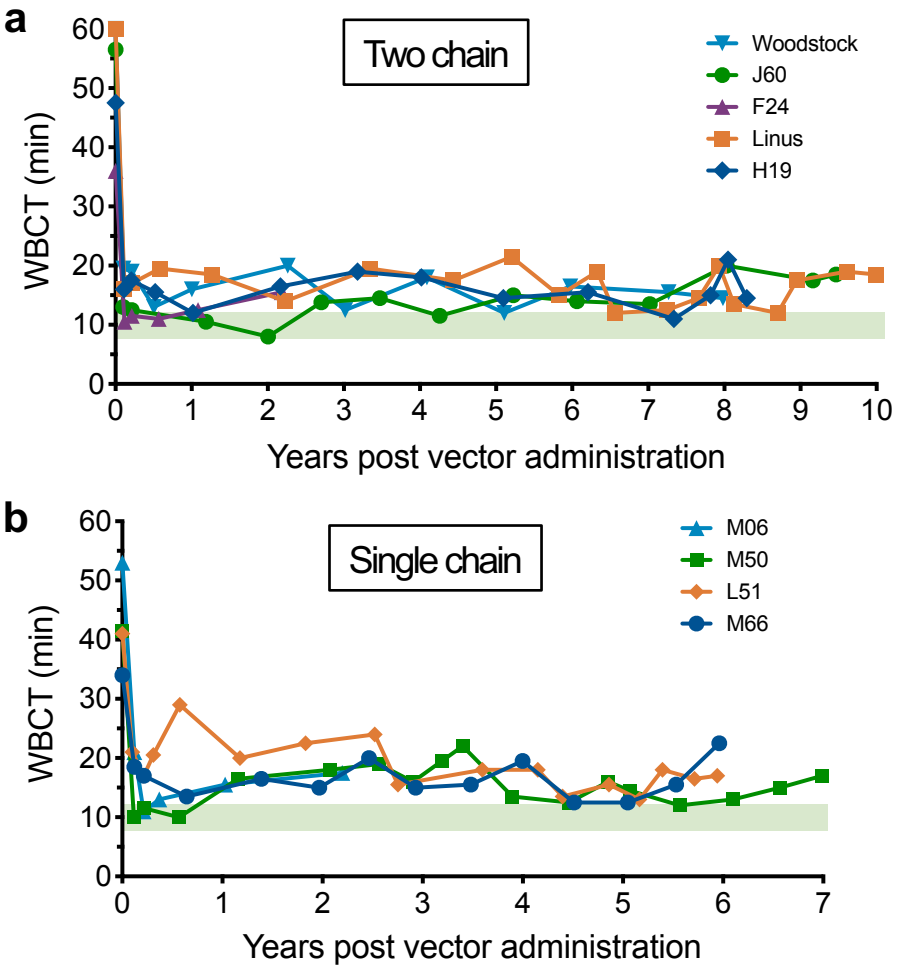
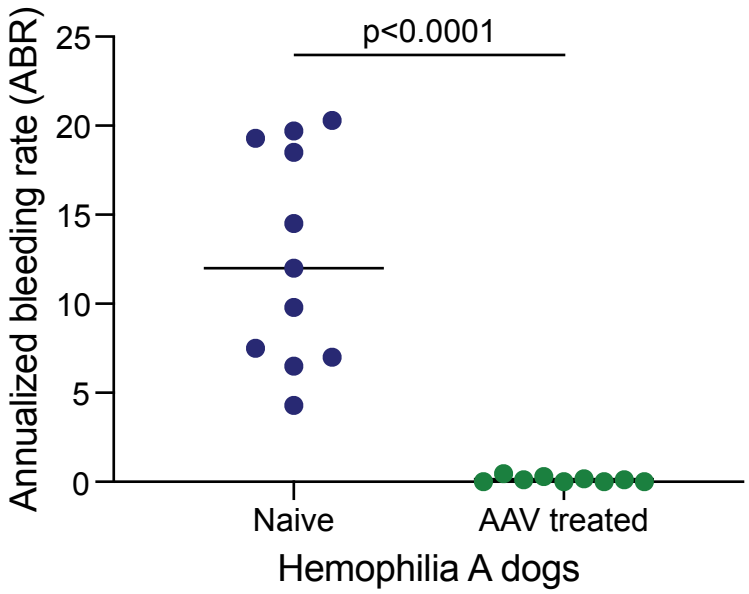


Supplementary Figure 1

Whole blood clotting time in the AAV-treated hemophilia A dogs.

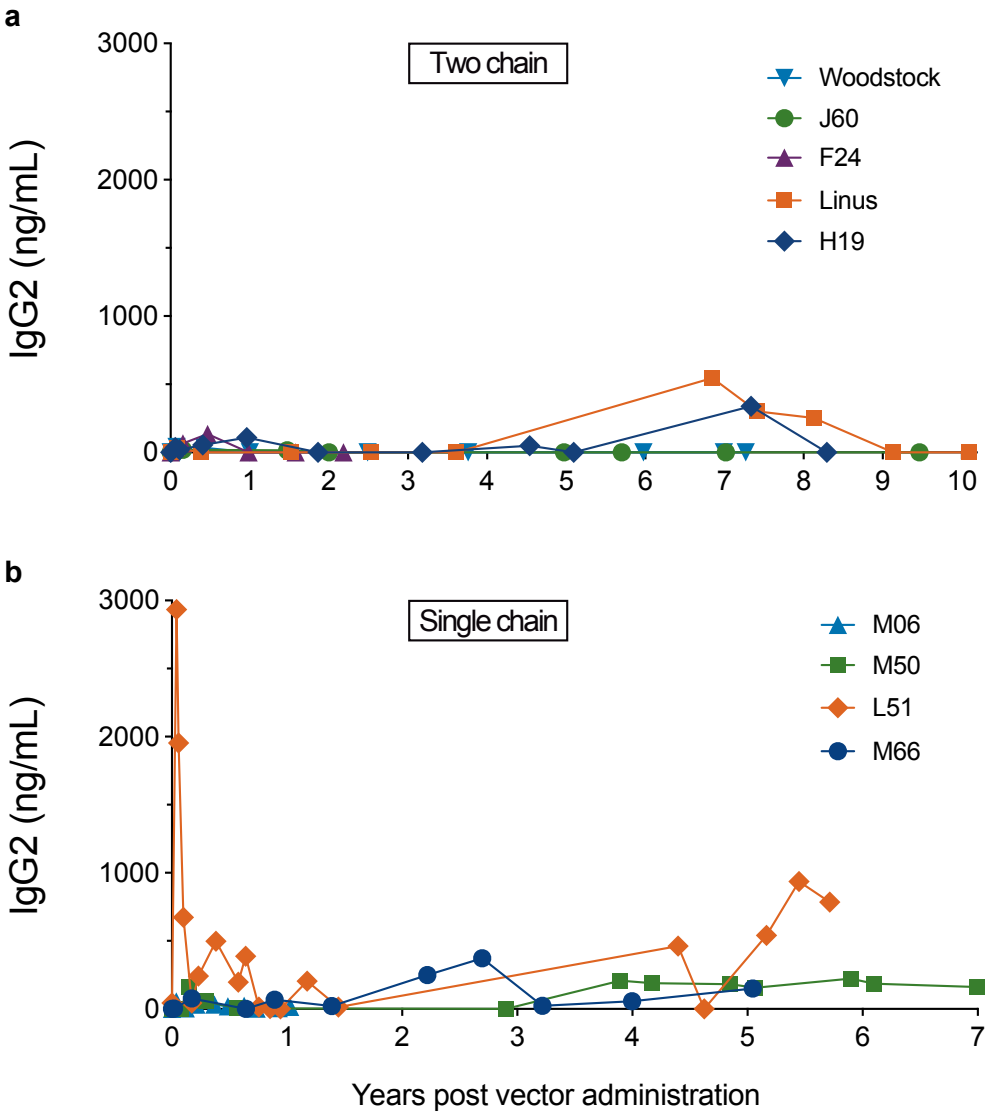
(a) Whole blood clotting time (WBCT) after two chain AAV administration in hemophilia A dogs. At baseline the WBCT (min) was >35 minutes. After AAV administration the WBCT Shortened to near or within the normal range for dogs (8-12 min, green highlight). (b) Whole blood clotting time (WBCT) after single chain AAV administration in hemophilia A dogs.



Supplementary Figure 2

Annualized bleeding rate (ABR) in the hemophilia A dogs after AAV administration.

