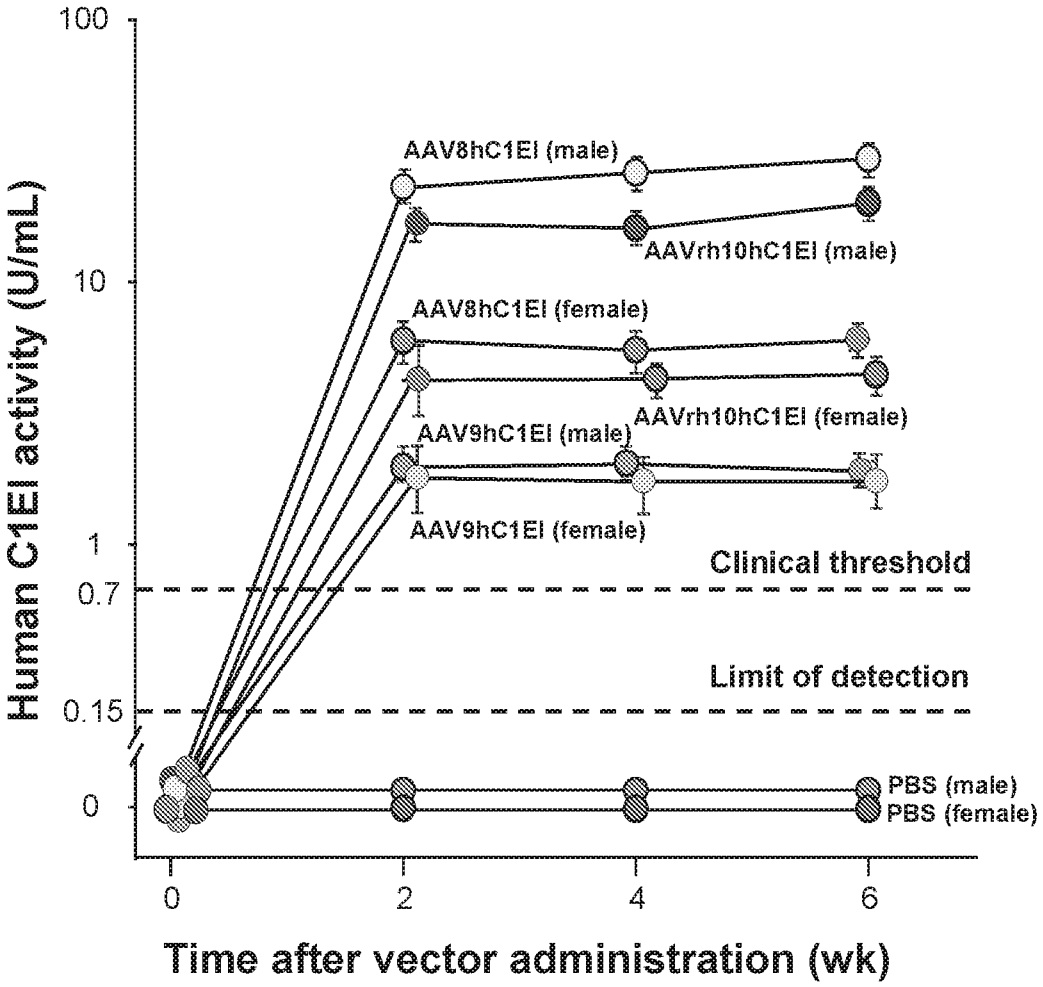


Figure 6

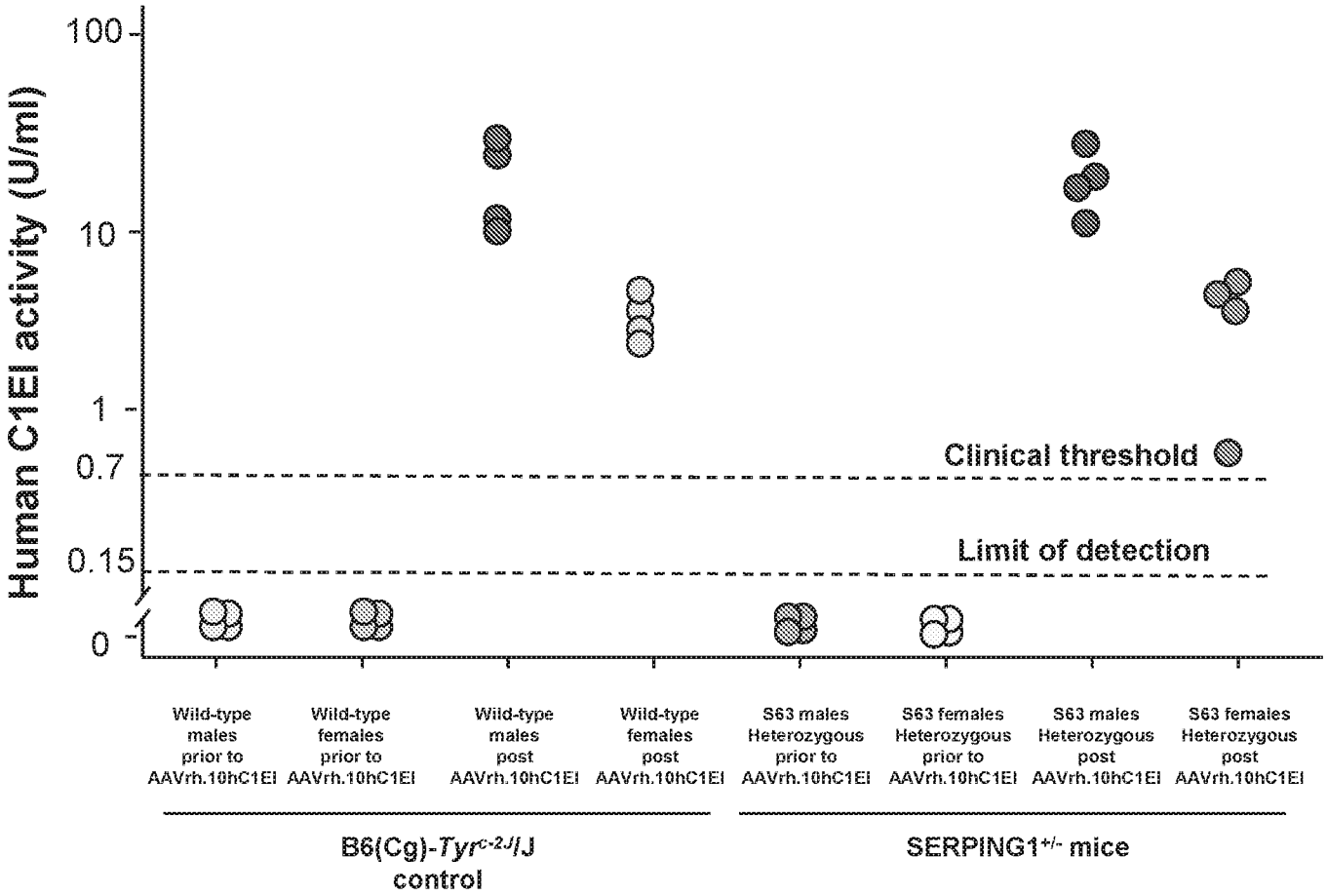

Human C1EI activity (U/ml)
100
10
1
0.7
0.15
0
Clinical threshold
Limit of detection
Wild-type males prior to AAVrh.10hC1EI
Wild-type females prior to AAVrh.10hC1EI
Wild-type males post AAVrh.10hC1EI
Wild-type females post AAVrh.10hC1EI
S63 males Heterozygous prior to AAVrh.10hC1EI
S63 females Heterozygous prior to AAVrh.10hC1EI
S63 males Heterozygous post AAVrh.10hC1EI
S63 females Heterozygous post AAVrh.10hC1EI
B6(Cg)-Tyr^c-2J/J control
SERPING1+/- mice

