Genetic Diversity Testing for American Hairless Terrier

Overview

The Veterinary Genetics Laboratory (VGL), in collaboration with Dr. Niels C. Pedersen and staff, has developed a panel of short tandem repeat (STR) markers to determine genetic heterogeneity and diversity across the genome and in the Dog Leukocyte Antigen (DLA) class I and II regions for specified dog populations. This test panel is useful to dog breeders who wish to use DNA-based testing to track and distribute genetic diversity as a supplement to in-depth pedigrees. Information on genetic heterogeneity and diversity, along with DNA testing results for desired phenotypes and health traits, can aid in informing breeding decisions in order to improve the overall genetic health of a breed.

Genetic diversity testing in the American Hairless Terrier has been established, and almost all existing alleles at the 33 STR loci and 7 DLA class I and II regions have potentially been identified. As of December of 2022, 179 American Hairless Terriers from the United States (n = 147), Czech Republic (n = 21), Finland (n = 6), and Belgium (n = 5) were tested to assess genetic diversity in the breed. Allele and DLA haplotype frequencies will be updated as more dogs are tested.

Results reported as:

Short tandem repeat (STR) loci: A total of 33 STR loci from different regions of the genome were used to assess genetic heterogeneity and existing genetic diversity within an individual as well as across the breed. The alleles inherited from each parent are displayed graphically to highlight heterozygosity and genetic diversity in individuals as well as breed-wide.

DLA haplotypes: Seven STR loci linked to DLA class I and II genes were used to assess genetic diversity within a region that regulates immune responses and self/non-self-recognition. Problems with self/non-self-recognition, along with environmental factors, are responsible for autoimmune disease, allergies, and susceptibility to infectious agents.

Internal Relatedness (IR): The IR value is a measure of the genetic relatedness of an individual's parents. The value takes into consideration both heterozygosity of alleles at each STR loci and their relative frequency in the population. Therefore, IR values heterozygosity over homozygosity and uncommon alleles over common alleles. IR values are unique to each dog; two individuals from different sources may have identical IR values, but a quite different genetic makeup.

I. Introduction to the American Hairless Terrier

A. Breed History [1-3]

The American Hairless Terrier originated in Louisiana in 1972 as a natural variation of the Rat Terrier, being the only hairless dog breed native to the United States. That year, a hairless bitch pup was born in a litter of purebred Rat Terriers. The bitch, named Josephine, was owned by Edwin and Willie Scott from Trout, Louisiana. Josephine's first litter contained another hairless bitch pup, Gypsy. For eight years thereafter, neither bitch produced another hairless puppy, when in 1981, Josephine (then 9 years old) produced two hairless pups: a male (Snoopy) and a female (Jemima) (**Figure 1**). In 1983, the Scotts bred Snoopy to his hairless sister and several hairless puppies were born, establishing the foundation stock for the breed. In 1999, the Rat Terrier sought United Kennel Club (UKC) recognition as a breed, and the hairless variety was accepted alongside their parent breed at that time. The American Hairless Terrier was the Hairless Variety of the Rat Terrier until 2004, when the American Hairless Terrier officially separated from the Rat Terrier. All "Rat Terriers" with any known hairless relatives were officially re-registered as American Hairless Terriers (coated/hairless variety) at that time. The American Hairless Terrier Club of America was established in 2009, with American Kennel Club (AKC) Foundation Stock Service (FSS) recognition in 2011 followed by full AKC recognition in 2016. As of 2021, the breed ranked 135 of 284 in popularity among the AKC registries.

Figure 1. The American Hairless Terrier foundation dogs (from left to right): Jemima, Josephine, Snoopy, and Gypsy

B. Appearance [1-3]

The American Hairless Terrier is small to medium sized, with an ideal height between 12 and 16 inches although breed standard does not disqualify or fault dogs that are over/under "ideal" height. Their weight ranges from 12 to 32lbs, with an average weight of 15-23 lbs. They can come in both coated and hairless varieties – hairless dogs can have eyebrows and whiskers, while the coated variety has a short, smooth, dense, and shiny coat. Their body is rectangular, being slightly longer than tall (10:9 ratio). The skull is broad and tapers slightly toward the muzzle; skull and muzzle

are of equal length. The nose is solid-colored; eye color varies from darkest brown to amber and hazel. Blue eyes are acceptable in blue or blue fawn dogs, but gray is preferred. The ears are set at the outside edge of the skull and V-shaped. While erect ear are preferred, button and tipped are acceptable. Ear carriage must match.