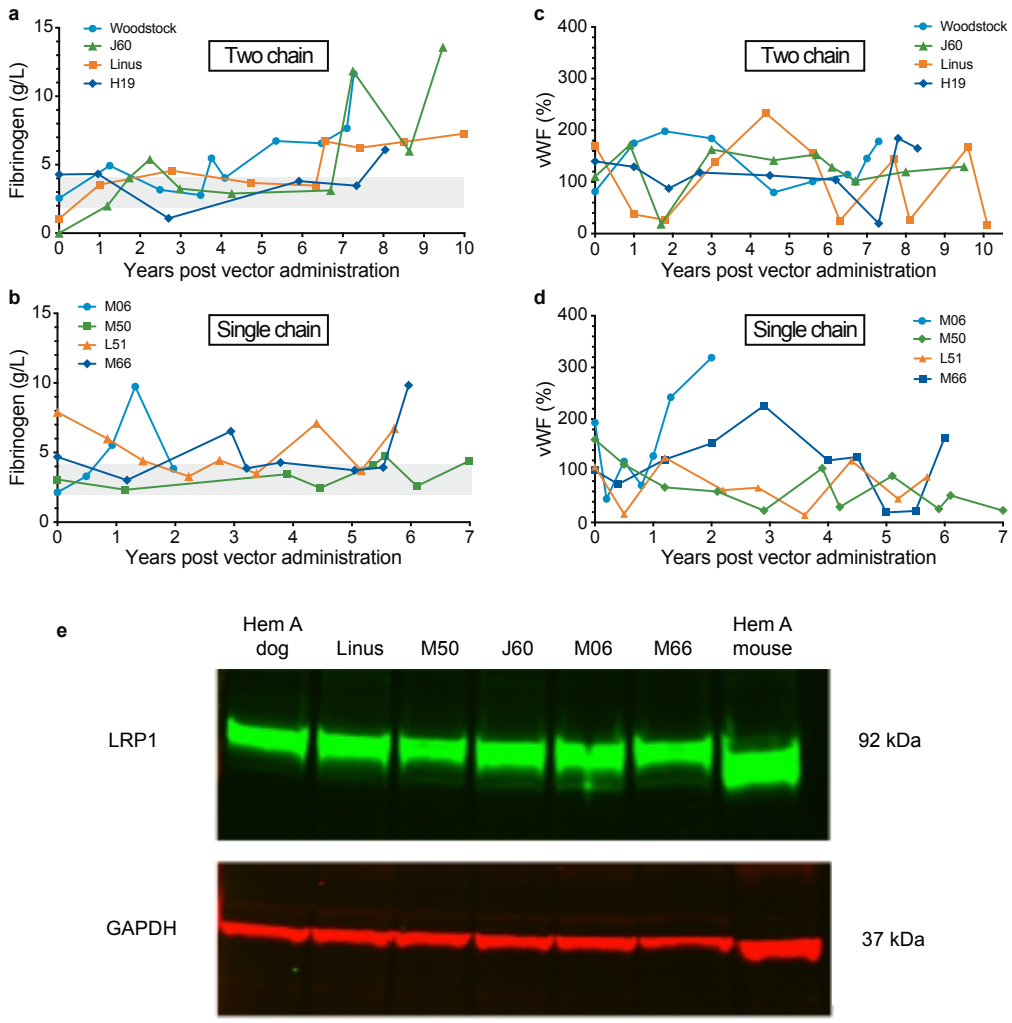
Naïve hemophilia A dogs (n=11 biologically independent animals) from two litters were followed prospectively for 4 years to obtain a detailed bleeding history for the dogs (ABR 12.7 ± 6.0, Mean ± Standard Deviation). The AAV treated dogs (n=9 biologically independent animals) were monitored for bleeding events for the duration of the study (ABR 0.13 ± 0.16). The ABR was calculated based on the total number of bleeding events/number of years on the study. Each data point represents a hemophilia A dog. After AAV administration, four of the dogs (F24, J60, M50, M66) had FVIII activity levels that were in a range that produces a mild (n=3) or moderate (n=1) hemophilia A phenotype in humans and had no bleeding episodes. The four dogs that had one bleeding episode during the course of the study (Woodstock, H19, M06, L51) had levels of FVIII activity after AAV administration in the severe (n=2), moderate (n=1) or mild range (n=1). Two of these bleeding episodes were documented to be in response to a trauma. Eight of the dogs had either none (n=4) or only one (n=4) documented bleed during the study; one dog (Linus) had three. Notably, Linus had these bleeding episodes during the first two years after AAV administration, when his cFVIII activity levels were between 1-2%; no bleeds were detected at later time points when his cFVIII activity was >2%. Thus, these data suggest that even low levels of FVIII expression after gene therapy improved the bleeding phenotype and correlate with the human clinical phenotype. Two-tailed non-parametric Mann-Whitney U test, $p<0.0001$.



Supplementary Figure 3

Anti-cFVIII IgG after AAV administration.

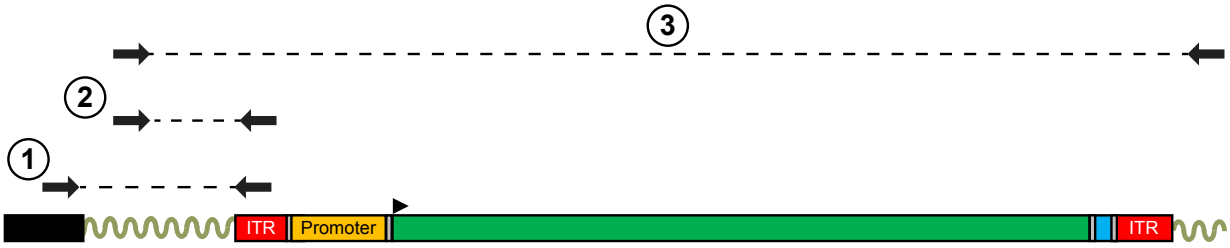
IgG2 was assayed by ELISA specific for anti-cFVIII antibodies throughout the study. (a) Anti-cFVIII IgG after AAV delivery in the two chain treated dogs. (b) Anti-cFVIII IgG after AAV delivery in the single chain treated dogs. L51 had an elevation in IgG2 that peaked at 24 days and returned to baseline levels by 50 days after vector administration as we previously reported[6]. In the final year of the study L51 had a low level of anti-cFVIII IgG2 but no neutralizing anti-cFVIII antibodies were detected (0 BU). Hemophilia A dogs with an intron 22 inversion have been shown to develop inhibitors to canine FVIII in both the Chapel Hill and Queen's colonies[56] and this dog was a member of a pedigree containing several litters of inhibitor prone dogs. None of the other dogs had elevated IgG2 levels. No anti-cFVIII IgG1 antibodies were detected. The pre-treatment baseline sample for each dog serves as the control for each respective dog and are shown as zero as described in the Methods. As described in our previous report, we challenged the dogs with cFVIII protein and confirmed that they were tolerant to cFVIII after AAV AAV delivery[6].



Supplementary Figure 4

Analysis of fibrinogen, vWF and clearance receptor, LRP1.

(a) Fibrinogen levels after AAV administration in the two chain treated hemophilia A dogs. (b) Fibrinogen levels after AAV administration in the single chain treated hemophilia A dogs. Fibrinogen levels have been associated with inflammation and some cancers. Fibrinogen levels were assayed at multiple time points in the dogs to determine if there were elevations in the levels suggestive of abnormal liver function but fibrinogen levels remained in the normal range (2-4 g/L; gray highlight) for most of the dogs during the first years of follow-up after AAV delivery. A consistent elevation in plasma fibrinogen levels was observed that increased proportionally with age, which is commonly seen in healthy humans. One dog, M06, had elevated fibrinogen levels beginning at age 1.5 y.o. which correlated with the onset of bleeding associated with mucosal polyps. There was no association with the increase in FVIII levels in Linus and M50 and the onset of the increase in fibrinogen levels. (c) von Willibrand Factor (vWF) levels after AAV administration in the two chain treated hemophilia A dogs. (d) von Willibrand Factor (vWF) levels after AAV administration in the single chain treated hemophilia A dogs. Since the clearance of FVIII is determined by its association with vWF which could influence the FVIII levels in the circulation, the levels of vWF were tested in the dogs over time. Levels of vWF in the plasma after AAV administration ranged between 15 and 230% of normal levels in the AAV treated dogs. Normal canine vWF antigen levels range from 70-180%. The broad range and variability can be attributed to multiple factors including age, genetic variability and acute-phase response that can be influenced by exercise or infections. No correlation was observed between the increase in circulating FVIII in Linus and M50 and the vWF levels. (e) Western Blot analysis of LRP1 levels in the hemophilia A dogs (representative of two independent blots). The clearance of FVIII and vWF is modulated by multiple receptors with LRP1 serving as one of the primary receptors and alterations in the expression of these receptors can influence the clearance of these proteins. Protein was isolated from liver tissue at the terminal time point for each AAV treated hemophilia A dog and an untreated hemophilia A dog. The levels of LRP1 in the livers were determined by Western blot and were analyzed by densitometry. No difference was observed in the LRP1 protein levels in Linus and M50 compared to the other hemophilia A dogs. Thus, the increased levels of FVIII in Linus and M50 are not related to the levels of LRP1.



1 Integration site analysis

2 Targeted validation using one dog genomic DNA primer and one AAV primer

3 Amplification of internal fragment plus junction with dog genome

PCR primer

Amplicon

Adaptor ligated to permit PCR amplification

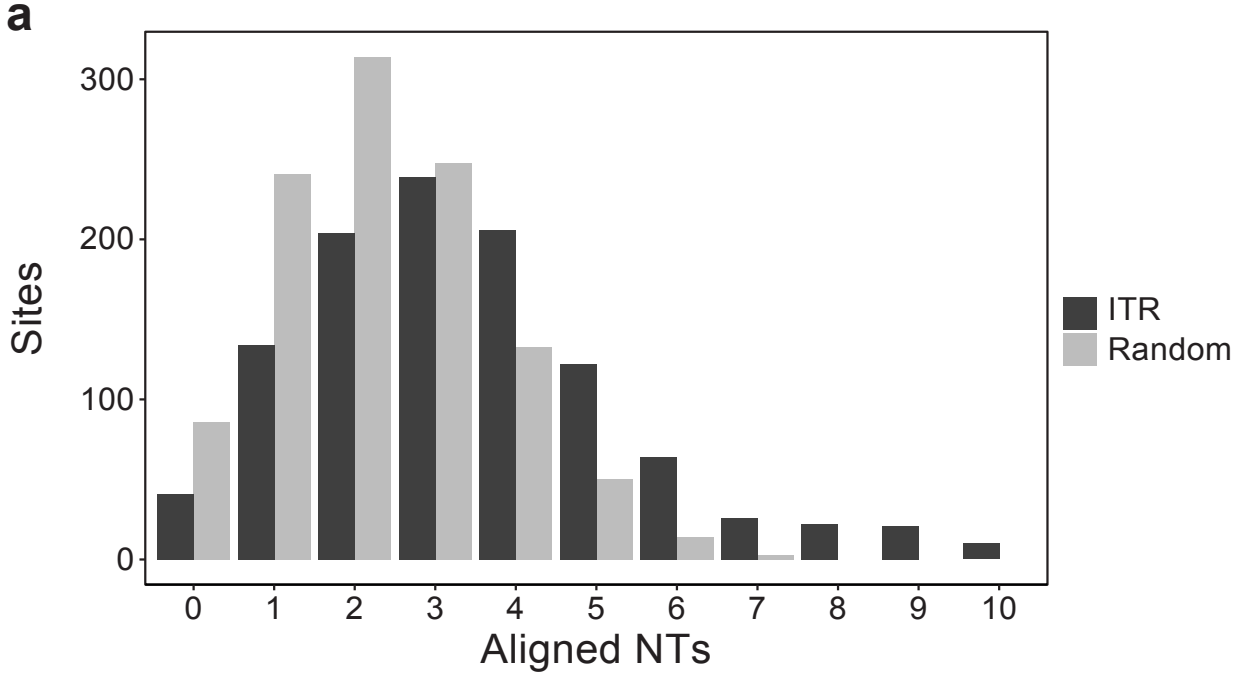
Dog genomic DNA

Supplementary Figure 5

Diagram of the PCR strategies used to generate templates for DNA sequencing of junctions between AAV vector sequences and dog genomic DNAs.