Figure 7A

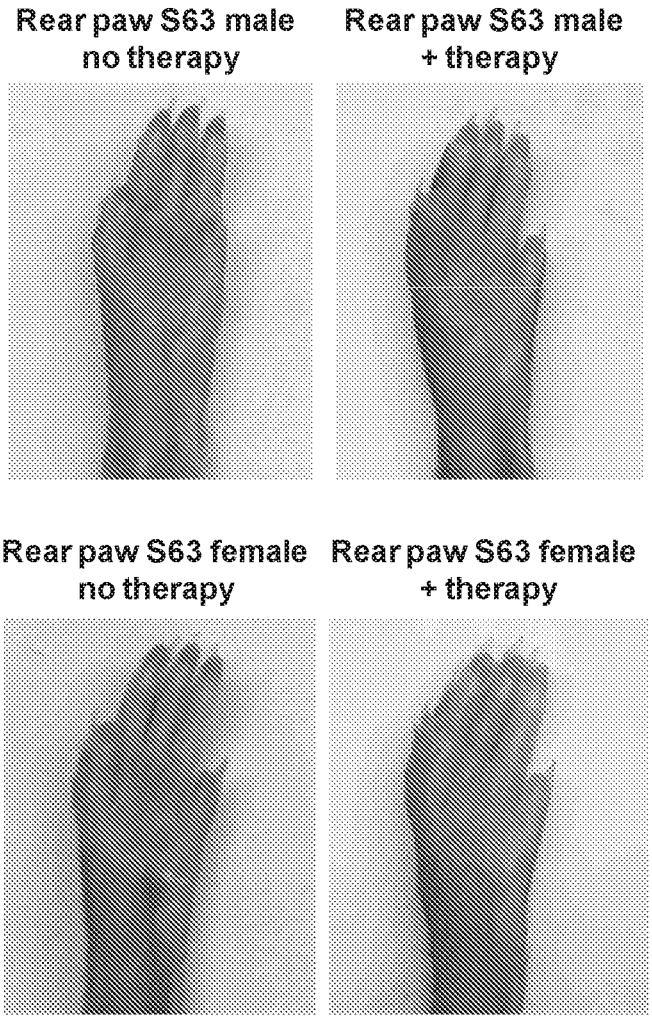

Rear paw S63 male
no therapy
Rear paw S63 male
+ therapy
Rear paw S63 female
no therapy
Rear paw S63 female
+ therapy