Hairless puppies are born with a soft coat called "birth coat", which disappears around 8-10 weeks of age. An adult hairless dog should be completely devoid of hair except for whiskers and guard hairs on the eyebrows and muzzle. Their skin is smooth and warm to the touch. In the coated variety, dogs are covered with a smooth, short and dense coat. Any color or combination of colors is allowed in the American Hairless Terrier, except for albino and merle.

Disqualifications include: hanging ears; bobtail or docked tail in the hairless variety; wire, broken or long coat in the coated variety; merle coat color; albinism.

C. Temperament [1-4]

The American Hairless Terrier is alert, curious and intelligent. Aggressiveness or extreme shyness are not desirable. The breed gets along well with children when socialized properly/early with them; dogs that were not raised with kids typically do not tolerate them well. They are well adapted to life indoors, but enjoy spending time outdoors. It is advised to protect hairless individuals from sun exposure (sunscreen/clothing), but coated dogs have no limitation on that. American Hairless Terriers may not require the same amount of exercise as some breeds, but they are outstanding athletes and excel at a wide variety of performance events including agility, lure coursing, barn hunt, scent work, etc.

D. Health

1. Lifespan

The American Hairless Terrier is a generally healthy breed, with a lifespan of 12 to 15 years.

2. Diseases

Reports indicate that the incidence of Microvascular Dysplasia (MVD) has been increasing in the breed. Currently, a minimum of 27% of all American Hairless Terriers have MVD according to serum bile acid (SBA) testing, with another 22% falling in the equivocal range (diagnosis is confirmed via 3 lobe liver biopsy). Additionally, 2% have confirmed shunt.

The American Hairless Terrier is a CHIC breed with OFA. For CHIC certification of breeding stock, not all results need to be normal, but they must all be in the public domain. This way, responsible breeders can make informed breeding decisions based on test results. The following basic health screening tests are recommended for all American Hairless Terrier breeding stock:

a. Cardiac Evaluation – one of the following: congenital cardiac exam, basic cardiac exam, or advanced cardiac exam;
b. Hip Dysplasia – one of the following: OFA evaluation or PennHIP evaluation;

c. Patellar Luxation – OFA evaluation;
d. Legg-Calve-Perthes Disease – OFA evaluation;
e. Congenital Deafness – OFA evaluation based on BAER test;
f. Primary Lens Luxation – DNA-based PLL test from an approved laboratory;
g. ACVO Eye Exam – optional: annual eye examinations until 8 years old;
h. Elbow Dysplasia – optional: OFA evaluation;
i. Progressive Retinal Atrophy (PRA) – optional: DNA based prcd-PRA test from an approved laboratory.

For a complete list of diseases that have been reported in the American Hairless Terrier, please visit https://ahtca.info/breed-health.html.

II. Results on Genetic Diversity of American Hairless Terriers

A. Population genetics based on 33 STR loci on 25 chromosomes

STR markers are highly polymorphic and have great power to determine genetic differences among individuals and breeds. The routine test panel contains 33 STRs consisting of those that are recommended for universal parentage determination for domestic dogs by the International Society of Animal Genetics (ISAG) and additional markers developed by the VGL for forensic purposes [5,6]. The average number of alleles identified per locus across the dog breeds tested at the VGL to date is 15.4 alleles/locus. Dog breeds, having evolved from a small number of founders and having been exposed to artificial population bottlenecks, will end up with only a portion of the total available genetic diversity found in canids. Artificial genetic bottlenecks can include phenomena such as sire effects, geographic isolation, catastrophes, outbreaks of disease, and variation in popularity, which can lead to a decrease in population size. The alleles identified at each of the 33 STR loci and their relative frequencies for the 179 American Hairless Terriers are listed on **Table 1**.

Table 1. Alleles and their frequencies for 33 STR markers in American Hairless Terriers (n=179). The allele that occurs at the highest frequency at each locus is bolded.

AHT121	AHT137	AHTH130	AHTh171-A	AHTh260	AHTk211
92 (0.078)	131 (0.190)	113 (0.123)	219 (0.056)	238 (0.176)	**87 (0.489)**
94 (0.095)	**133 (0.304)**	119 (0.254)	221 (0.003)	242 (0.142)	89 (0.358)
96 (0.070)	137 (0.257)	121 (0.061)	223 (0.003)	244 (0.117)	91 (0.115)
98 (0.056)	141 (0.067)	123 (0.034)	**225 (0.411)**	**246 (0.486)**	95 (0.031)
100 (0.047)	147 (0.142)	**125 (0.385)**	227 (0.003)	248 (0.025)	97 (0.008)
102 (0.374)	151 (0.039)	127 (0.089)	229 (0.352)	250 (0.034)	
104 (0.109)		129 (0.025)	233 (0.075)	252 (0.011)	
106 (0.156)		137 (0.028)	235 (0.070)	254 (0.008)	
108 (0.011)			237 (0.028)		
110 (0.003)					