The AAV vector genome is shown, flanked by dog genomic sequence (wavy green lines). The PCR strategies are numbered. Strategy 1 was used for the large scale integration site analysis, involving cleaving dog liver genomic DNA with sonication, ligation of DNA adaptors to the broken DNA ends, then PCR amplification from the adaptor to the flanking vector DNA sequence. Methods 2 and 3 rely on advanced knowledge of the integration sites derived from method 1. In method 2, primers were designed to anneal to flanking dog DNA and vector DNA, so that PCR would generate a junction fragment, allowing confirmation of integration sites first detected with method 1. In method 3, two primers are designed to bind each segment of the dog genome flanking the site of vector integration site inferred from the sequence of the vector-dog DNA junction. Method 3 allowed analysis of the full integrated vector sequence. For methods 1 and 3, sequence information was acquired using the Illumina sequencing technology; for method 2 Sanger sequencing was used.

a



b

chr3+62101419 | 10 aligned NTs | POLN

AACCCCTAGTGATGGAGTTGGCCACTCCC
GAAGGGGCTTCTCCAAGTTGGCCACTCCC

chr25+34592334 | 9 aligned NTs | EGR3

AACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGTACGGGCGA
CGGTAGAGGCTTCGGTTCTCCCGGGTGGGGGCAGCCGCCGACCAGAGGGAGGTAGGTACGAGCGA

chr25+34592383 | 8 aligned NTs | EGR3

AACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGC
GGGTTCTCCACTTAGGGGGCGCGATCGCCAGGCTGCGCGC

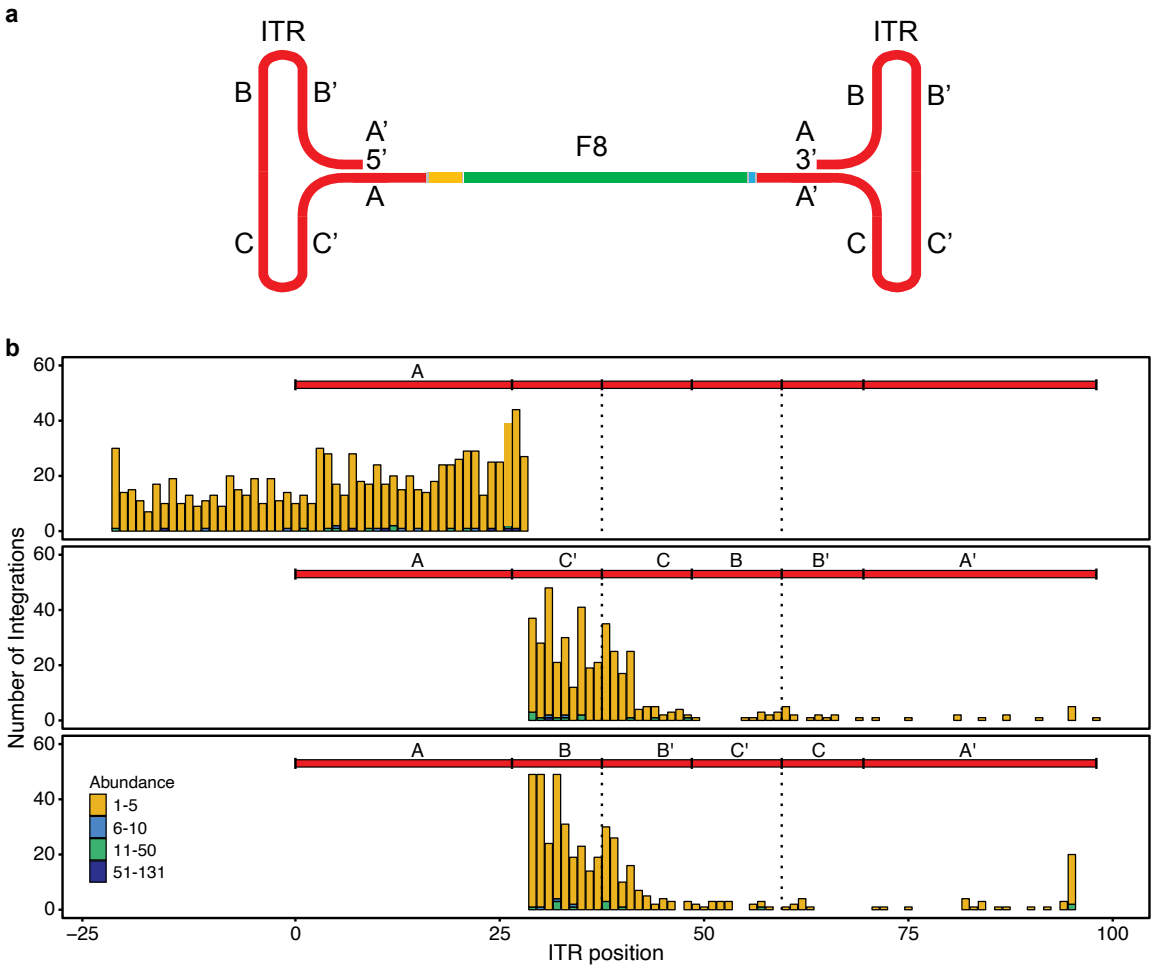
chr4+14782170 | 7 aligned NTs | EGR2

AACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCATTGA
ATCCATTTTAATCCAAGTCTTTGATATTTAAAAAAACGGAGATTCCTTTAATTGA

Supplementary Figure 6

AAV ITR micro-homology analysis.

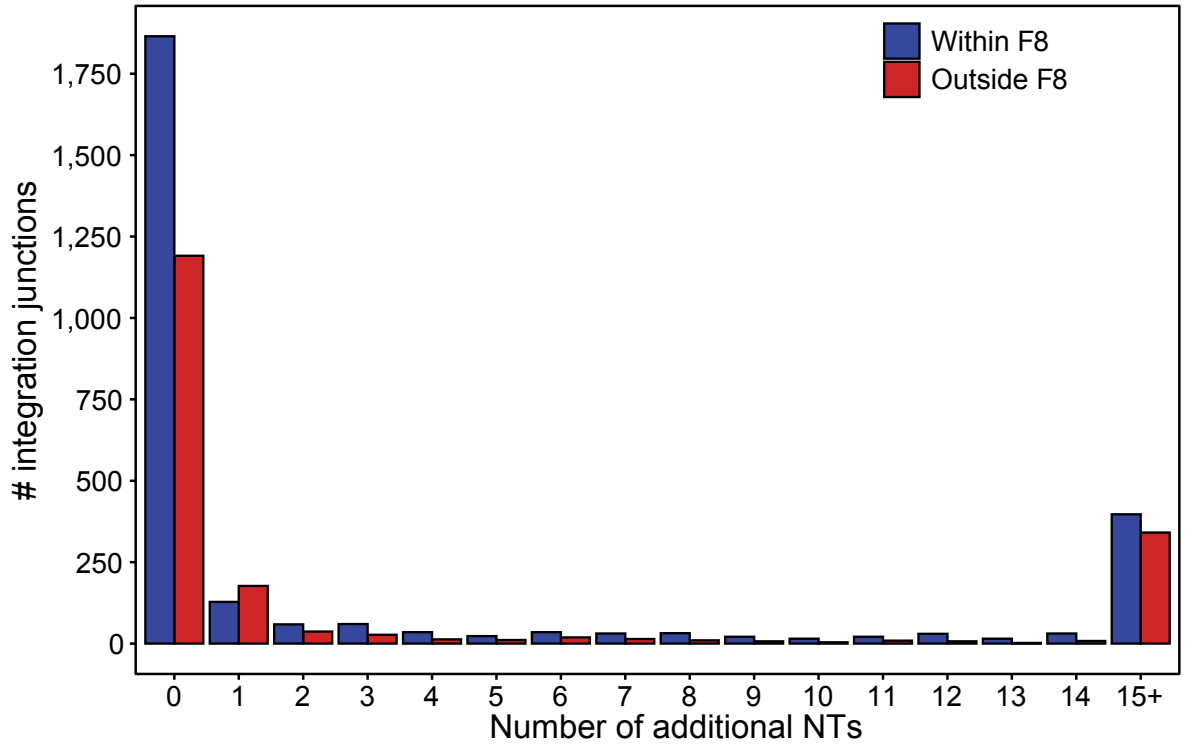
DNA sequence homology between AAV vectors and genomic DNA has the potential to promote integrative recombination. Thus, homology at junctions was assessed statistically. (a) Alignment of the last 10 nucleotides of ITR remnant sequences (1,067 unique integrations) to genomic sequences preceding integration positions yields significantly different distributions of alignment scores compared to randomly selected genome positions where the average of 1,000 different sets of random sequence sets are shown (Bonferroni adjusted Wilcox Rank Sum test p-values of alignment scores ranged from 6.8e-54 to 3.2e-33). (b) Select examples of alignments between ITR remnant sequences and genomic sequences where the ITR remnant sequences (top sequence) are shown with genomic sequences (bottom sequence).



Supplementary Figure 7

Overview of locations of integration junctions between the AAV ITR and novel flanking sequences.

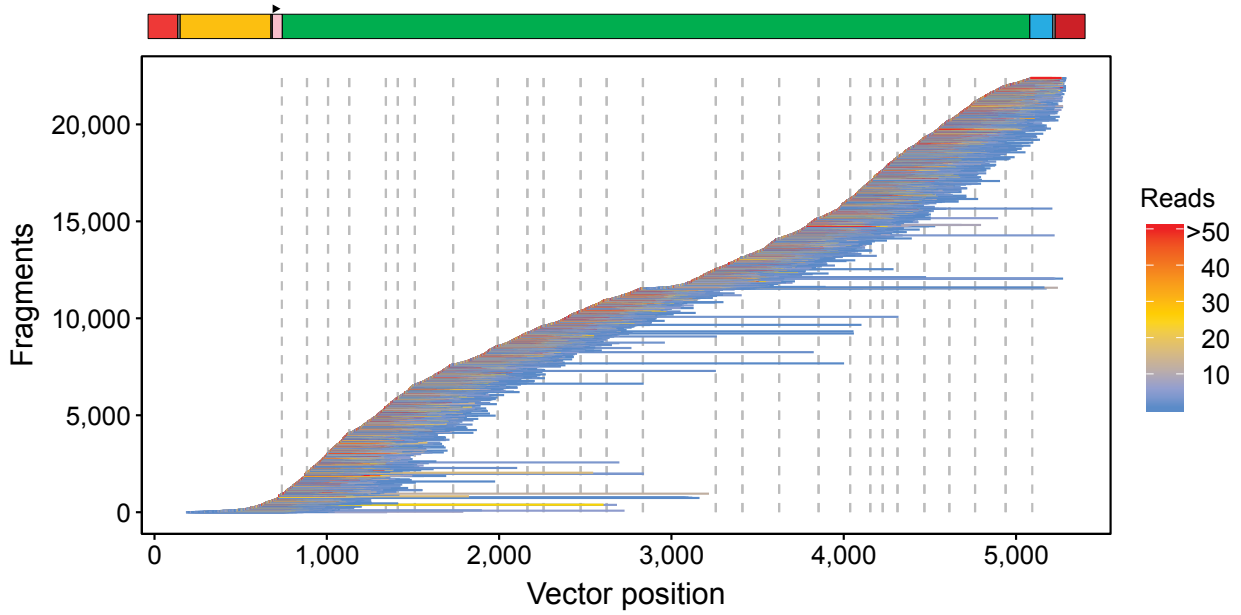
a) Schematic of the AAV vector construct, illustrating the labeling of the ITR subsequences. b) Sequences at junctions between AAV DNA and dog DNA, illustrating truncation of the terminal ITR sequences. Note that because of the locations of the amplification primers, it was not possible to judge the end of the molecule tested for break points within A. Break points more distal in the ITR could be mapped unambiguously to either end. “Abundance” indicates the sonic abundance of the indicated sequence.