Figure 7B

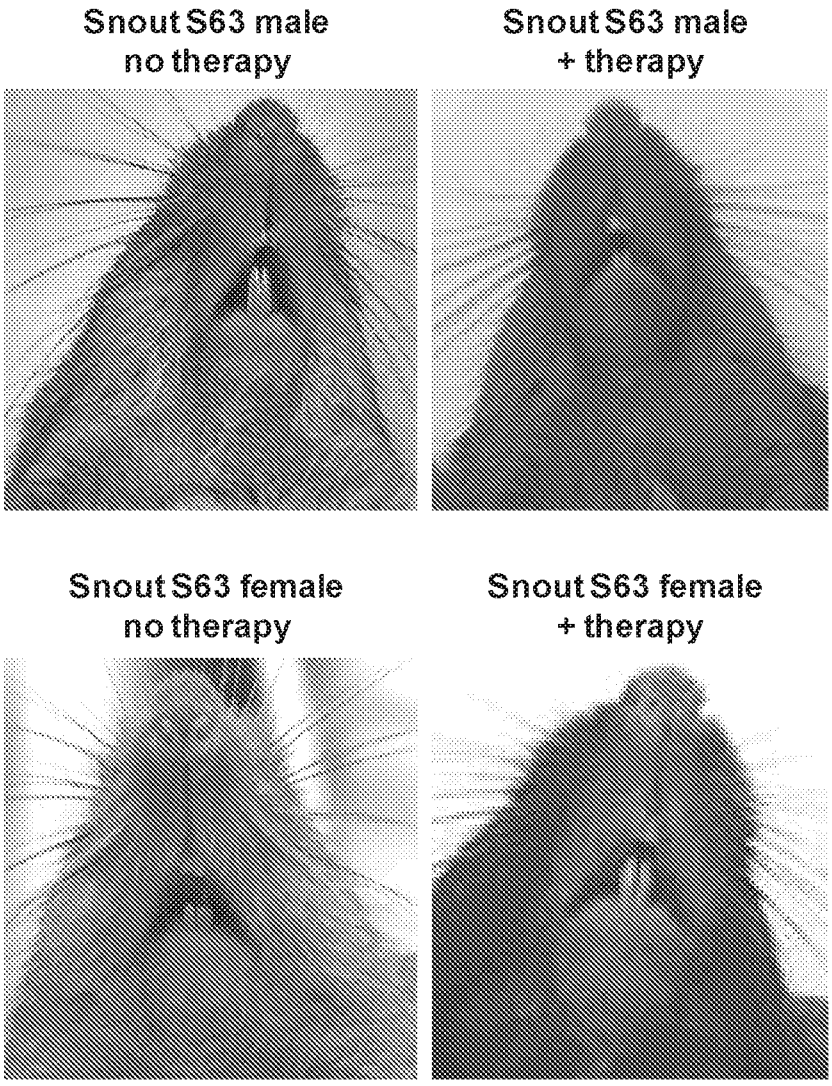

Snout S63 male
no therapy
Snout S63 male
+ therapy
Snout S63 female
no therapy
Snout S63 female
+ therapy