AHTk253	C22.279	FH2001	FH2054	FH2848	INRA21
286 (0.075)	**116 (0.433)**	128 (0.003)	148 (0.162)	230 (0.006)	95 (0.154)
288 (0.369)	118 (0.204)	**132 (0.682)**	152 (0.168)	232 (0.059)	97 (0.064)
290 (0.204)	120 (0.017)	136 (0.006)	**156 (0.265)**	234 (0.008)	99 (0.263)
292 (0.349)	124 (0.156)	144 (0.084)	160 (0.159)	**236 (0.662)**	**101 (0.332)**
294 (0.003)	126 (0.168)	148 (0.064)	164 (0.115)	238 (0.056)	103 (0.042)
	128 (0.022)	152 (0.156)	168 (0.101)	240 (0.112)	105 (0.145)
		156 (0.006)	172 (0.014)	242 (0.042)	
			176 (0.017)	244 (0.056)	

INU005	INU030	INU055	LEI004	REN105L03	REN162C04
110 (0.031)	144 (0.223)	204 (0.034)	85 (0.115)	227 (0.003)	198 (0.025)
124 (0.637)	146 (0.056)	208 (0.014)	**95 (0.679)**	229 (0.053)	200 (0.008)
126 (0.268)	148 (0.025)	210 (0.173)	97 (0.067)	231 (0.168)	**202 (0.330)**
128 (0.053)	**150 (0.394)**	212 (0.159)	101 (0.020)	233 (0.025)	204 (0.285)
132 (0.011)	152 (0.031)	**214 (0.439)**	107 (0.120)	235 (0.159)	206 (0.265)
	156 (0.271)	216 (0.103)		237 (0.031)	208 (0.070)
		218 (0.056)		**239 (0.469)**	210 (0.017)
		220 (0.020)		241 (0.089)	
		222 (0.003)		245 (0.003)	

REN169D01	REN169O18	REN247M23	REN54P11	REN64E19	VGL0760
202 (0.073)	162 (0.011)	266 (0.168)	222 (0.117)	139 (0.017)	12 (0.173)
212 (0.081)	164 (0.148)	**268 (0.732)**	**226 (0.430)**	143 (0.045)	14 (0.003)
214 (0.039)	166 (0.008)	272 (0.101)	232 (0.098)	145 (0.142)	15 (0.006)
216 (0.709)	**168 (0.550)**		234 (0.142)	147 (0.229)	18.2 (0.151)
218 (0.070)	170 (0.282)		236 (0.047)	**149 (0.430)**	19.2 (0.142)
220 (0.028)			238 (0.165)	151 (0.003)	**20.2 (0.184)**
				153 (0.103)	21.2 (0.078)
				155 (0.003)	22.2 (0.067)
				157 (0.028)	23.2 (0.115)
					24.2 (0.050)
					25.2 (0.006)
					26.2 (0.025)

VGL0910	VGL1063	VGL1165	VGL1828	VGL2009	VGL2409
13 (0.025)	8 (0.006)	14 (0.025)	14 (0.070)	9 (0.204)	13 (0.003)
14 (0.475)	9 (0.031)	17 (0.047)	16 (0.036)	10 (0.106)	14 (0.047)
15 (0.014)	10 (0.003)	18 (0.008)	17 (0.047)	11 (0.008)	15 (0.226)
15.1 (0.008)	12 (0.081)	20 (0.003)	19 (0.260)	12 (0.031)	16 (0.237)
16.1 (0.031)	13 (0.162)	21 (0.330)	20 (0.070)	13 (0.115)	17 (0.168)
17.1 (0.081)	**14 (0.466)**	22 (0.047)	21 (0.034)	**14 (0.318)**	**18 (0.307)**
18.1 (0.022)	15 (0.045)	25 (0.036)	**22 (0.366)**	15 (0.218)	19 (0.011)
19.1 (0.140)	17 (0.142)	26 (0.025)	23 (0.117)		
20.1 (0.008)	18 (0.022)	27 (0.020)			