Supplementary Figure 8

High frequency of integration of AAV vector sequences in dog liver samples in F8.

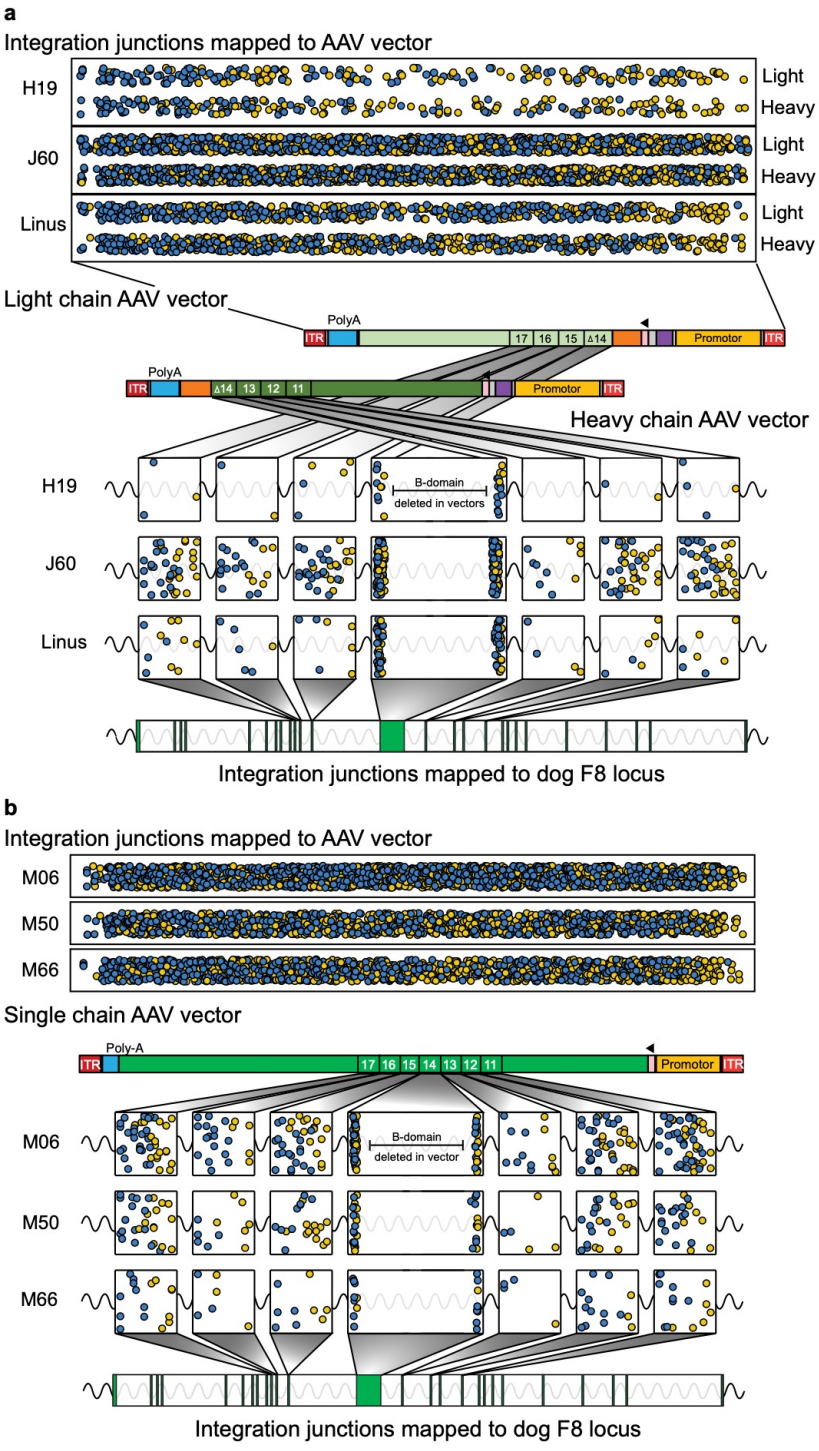
The figure plots the relative frequency of integration site junctions, where ITR sequences are linked to dog genomic DNA outside the F8 locus versus within the canine F8 locus (representing vector autointegration). Some integration sites showed insertions between the ITR and other DNA; the x-axis displays the number of additional bases present. As can be seen, the majority of mapped integration events are actually within F8.



Supplementary Figure 9

Joining of AAV ITRs to the vector F8 gene and not the chromosomal canine F8 gene

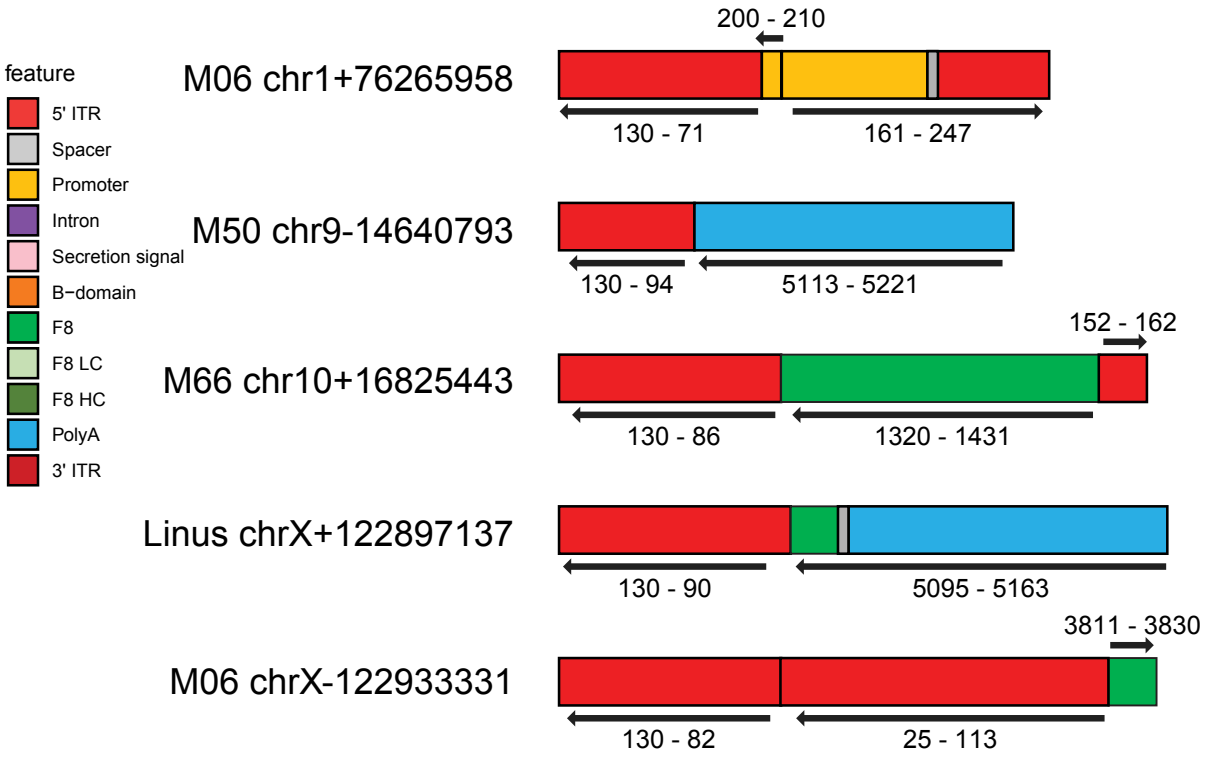
The figure shows the positions of mapped junctions between ITRs and FVIII sequences, mapped on to the vector sequence. The x axis shows the position on the vector map, the y axis shows the cumulative fragment number from bottom to top. The dashed vertical lines show exon junctions, which are present in the vector cDNA but not the chromosomal F8 copy. All reads plotted crossed exon boundaries. In addition, no integration site junctions were found involving F8 intron sequences. These findings indicate that junctions involved the vector FVIII cDNA and not the chromosomal F8 gene.



Supplementary Figure 10

Mapping sites of autointegration/rearrangements within the AAV vector.

a) Results are shown for the two chain vector. The blue and yellow dots show the positions of integration sites from junctions between ITRs and other vector sequences. Junctions are color coded to show orientation of the integrated segment (blue indicates +, yellow indicates - with respect to the dog genome). Data for each dog is shown as a separate row. The bottom display shows the locations of apparent integration sites in a part of the canine F8 locus. All integration sites are in exons and not introns, and the region encoding the FVIII B domain that is missing in the vector lacks integration sites. For AAV sequences common to both the heavy and light chain vectors, integration sites could map equally well to either. b) as in a), but showing results for dogs treated with the single chain vectors.



Supplementary Figure 11

Examples of rearranged AAV vector sequences, determined by priming from the ITR (Supplementary Figure 5, method 1). The numbers refer to the coordinate in each AAV FVIII vector genome.

Supplementary Table 1. Liver pathology of AAV-treated hemophilia A dogs.