Figure 8A

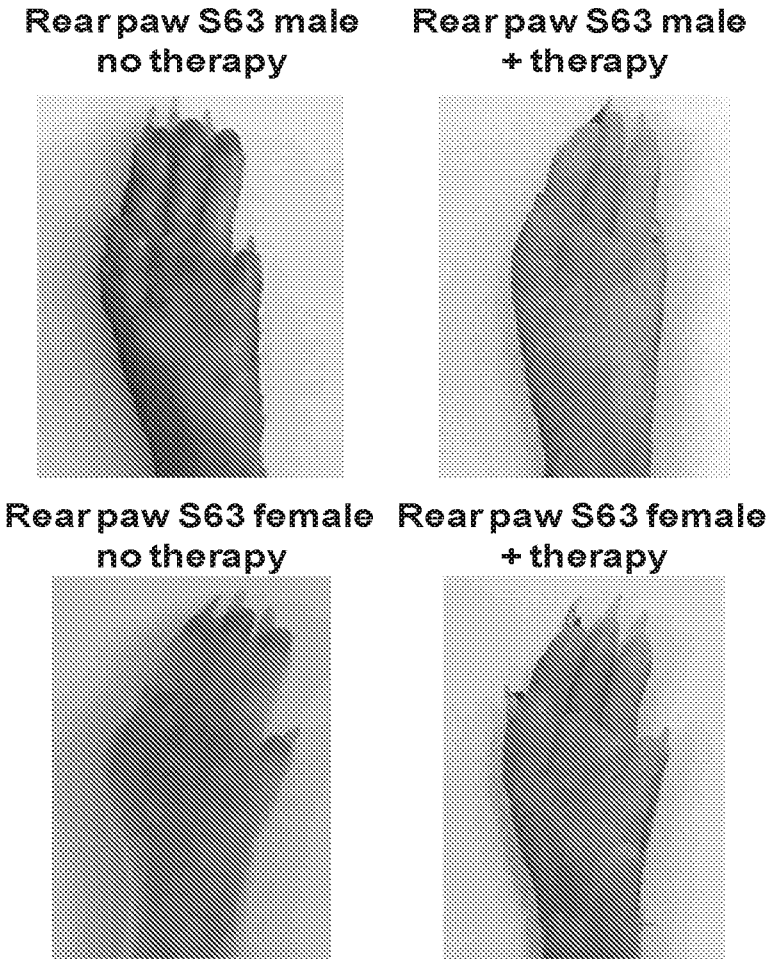
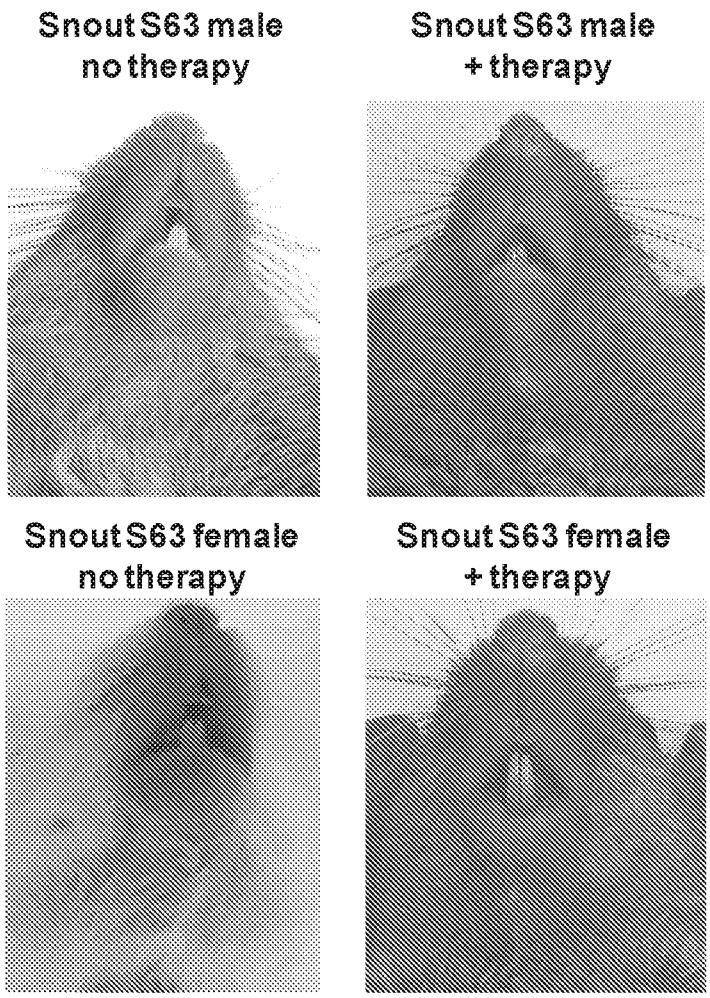

Rear paw S63 male
no therapy
Rear paw S63 male
+ therapy
Rear paw S63 female
no therapy
Rear paw S63 female
+ therapy

Figure 8B


Snout S63 male
no therapy
Snout S63 male
+ therapy
Snout S63 female
no therapy
Snout S63 female
+ therapy