Genotype	Dog ID	Years Post-AAV Administration	Liver Sample	AAV Delivery Approach	Age at necropsy/ biopsy (years)	Hepatocellular necrosis	Increased connective tissue	Bile duct hyperplasia	Mixed inflammatory cell infiltrates	Pigment lipogranulomas	Hemosiderin-laden macrophages	Hepatic cord atrophy	Nodular hyperplasia	Hepatocellular swelling and clearing
Hem A	Woodstock	Pre-AAV	WS-Pre	TC	NA	0	0	2	0	0	0	0	0	3
		8.2 Final	WS Final		12.5	0	1	1	0	1	0	0	1	3
	J60	9.5 Final	Lobe 1	TC	10.5	0	1	1	1	1	0	0	0	1
			Lobe 2			0	1	1	0	1	0	0	0	1
			Lobe 3			0	0	0	0	1	0	0	0	0
			Lobe 4			0	0	1	0	1	0	1	1	0
			Lobe 5			0	1	1	1	1	0	0	0	1
	Linus	Pre-AAV	Linus-Pre	TC	NA	0	0	1	0	0	0	0	0	3
		6.0	Biopsy		10	0	0	2	0	0	0	0	0	3
		10.1 Final	Lobe 1		14.3	0	0	1	0	1	0	0	0	1
			Lobe 2			0	0	2	0	1	2	0	0	1
			Lobe 3			0	1	1	0	1	0	0	0	1
			Lobe 4			0	0	1	0	1	0	0	0	3
			Lobe 5			0	0	1	0	1	0	0	0	2
	H19	8.3 Final	H19 Final	TC	9.3	2	2	2	2	1	2	0	0	2
	M06	2.3 Final	M06 Final	SC	2.7	0	1	1	2	1	0	0	0	3
	M50	7.3 Final	Lobe 1	SC	7.9	0	2	1	1	1	2	0	0	2
			Lobe 2			0	1	1	0	1	0	0	0	2
			Lobe 3			0	1	1	0	1	0	0	0	2
			Lobe 4			0	1	1	0	1	0	0	0	2
			Lobe 5			0	2	1	1	1	0	0	0	2
	L51	6.1 Final	L51 Final	SC	6.5	1	2	2	2	3	3	0	0	0
	M66	6.0 Final	Lobe 1	SC	7.5	0	2	1	0	1	2	0	0	1
			Lobe 2			0	2	1	0	1	0	0	0	1
			Lobe 3			0	2	1	0	1	2	0	0	1
			Lobe 4			0	2	1	0	1	0	0	0	1
			Lobe 5			0	1	1	0	1	0	0	0	0

0 Unremarkable
1 Minimal change
2 Mild change
3 Moderate change
4 Severe change

Supplementary Table 2. Liver pathology of naive hemophilia A, hemophilia B and normal dogs.

Genotype	Dog ID	Age at necropsy	Mean age at necropsy (years)	Hepatocellular necrosis	Increased connective tissue	Bile duct hyperplasia	Mixed inflammatory cell infiltrates	Pigment lipogranulomas	Hemosiderin-laden macrophages	Hepatic cord atrophy	Nodular hyperplasia	Hepatocellular swelling and clearing
Hem A	S32	3.7	5.5 ± 2.2	0	0	0	0	0	0	0	0	4
	P19	6.7		1	2	2	1	2	2	0	0	0
	T03-Lawrence	2.3		0	1	1	0	0	0	0	0	0
	O94	5.8		0	0	0	0	0	3	0	0	0
	L57	5.4		0	1	1	0	0	0	0	0	0
	Diamond	9.2		0	2	2	1	3	1	0	0	0
	F26	7.7		0	1	1	1	1	0	0	0	0
	G56-Daisy	2.7		0	1	1	0	3	3	0	0	0
	Black Jack	7.0		0	1	1	0	2	1	0	0	0
	E02	4.8		0	1	1	0	0	0	0	0	0
Hem B	S12	5.0	5.6 ± 3.1	0	2	2	2	2	1	0	0	2
	S14	5.0		0	2	2	0	1	0	0	0	0
	P41	6.7		0	1	2	0	1	1	0	0	0
	P05	6.2		0	1	1	0	1	0	0	0	0
	O40	4.7		0	0	0	0	1	0	0	0	0
	G35	11.6		0	2	2	2	3	2	0	0	0
	O24	3.0		0	0	0	1	1	0	0	0	0
	L11	1.3		0	2	2	0	1	0	0	0	0
	Z91	8.8		0	1	1	0	1	1	0	0	0
WT	D22	12.3	11.7 ± 2.4	0	1	1	0	1	0	0	0	0
	Elton	14.0		0	2	1	1	1	0	0	0	2
	I34	13.0		0	2	1	1	1	0	0	0	2
	I32	12.9		0	3	1	1	1	1	0	3	2
	I23	10.7		0	1	0	0	0	0	0	0	0
	I31	9.3		0	2	1	1	3	1	0	0	4
	J42	6.4		0	3	2	1	1	1	0	0	2
	E16	9.8		0	3	2	2	2	0	0	0	1
	X13	12.1		0	2	2	0	2	0	0	0	1

0 Unremarkable
1 Minimal change
2 Mild change
3 Moderate change
4 Severe change

Supplementary Table 3. Anti-AAV8 neutralizing antibody titers after AAV administration.

Hem A Dog	Total Vector Dose (vg/kg)	Baseline Anti-AAV8 NAb titer	Anti-AAV8 NAb titer post vector administration					Final Timepoint (yr)
			0.5 month	6 months	1 year	4 years	Final	
F24	2.5×10^{13}	<1:1	>1:3155	>1:3155	>1:3155	ND	>1:3155	2.2
Linus	1.2×10^{13}	<1:1	>1:3155	>1:3155	>1:3155	>1:3155	1:316 to 1:1000	10.0
M06	4.0×10^{13}	<1:1	>1:3155	>1:3155	>1:3155	ND	>1:3155	2.0
M50	4.0×10^{13}	<1:1	>1:3155	>1:3155	>1:3155	>1:3155	1:1000 to 1:3155	7.0
L51	2.0×10^{13}	<1:1	>1:3155	>1:3155	>1:3155	>1:3155	>1:3155	5.7
M66	2.0×10^{13}	1:1 to 1:3.16	>1:3155	>1:3155	>1:3155	>1:3155	1:1000 to 1:3155	6.0

Supplementary Table 4. Comparison of AAV administration details for Linus and M50.

	Linus	**M50**
AAV serotype	AAV8	AAV8
Vector delivery approach	Two Chain	Single Chain
Promoter	TBG	hAAT
Total vector dose (vg/kg)	1.2×10^{13}	4×10^{13}
Age at vector administration (yrs)	4	0.6
Clinical concerns	None	None

Supplementary Table 5. Vector copy number analysis per liver lobe in the hemophilia A dogs.

Hem A Dog	Lobe	# Liver samples/lobe	Mean VCN ± SD
J60	1	5	2.13 ± 0.82
	2	6	4.03 ± 2.21
	3	6	3.91 ± 2.87
	4	6	4.09 ± 3.30
	5	6	2.78 ± 1.65
Linus	1	3	0.36 ± 0.22
	2	3	0.15 ± 0.20
	3	3	0.33 ± 0.17
	4	3	0.39 ± 0.30
	5	3	0.19 ± 0.12
M50	1	6	0.38 ± 0.34
	2	5	0.64 ± 0.43
	3	6	0.18 ± 0.26
	4	6	0.20 ± 0.26
	5	6	0.41 ± 0.30
M66	1	3	0.09 ± 0.16
	2	2	0.33
	3	3	0.18 ± 0.11
	4	3	0.45 ± 0.03
	5	3	0.40 ± 0.22

Supplementary Table 6. Integration site data sets studied.

Dog	Sample ID	Liver Lobe	Years Post-AAV	Delivery Approach	VCN	Sample Mass	Number of Sites in Canine Genome	Number of in Vector Sites*	Percent Sites in Vector
M50	GTSP2160	4	7	Single Chain	0.27	110.31	50	278	84.75
M50	GTSP2161	4	7	Single Chain	1.14	123.83	111	413	84.66
M50	GTSP2162	4	7	Single Chain	0.65	112.62	99	352	82.61
M66	GTSP2163	2	6	Single Chain	0.27	110.47	54	273	87.07
M66	GTSP2164	1	6	Single Chain	0.23	154.32	74	344	87.39
M66	GTSP2165	3	6	Single Chain	0.42	126.71	33	330	94.00
M06	GTSP2175	1	2	Single Chain	0.78	221.69	318	3033	70.37
M06	GTSP2176	3	2	Single Chain	2.04	100.26	162	2135	81.56
M06	GTSP2177	8	2	Single Chain	1.22	218.04	288	3079	72.31
Linus	GTSP2166	2	10	Two Chain	0.54	73.89	30	285	91.80
Linus	GTSP2167	3	10	Two Chain	0.14	59.22	31	98	76.52
Linus	GTSP2168	3	10	Two Chain	0.62	148.12	70	399	86.77
H19	GTSP2169	3	8.5	Two Chain	0.14	157.31	73	127	66.05
H19	GTSP2170	6	8.5	Two Chain	0.07	123.90	53	104	66.67
H19	GTSP2171	9	8.5	Two Chain	0.18	244.65	34	84	72.00
J60	GTSP2172	1	9.5	Two Chain	7.28	194.45	110	4075	89.11
J60	GTSP2173	2	9.5	Two Chain	3.06	123.72	96	2936	90.09
J60	GTSP2174	1	9.5	Two Chain	1.33	111.78	65	1079	87.68

* Sites arising from reads aligning to vector elements shared between the heavy and light chain vectors were averaged

Supplementary Table 7. Results of validation attempts for selected integration sites using targeted PCR and Sanger sequencing.

Dog	Site (Chromosome Position)	Sonic Abundance	Nearest Gene	Sanger Sequence Validation
M50	25_34590970	28.5%	EGR3	Yes
M50	14_55620581	13.0%	MET	Yes
M50	15_42531469	7.3%	GLT8D2	Yes
M50	4_14832997	13.4%	EGR2	Yes
M50	4_14757686	10.6%	EGR2	Yes
M50	12_38081605	17.3%	RPLPOP2	No
M66	4_14709696	36.2%	EGR2	No
Linus	4_14733827	20.3%	EGR2	Yes
Linus	25_34587602	21.4%	EGR3	Yes
Linus	37_13443531	15.1%	PQRD3	Yes
Linus	4_14681249	6.7%	ADO	No
Linus	18_48493167	4.3%	LTO	No
Linus	22_1840213	34.7%	DLEU2	Yes
J60	18_48600092	17.1%	CCND1	Yes
J60	25_34458017	25.9%	PEBP4	Yes
J60	4_14552338	9.8%	ZNF365	Yes
J60	18_48578102	4.3%	CCND1	No
J60	25_34548677	44.4%	PEBP4	Yes
HO2	10_19438765	2.0%	TBC1D22A	No
HO2	21_30040507	2.0 %	GVINP1	No

Supplementary Table 8. Calculated numbers of targeted AAV-host junctions in samples used for validation attempts.

Primer Target Site (Chromosome Position)	Direction	VCN	Relative Sonic Abundance	Abundance of Integration Per Nanogram DNA	Number of Integration Site Junctions in Reaction	Nanograms DNA in Reaction
25_34590970	Forward	0.27	0.285	13.99	165.0	11.8
25_34590970	Reverse	0.27	0.285	13.99	70.0	5.0
14_55620581	Forward	1.14	0.13	26.95	140.0	5.2
14_55620581	Reverse	1.14	0.13	26.95	70.0	2.6
15_42531469	Forward	1.14	0.073	15.13	140.0	9.3
15_42531469	Reverse	1.14	0.073	15.13	70.0	4.6
4_14832997	Forward	0.65	0.134	15.84	41.0	2.6
4_14832997	Reverse	0.65	0.134	15.84	27.0	1.7
4_14757686	Forward	0.65	0.106	12.53	41.0	3.3
4_14757686	Reverse	0.65	0.106	12.53	41.0	3.3
12_38081605	Forward	0.65	0.173	20.45	41.0	2.0
12_38081605	Reverse	0.65	0.173	20.45	41.0	2.0
4_14709696	Forward	0.42	0.362	27.64	37.6	1.4
4_14709696	Reverse	0.42	0.362	27.64	37.6	1.4
4_14733827	Forward	0.54	0.203	19.93	82.0	4.1
4_14733827	Reverse	0.54	0.203	19.93	82.0	4.1
25_34587602	Forward	0.54	0.214	21.01	82.0	3.9
25_34587602	Reverse	0.54	0.214	21.01	52.0	2.5
37_13443531	Forward	0.14	0.151	3.84	15.0	3.9
37_13443531	Reverse	0.14	0.151	3.84	31.0	8.1
4_14681249	Forward	0.62	0.067	7.55	31.0	4.1
4_14681249	Reverse	0.62	0.067	7.55	31.0	4.1
18_48493167	Forward	0.62	0.043	4.85	2.5	0.5
18_48493167	Reverse	0.62	0.043	4.85	2.5	0.5
22_1840213	Forward	0.62	0.347	39.12	103.00	2.6
22_1840213	Reverse	0.62	0.347	39.12	103.00	2.6
18_48600092	Forward	7.28	0.171	226.34	1150.0	5.1
18_48600092	Reverse	7.28	0.171	226.34	1150.0	5.1
25_34458017	Forward	3.06	0.259	144.10	600.0	4.2
25_34458017	Reverse	3.06	0.259	144.10	600.0	4.2
4_14552338	Forward	1.33	0.098	23.70	113.0	4.8
4_14552338	Reverse	1.33	0.098	23.70	370.0	15.6
18_48578102	Forward	1.33	0.043	10.40	5.0	0.5
18_48578102	Reverse	1.33	0.043	10.40	5.0	0.5
25_34548677	Forward	1.33	0.444	107.37	226.00	2.1
25_34548677	Reverse	1.33	0.444	107.37	226.00	2.1
10_19438765	Forward	0.27	0.02	0.98	3.8	3.9
10_19438765	Reverse	0.27	0.02	0.98	3.8	3.9
21_30040507	Forward	0.27	0.02	0.98	3.8	3.9
21_30040507	Reverse	0.27	0.02	0.98	3.8	3.9

Supplementary Table 9. KEGG pathway enrichment analysis.

Term ID	Protein	Hits	p Value*	p Value FDR**	Term Description
04520	70	5	0.0000	0.0001	Adherens junction
05218	69	4	0.0000	0.0009	Melanoma
05100	73	4	0.0000	0.0009	Bacterial invasion of epithelial cells
05200	320	6	0.0001	0.0025	Pathways in cancer
04330	47	3	0.0002	0.0039	Notch signaling pathway
04310	135	4	0.0003	0.0041	Wnt signaling pathway
05166	250	5	0.0003	0.0041	HTLV-I infection
05161	139	4	0.0003	0.0041	Hepatitis B
04390	146	4	0.0003	0.0044	Hippo signaling pathway
05203	181	4	0.0008	0.0089	Viral carcinogenesis
05215	85	3	0.0010	0.0092	Prostate cancer
04151	336	5	0.0010	0.0092	PI3K-Akt signaling pathway
01100	1161	9	0.0011	0.0092	Metabolic pathways
04510	202	4	0.0012	0.0092	Focal adhesion
04015	204	4	0.0012	0.0092	Rap1 signaling pathway
04919	115	3	0.0023	0.0166	Thyroid hormone signaling pathway
04530	127	3	0.0031	0.0206	Tight junction
05206	143	3	0.0043	0.0272	MicroRNAs in cancer
04630	154	3	0.0053	0.0317	Jak-STAT signaling pathway
05014	50	2	0.0059	0.0317	Amyotrophic lateral sclerosis (ALS)
05213	50	2	0.0059	0.0317	Endometrial cancer
00330	57	2	0.0076	0.0374	Arginine and proline metabolism
05131	57	2	0.0076	0.0374	Shigellosis
05211	64	2	0.0095	0.0439	Renal cell carcinoma
04144	192	3	0.0097	0.0439	Endocytosis
04115	66	2	0.0101	0.0439	p53 signaling pathway
04917	69	2	0.0110	0.0460	Prolactin signaling pathway
04810	208	3	0.0121	0.0477	Regulation of actin cytoskeleton
03008	73	2	0.0122	0.0477	Ribosome biogenesis in eukaryotes

* KEGG enrichment computed using a hypergeometric test
**False discovery rate (FDR) calculated using the Benjamini-Hochberg procedure

Supplementary Table 10. Integration site clusters identified using Scan Statistics (FDR 0.2; length <0.5Mb)

Chromosome	Start	End	Width	Gene	Hits*
4	14530145	14924592	394448	EGR2	7
4	39589684	39589877	194	DUSP1	26
13	62155847	62632404	476558	ALB	5
18	48484014	48821243	337230	CCND1	14
25	34458017	34601125	143109	EGR3	15

* Number of calls against 50 random sets

Supplementary Table 11. Primer sequences for integration site experiments.

Primer (Validation Primers Listed as Target Site Chromosome Position)	Direction	Sequence
PCR1 linker primer	Forward	GCCATGCTACTTATCTACGTAGCCATGC
PCR2 linker primer	Forward	GGTTCCTTGTAGTTAATGATTAACCCGCC
ITR inner boundary primer	Reverse	AGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTTGTAGT TAATGATTAACCCGCCATGCTACTTATCTACGTAGCCATGC
SEQ primer	N/A	CCTTGTAGTTAATGATTAACCCGCC
25_34590970	Forward	CCACTCGCGAAGAACTCCG
25_34590970	Reverse	CGACGTCACAATGGAAGCTCC
14_55620581	Forward	CTCCAGCACGTGACTACACC
14_55620581	Reverse	GACCACAGTTTAAACTGGAAAGGTCTATGG
15_42531469	Forward	GCCTCAGTCAGTGAAGAATCTGC
15_42531469	Reverse	GGAGTCTGCAACAATAGTCTTCATTGTTGG
4_14832997	Forward	GGCAAAGGAGCAACATGATCAGG
4_14832997	Reverse	CGGACAGTGAGTTCTTAGATGGGC
4_14757686	Forward	CCCATCTATTCAAAATTGCTAACAGTATCTTTCATGG
4_14757686	Reverse	GTCACATTCTGAAGAACCAGGGTTAGG
12_38081605	Forward	GCAGGATTGCAGGATACTAGGC
12_38081605	Reverse	CTACATCAAGAATCTCTCTCCCATGTTCC
4_14709696	Forward	ATCCAACAAATAAAACTAGCAAACAAGTTGCTGG
4_14709696	Reverse	GTATGCAAATCGGCCATGTGACG
4_14733827	Forward	CCAAGGAGGTTGCAGAAGAGG
4_14733827	Reverse	CAGTGAAAAGGGTACGTGCAAGG
25_34587602	Forward	CCTTGGCATTCTCACCTGAGC
25_34587602	Reverse	GCTGCCTCTGTAAGCAGGG
37_13443531	Forward	GCTAACAACTTTTGGAAATAGGGGAATGG
37_13443531	Reverse	CTATTATCAGGGTTTTGCGAGGATAGCC
4_14681249	Forward	GGAAATTAGACCTTTCTCTGATGTGTCAATTGC
4_14681249	Reverse	CTATTCAAAAGTTTGTCCAATAGCCACATGC
18_48493167	Forward	GTTGACCAGAGACAGGTGGG
18_48493167	Reverse	GTATCGCCCGAGACAGAACC
22_1840213	Forward	GAGAGACGGAGAGCCTATCAAGC
22_1840213	Reverse	CTGAGAACCAGTGGACTTAGGTATATTTACCC
18_48600092	Forward	CCTGGGGAGAATGTATCTAGTGGG
18_48600092	Reverse	CCGGGCACCTCTGTAACC
25_34458017	Forward	GCATGTGCATGACACTTAGATGGG
25_34458017	Reverse	CACAGCAAGTGGATGCAGAGC
4_14552338	Forward	CACAGTGTGGGTACACACTCC
4_14552338	Reverse	CAAGCTTGCCTGTGACCATCC
18_48578102	Forward	CAGCCAGGACGTATGAACAGG
18_48578102	Reverse	CAGATGGACACACAGCAGTGG
25_34548677	Forward	GGTTTCACAGAACCGCCAGG
25_34548677	Reverse	GGCTTCCATACTCAGCTCTAGTGG
10_19438765	Forward	GCCCAGAGCCCATCTTACC
10_19438765	Reverse	GCCGGAGTCTCTTGACAGG
21_30040507	Forward	CCACAGTTGTCCCTGAAGGG
21_30040507	Reverse	GTCCATGGCCTGTGTCAGC
AAV ITR Primer	N/A	GCATGGCTACGTAGATAAGTAGCATGG

Supplementary Table 12. Integration sites in the dog genome that were recovered from two or more cells independently (sonic abundance of two or more).