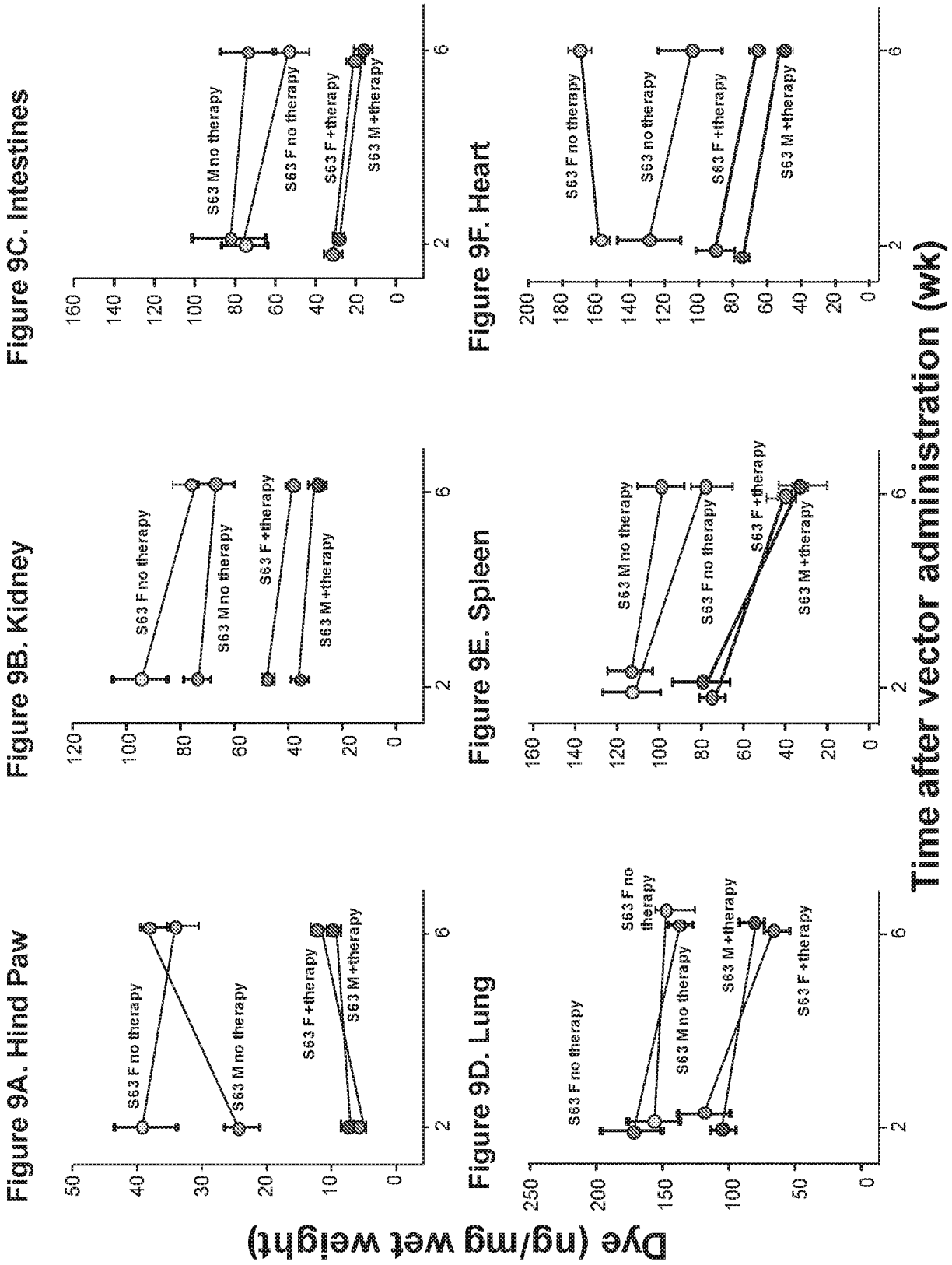
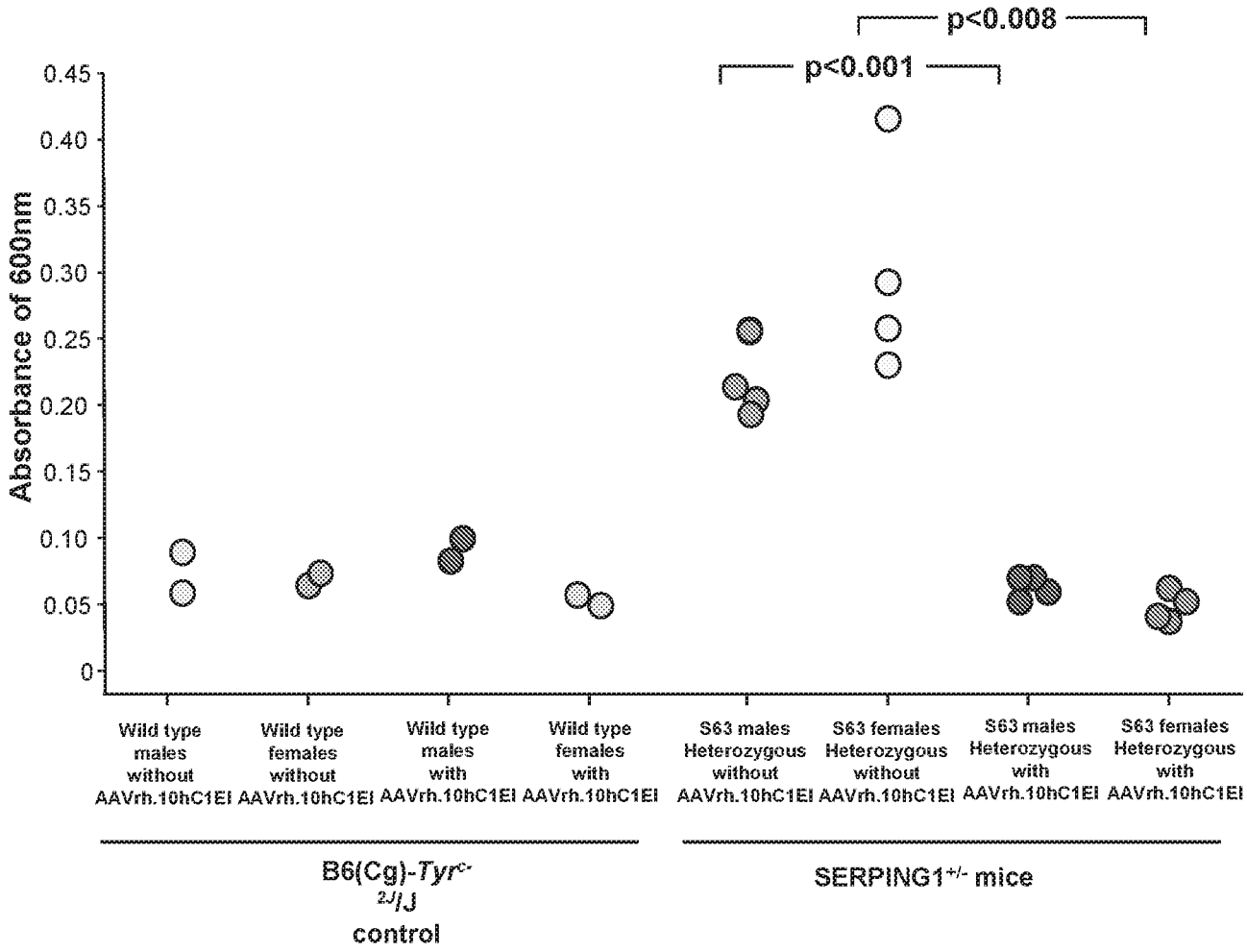

Figure 9A. Hind Paw
Figure 9B. Kidney
Figure 9C. Intestines
Figure 9D. Lung
Figure 9E. Spleen
Figure 9F. Heart
S63 F no therapy
S63 M no therapy
S63 F +therapy
S63 M +therapy
Dye (ng/mg wet weight)
Time after vector administration (wk)

Figure 10


p<0.008
p<0.001
Absorbance of 600nm
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
Wild type males without AAVrh.10hC1EI
Wild type females without AAVrh.10hC1EI
Wild type males with AAVrh.10hC1EI
Wild type females with AAVrh.10hC1EI
S63 males Heterozygous without AAVrh.10hC1EI
S63 females Heterozygous without AAVrh.10hC1EI
S63 males Heterozygous with AAVrh.10hC1EI
S63 females Heterozygous with AAVrh.10hC1EI
B6(Cg)-Tyrc-2J/J control
SERPING1+/- mice