Dog	Timepoint	Position	Abundance	ITR Remnant length	Nearest Gene	Distance	Nearest oncogene	Distance	Validated
J60	y9.5	chr25-34548677	130	39	PEBP4	0	EGR3	-42611	Sanger/Long PCR
Linus	y10	chr22-1840213	118	16	DLEU2,DLEU2L	0	DLEU2	0	Nextera
M50	y7	chr25-34590970	87	59	EGR3	-318	EGR3	-318	Nextera
J60	y9.5	chr18*48600108	59	63	CCND1	-90384	CCND1	-90384	Sanger/Long PCR
Linus	y10	chr25-34587602	54	58	EGR3	-3686	EGR3	-3686	Nextera
Linus	y10	chr25*34591227	54	43	EGR3	-100	EGR3	-100	NA
Linus	y10	chr25+34592325	50	56	EGR3	0	EGR3	0	NA
J60	y9.5	chr25-34458017	48	64	PEBP4	0	RHOBTB2	-128882	Sanger/Long PCR
Linus	y10	chr17*49576466	47	76	ALMS1,EGR4	0	LOXL3	965375	NA
Linus	y10	chr4+14733827	44	37	EGR2	-21855	EGR2	-21855	Sanger
M50	y7	chr12+38081605	37	44	RPLP0P2	674	PHIP	1816387	Short PCR
M50	y7	chr25-34591015	31	127	EGR3	-273	EGR3	-273	NA
J60	y9.5	chr4+14552338	30	67	ZNF365	0	EGR2	153044	Sanger/Long PCR
Linus	y10	chr37+13443531	28	41	PARD3,PARD3B	0	RAPH1	-1097001	Nextera
M50	y7	chr14-55620581	28	62	MET	-5864	MET	-5864	Sanger
Linus	y10	chr25+34592334	27	65	EGR3	0	EGR3	0	NA
J60	y9.5	chr4+14731055	26	72	EGR2	-19083	EGR2	-19083	NA
M50	y7	chr4-14832997	26	67	EGR2	-121025	EGR2	-121025	Sanger
M50	y7	chr4*14757682	24	127	EGR2	-45706	EGR2	-45706	Nextera
Linus	y10	chr4-14799029	23	53	EGR2	-87057	EGR2	-87057	NA
Linus	y10	chr23+25225414	22	64	TBC1D5	0	SATB1	530445	NA
J60	y9.5	chr4+14789031	21	61	EGR2	-77059	EGR2	-77059	NA
Linus	y10	chr4+14681204	21	26	ADO	-17060	EGR2	24178	Failed
M50	y7	chr4*14801145	20	51	EGR2	-89160	EGR2	-89160	Failed
M50	y7	chr15+42531619	19	44	GLT8D2	0	HSP90B1	57500	NA
M66	y6	chr4+14709696	18	61	EGR2	0	EGR2	0	Long PCR
Linus	y10	chr4-14712837	17	80	EGR2	-865	EGR2	-865	NA
Linus	y10	chr18*48556878	16	89	CCND1	-47154	CCND1	-47154	NA
M50	y7	chr15-42531469	16	66	GLT8D2	0	HSP90B1	57350	Nextera
Linus	y10	chr23+43995528	14	70	CP	0	HLTF	-76924	NA
M50	y7	chr4-14598472	14	61	ZNF365	13629	EGR2	106910	NA
M66	y6	chr4+14710334	14	64	EGR2	0	EGR2	0	NA
Linus	y10	chr18+48493167	13	33	LTO1	3195	CCND1	5806	Long PCR
Linus	y10	chr4+14732408	13	70	EGR2	-20436	EGR2	-20436	NA
M50	y7	chr4+14714125	13	64	EGR2	-2153	EGR2	-2153	NA
J60	y9.5	chr18*48578093	12	70	CCND1	-68377	CCND1	-68377	Failed
Linus	y10	chr4+14759642	12	36	EGR2	-47670	EGR2	-47670	NA
J60	y9.5	chr4+14802452	11	73	EGR2	-90480	EGR2	-90480	NA
Linus	y10	chr25+34591807	10	37	EGR3	0	EGR3	0	NA
Linus	y10	chr21-39487582	10	45	PLEKHA7	0	MYOD1	-770244	NA
Linus	y10	chr5-78404628	10	61	ZFHX3	46069	ZFHX3	46069	NA
J60	y9.5	chr4+14849034	9	63	NRBF2	-109158	EGR2	-137062	NA
J60	y9.5	chr18-48785343	9	64	TPCN2	167424	CCND1	-275635	NA
Linus	y10	chr18-48501832	9	54	CCND1	0	CCND1	0	NA
M50	y7	chr18+48484620	9	21	LTO1	0	CCND1	14353	NA
Linus	y10	chr25+34591962	7	42	EGR3	0	EGR3	0	NA
Linus	y10	chr18-48760360	7	66	TPCN2	192407	CCND1	-250652	NA
M06	y2	chr12-53183015	7	62	CELF4	0	EPHA7	-877840	NA
M50	y7	chr4-14832991	7	67	EGR2	-121019	EGR2	-121019	NA
J60	y9.5	chr4+14563609	6	47	ZNF365	0	EGR2	141773	NA
J60	y9.5	chr4+14711850	6	65	EGR2	0	EGR2	0	NA
J60	y9.5	chr3+2490737	5	72	MAN2A1	-13287	APC	-2110233	NA
Linus	y10	chr18+48493174	5	33	LTO1	3202	CCND1	5799	NA
M50	y7	chr4-14709564	5	31	EGR2	0	EGR2	0	NA
H19	y8.5	chr32-4667479	4	71	CFAP299	0	FGF5	134689	NA
Linus	y10	chr18+48501970	4	71	CCND1	0	CCND1	0	NA
Linus	y10	chr13-21450894	4	41	DERL1	0	RNF139	-1108984	NA
Linus	y10	chr4-14709639	4	43	EGR2	0	EGR2	0	NA
Linus	y10	chr4+14782170	4	55	EGR2	-70198	EGR2	-70198	NA
M06	y2	chr4-39589762	4	67	DUSP1	0	MIXL1	-165217	NA
M50	y7	chr18-48543799	4	47	CCND1	-34091	CCND1	-34091	NA
M50	y7	chr18-48623683	4	36	CCND1	-113975	CCND1	-113975	NA
H19	y8.5	chr8+72693342	3	61	JAG2,PACS2,TMEM	0	JAG2	0	NA
J60	y9.5	chr18+48736726	3	64	TPCN2	216041	CCND1	-227018	NA
J60	y9.5	chr11*26044659	3	64	EGR1	-1288	EGR1	-1288	NA
J60	y9.5	chr15+6230997	3	50	AGO3	0	THRAP3	-208604	NA
J60	y9.5	chr18+48500622	3	71	CCND1	0	CCND1	0	NA
J60	y9.5	chr2*32199118	3	69	PITRM1	0	KLF6	535042	NA
J60	y9.5	chr4-14789791	3	54	EGR2	-77819	EGR2	-77819	NA
Linus	y10	chr4-14785464	3	26	EGR2	-73492	EGR2	-73492	NA
Linus	y10	chr4-14713726	3	65	EGR2	-1754	EGR2	-1754	NA
Linus	y10	chr18-48584297	3	52	CCND1	-74589	CCND1	-74589	NA
Linus	y10	chr18*48722018	3	67	CCND1	-212308	CCND1	-212308	NA
Linus	y10	chr18+48584456	3	69	CCND1	-74748	CCND1	-74748	NA
Linus	y10	chr25-30507351	3	32	STMN4	155046	CLU	506629	NA
M50	y7	chr21-6506179	3	64	MRE11	0	MRE11	0	NA
M50	y7	chr25-34590999	3	40	EGR3	-289	EGR3	-289	NA
M50	y7	chr7+67593155	3	58	YES1	0	YES1	0	NA
M50	y7	chrX+71350380	3	19	ACTN1	230697	HNRNPK	-1711394	NA
M50	y7	chr2-66688859	3	70	SIAH1	-16203	ZNF423	908202	NA
M50	y7	chr18-48513636	3	41	CCND1	-3928	CCND1	-3928	NA
M50	y7	chr4-14788834	3	71	EGR2	-76862	EGR2	-76862	NA
M66	y6	chr4*14722170	3	22	EGR2	-10148	EGR2	-10148	NA
H19	y8.5	chr1-45651422	2	61	LOC105378068	398922	ARID1B	-719139	NA
H19	y8.5	chr10-45097655	2	35	FAM178B	0	CNNM4	59781	NA

H19	y8.5	chr15+39094941	2	74	ANKS1B	0	APAF1	977914	NA
H19	y8.5	chr30-23830049	2	21	MINDY2	2558	GCNT3	-654693	NA
H19	y8.5	chr33+11774631	2	67	CBLB	-302183	CBLB	-302183	NA
H19	y8.5	chr36-24205150	2	63	UBE2E3,UBE2E4P	0	PDE11A	-2475504	NA
H19	y8.5	chr9-36088961	2	28	C17orf64	-6674	USP32	-79132	NA
H19	y8.5	chr1+116987164	2	46	RBM42	-1439	FXYD5	425710	NA
H19	y8.5	chr1+116987171	2	46	RBM42	-1446	FXYD5	425703	NA
H19	y8.5	chr10+1129800	2	76	SDR9C7	-9069	NAB2	-96754	NA
H19	y8.5	chr2+73264837	2	65	GPN2	3291	ZDHHC18	9346	NA
H19	y8.5	chr34+21096771	2	50	LPP	0	LPP	0	NA
H19	y8.5	chr5+61633275	2	73	ERRFI1	0	ERRFI1	0	NA
H19	y8.5	chr7-40039717	2	13	NVL	-2038	TP53BP2	-256559	NA
H19	y8.5	chr7+61474770	2	69	CHST9	-96960	SS18	-1016075	NA
H19	y8.5	chr8-7267761	2	68	AK3	-161625	FOXG1	-1010286	NA
H19	y8.5	chr9+4143400	2	49	ST6GALNAC2	-14478	ST6GALNAC1	19437	NA
H19	y8.5	chr1+38773155	2	38	SAMD5	203006	LATS1	1656972	NA
J60	y9.5	chr1-86823525	2	66	TRPM3	0	HMGN2P46	-373233	NA
J60	y9.5	chr10-331748	2	69	SUOX	0	ERBB3	-8201	NA
J60	y9.5	chr18+48736654	2	41	TPCN2	216113	CCND1	-226946	NA
J60	y9.5	chr34+38763204	2	27	NAALADL2	0	ECT2	1803894	NA
J60	y9.5	chr36-9749057	2	61	GRB14	0	LRP2	4161391	NA
J60	y9.5	chr4*14701825	2	76	ADO	0	EGR2	3561	NA
J60	y9.5	chr4-14924592	2	62	NRBF2	-33600	EGR2	-212620	NA
J60	y9.5	chr4+14715301	2	62	EGR2	-3329	EGR2	-3329	NA
J60	y9.5	chr13+62168428	2	61	ALB	0	RASSF6	130134	NA
J60	y9.5	chr18-44600867	2	58	CD82	57628	CD82	57628	NA
J60	y9.5	chr18-48821243	2	75	TPCN2	131524	MAP2K1	258795	NA
J60	y9.5	chr4*14641819	2	65	ADO	-56469	EGR2	63587	NA
J60	y9.5	chr4-14713052	2	59	EGR2	-1080	EGR2	-1080	NA
J60	y9.5	chr4-14841073	2	27	NRBF2	-117119	EGR2	-129101	NA
J60	y9.5	chr4+14805710	2	53	EGR2	-93738	EGR2	-93738	NA
J60	y9.5	chr8-3461643	2	72	SLC7A8	0	BCL2L2	-107759	NA
Linus	y10	chr10+34424210	2	27	SH3RF3	0	RANBP2	662940	NA
Linus	y10	chr18-48645201	2	16	CCND1	-135493	CCND1	-135493	NA
Linus	y10	chr2-20988823	2	63	MINDY3	0	CUBN	947319	NA
Linus	y10	chr2+59618697	2	64	MT3	6153	AMFR	-149364	NA
Linus	y10	chr22+2544527	2	68	FNDC3A	0	RB1	517092	NA
Linus	y10	chr25-34591177	2	43	EGR3	-111	EGR3	-111	NA
Linus	y10	chr12-15583942	2	64	CD2AP	0	RUNX2	1740306	NA
Linus	y10	chr14-15091597	2	65	ZNF804B	0	SRI	-817304	NA
Linus	y10	chr18+48491590	2	54	LTO1	1618	CCND1	7383	NA
Linus	y10	chr25+34592383	2	40	EGR3	0	EGR3	0	NA
Linus	y10	chr30+16775516	2	12	AP4E1	0	CYP19A1	178885	NA
Linus	y10	chr1-118074774	2	44	LSM14A	0	FXYD5	-650607	NA
Linus	y10	chr11-26058613	2	61	EGR1	8808	EGR1	8808	NA
Linus	y10	chr18*48522347	2	55	CCND1	-12627	CCND1	-12627	NA
Linus	y10	chr18+48771203	2	29	TPCN2	181564	CCND1	-261495	NA
Linus	y10	chr22-1840015	2	38	DLEU2,DLEU2L	0	DLEU2	0	NA
Linus	y10	chr30+2461957	2	59	GJD2	15390	GREM1	-230128	NA
Linus	y10	chr4+14753192	2	75	EGR2	-41220	EGR2	-41220	NA
M06	y2	chr1-110141910	2	65	ERCC1,GPR68	0	ERCC1,GPR68	0	NA
M06	y2	chr12-25761444	2	61	KHDRBS2	0	DST	-1566251	NA
M06	y2	chr15+35765032	2	73	HAL	1609	ELK3	-185502	NA
M06	y2	chr18-9500676	2	62	SUGCT	0	RALA	521817	NA
M06	y2	chr21-999882	2	75	LYAR	-28458	MAML2	-3823223	NA
M06	y2	chr26-13854842	2	107	NOS1	0	PEBP1	-667262	NA
M06	y2	chr28-15948142	2	61	SH3PXD2A	0	SUFU	832642	NA
M06	y2	chr3+74490062	2	39	RELL1	-3132	KLF3	-826168	NA
M06	y2	chr34+17067867	2	53	DVL3	0	PSMD2	-112224	NA
M06	y2	chr37-18405952	2	83	CPS1	0	ERBB4	623748	NA
M06	y2	chr4-39589745	2	62	DUSP1	0	MIXL1	-165200	NA
M06	y2	chr4-39589762	2	56	DUSP1	0	MIXL1	-165217	NA
M06	y2	chr4+73281440	2	59	PRLR	0	PRLR	0	NA
M06	y2	chr13-18262892	2	68	LOC101927513	17962	TNFRSF11B	-97856	NA
M06	y2	chr14+21392553	2	52	SLC25A13	0	TAC1	-1239456	NA
M06	y2	chr15+24557055	2	63	TMTC2	-72116	PAWR	-2403627	NA
M06	y2	chr17-58827471	2	66	PDZK1P1	0	PIAS3	-166716	NA
M06	y2	chr26+31747628	2	62	NEB	-343531	MAPK1	-614608	NA
M06	y2	chr28+10665763	2	45	RRP12	6319	FRAT1	27302	NA
M06	y2	chr31+29963191	2	74	RCAN1	0	RUNX1	203171	NA
M06	y2	chr35-19969893	2	52	LINC00581	37319	SOX4	-129023	NA
M06	y2	chr4-14746313	2	59	EGR2	-34341	EGR2	-34341	NA
M06	y2	chr4+39589807	2	61	DUSP1	0	MIXL1	-165262	NA
M06	y2	chr7-33241851	2	26	EXO1	0	FH	-314393	NA
M06	y2	chr1-42417078	2	67	SYNE1	0	SYNE1	0	NA
M06	y2	chr10-60378614	2	25	MIR4432HG	124107	BCL11A	209642	NA
M06	y2	chr11-27813251	2	46	KDM4C	0	KDM4C	0	NA
M06	y2	chr14-35388428	2	45	SP4	0	ABCB5	627021	NA
M06	y2	chr15-54263444	2	62	PDGFC	-23558	FBXW7	-3846235	NA
M06	y2	chr15+3625821	2	69	MACF1	0	MACF1	0	NA
M06	y2	chr20+17342340	2	67	AIMP1	-165032	CHL1	-357318	NA
M06	y2	chr23+8622032	2	23	SCN11A	0	XIRP1	227676	NA
M06	y2	chr28-5033380	2	65	KIF20B	362621	RET	-1039184	NA
M06	y2	chr32+10633798	2	59	AFF1	2387	AFF1	2387	NA
M50	y7	chr20-54608016	2	72	PTPRS	0	RFX2	496323	NA
M50	y7	chr22+50166197	2	61	PCCA	0	FGF14	1213603	NA
M50	y7	chr32-29986493	2	69	CFI	-622	EGF	-87256	NA
M50	y7	chr33+25455439	2	50	CASR	21486	CSTA	-22619	NA
M50	y7	chr4-17787487	2	20	CTNNA3	0	SIRT1	-1401120	NA
M50	y7	chr4+14711817	2	70	EGR2	0	EGR2	0	NA

M50	y7	chr6-65773858	2	67	ADGRL2	0	ADGRL2	0	NA
M50	y7	chr14+22874727	2	127	C1GALT1	0	COL28A1	118443	NA
M50	y7	chr25+34601125	2	70	EGR3	3980	EGR3	3980	NA
M50	y7	chr33+29230184	2	44	TFRC	0	TFRC	0	NA
M50	y7	chr38-1772649	2	17	TMCC2	0	RBBP5	-126482	NA
M50	y7	chr5-78694771	2	80	HCCAT5	-27367	ZFHX3	-84743	NA
M50	y7	chr6+17876405	2	65	PRRT2	0	MVP	-9712	NA
M50	y7	chr10-24124521	2	56	XPNPEP3,EP300	0	EP300	0	NA
M50	y7	chr14-1871659	2	25	OR2L5,OR2L3,OR2L	179566	WNT3A	-963029	NA
M50	y7	chr27+40595108	2	23	CCND2-AS1	0	CCND2-AS1	0	NA
M50	y7	chr28+15144698	2	43	ARL3	5147	SUFU	29198	NA
M50	y7	chr34-32001200	2	67	ZBBX	169637	MECOM	1746286	NA
M50	y7	chr4-14713093	2	62	EGR2	-1121	EGR2	-1121	NA
M50	y7	chr4+39589852	2	38	DUSP1	0	MIXL1	-165307	NA
M50	y7	chr4+65891299	2	13	FGF10	0	FGF10	0	NA
M50	y7	chr6-5975701	2	73	GTF2IRD1	-11819	LIMK1	287670	NA
M50	y7	chr8-38607187	2	73	SYNE2	0	SYNE2	0	NA
M66	y6	chr10-43140250	2	71	AFF3	25562	AFF3	25562	NA
M66	y6	chr15-56522259	2	67	HOXD-AS2	22810	EEF1A1	2330802	NA
M66	y6	chr16-18834023	2	67	SHH	-170782	SHH	-170782	NA
M66	y6	chr23+43994847	2	61	CP	0	HLTF	-76243	NA
M66	y6	chr3+48777081	2	62	SV2B	0	AKAP13	-214358	NA
M66	y6	chr32+3027326	2	57	ANXA3	0	FGF5	-1481518	NA
M66	y6	chr16+45738385	2	65	ACSL1	-14656	SORBS2	675110	NA
M66	y6	chr37+13896954	2	57	PARD3,PARD3B	0	ADAM23	-1099909	NA
M66	y6	chr37+169848	2	50	WDR75	0	KDM3A	45767	NA
M66	y6	chr5+41957696	2	21	PEMT	0	EWSR1	-182944	NA
M66	y6	chr15-42495602	2	42	TDG	0	HSP90B1	21483	NA
M66	y6	chr25-43821788	2	31	DIS3L2	0	PTMA	253801	NA
M66	y6	chr28+35981345	2	17	DOCK1	0	ADAM12	-496135	NA
M66	y6	chr8+33570819	2	45	ACTR10	-4588	ARID4A	-90734	NA

AAV Vector Sequences

Single Chain Vector

CAGCTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGT
GAGCGAGCGAGCGCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTTGTAGTTAATGATTAACCCGCCATGCT
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GGAATTTCGGTGGAGAGGAGCAGAGGTTGTCCTGGCGTGGTTTAGGTAGTGTGAGAGGGGAATGACTCCTTTCGGTAAGT
GCAGTGGAAGCTGTACACTGCCCAGGCAAAGCGTCCGGGCAGCGTAGGCGGGCGACTCAGATCCCAGCCAGTGGACTTAG
CCCCTGTTTGCTCCTCCGATAACTGGGGTGACCTTGGTTAATATTCACCAGCAGCCTCCCCCGTTGCCCCTCTGGATCCA
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Heavy Chain Vector

CAGCTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGT
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Light Chain Vector

CAGCTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGT
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