21.1 (0.020)	19 (0.006)	28 (0.006)
22.1 (0.036)	20 (0.034)	29 (0.003)
24.1 (0.006)	21 (0.003)	30 (0.034)
25.1 (0.047)		**31 (0.416)**
26.1 (0.087)		
VGL2918	**VGL3008**	**VGL3235**
12 (0.874)	15 (0.369)	13 (0.383)
13 (0.106)	16 (0.025)	14 (0.092)
15 (0.003)	17 (0.045)	15 (0.008)
16 (0.006)	**18 (0.447)**	**16 (0.413)**
17.3 (0.006)	19 (0.042)	17 (0.039)
18.3 (0.003)	20 (0.036)	18 (0.039)
21.3 (0.003)	21 (0.034)	19 (0.025)
	22 (0.003)	

Allele distribution within the 33 autosomal STR loci in the American Hairless Terrier is typical of most pure dog breeds, i.e., one or two alleles are observed at higher frequency than others (bold on **Table 1**). The number of alleles identified for each STR locus ranged from 3 (REN247M23) to 14 (VGL0910), with an average across loci of 7.61 alleles (**Table 2**). This figure corresponds to roughly half of the average number of alleles identified across dog breeds tested at the VGL (15.4 alleles/locus). Loss of alleles is a common feature of pure dog breeds, and reflects the small number of founders existing at the time a breed registry is closed which is the case of American Hairless Terriers. Another consequence of such bottleneck effect is the disproportionately high incidence of one or two alleles at some loci (**Table 1**). These high incidence alleles have been inherited by descent from founding dogs whose phenotypes (and consequently genotypes) were highly valued and therefore most conserved. A single allele occurred in 50% or more of the dogs tested at 8 of the 33 loci (**Table 1**), which suggests that these alleles were inherited from the foundation dogs and are linked to breed-defining phenotypic traits.

B. Assessment of population diversity using standard genetic parameters

Alleles for each of the 33 STR loci listed in Table 1 and their respective frequencies are used to determine basic genetic parameters for the population (**Table 2**). These parameters include the number of alleles found at each locus (**Na**); the number of effective alleles (**Ne**) per locus (i.e., the number of alleles that contribute most to genetic differences/heterozygosity); observed heterozygosity (**Ho**); expected heterozygosity (**He**) if the existing population was in Hardy-Weinberg equilibrium (i.e., randomly breeding); and the coefficient of inbreeding (**F**) derived from Ho and He values.

Table 2. Genetic Assessment of 179 American Hairless Terriers based on 33 autosomal STR loci. SE = standard error of the mean.

	Na	**Ne**	**Ho**	**He**	**F**
Mean	7.61	3.487	0.665	0.673	0.006
SE	0.42	0.213	0.022	0.023	0.01

The average number alleles (Na) known to exist at the 33 STR loci across breeds, based on all breeds tested at the VGL so far, is 15.4 (see section IIA). In American Hairless Terriers, this number was estimated at 7.61 (**Table 2**), which is higher than several other pure breeds. Therefore, approximately half of the known canid diversity has been retained during breed evolution. However, the average number of effective alleles (Ne) constitutes a more important metric for diversity, since these alleles have the greatest genetic influence on heterozygosity. This number was estimated at 3.487 in the American Hairless Terrier, again higher than many pure breeds that have been studied to this point. Additionally, this value indicates that the bulk of genetic diversity was determined by approximately 50% of the alleles segregating in the breed. This is typical for most pure dog breeds. The values for Ho (0.665) and He (0.673) were not significantly different from each other, yielding a breed-wide coefficient of inbreeding (F) close to zero (0.006). Therefore, standard genetic assessment values indicate that American Hairless Terriers have a relatively high genetic diversity, and that breeders are successfully maintaining Hardy-Weinberg equilibrium (*i.e.*, the cohort analyzed in this study is as genetically diverse as a random breeding population).

However, the aforementioned values were estimated for the entire cohort and not for individual dogs making up the population. Internal Relatedness (IR) scores provide a better picture of heterozygosity for each dog and should be used by breeders to select the most unrelated mates possible (see **section E** below).

C. Standard genetic assessment values for individual STR loci

Allele frequencies can be also used to perform a standard genetic assessment of heterozygosity at each STR locus (**Table 3**). This provides an estimate of genetic diversity in the genomic regions associated with each STR marker. In the American Hairless Terrier, the average number of effective alleles (Ne) per locus across individuals ranged from 1.29 (VGL2918) to 7.5 alleles (VGL0760). The lowest average observed heterozygosity (Ho) for an individual STR locus was 0.25 (VGL2918), whereas the highest was estimated at 0.84 (VGL0760). Average expected heterozygosity (He) values ranged from 0.22 (VGL2918) to 0.87 (VGL0760) (**Table 3**).

Loci with the lowest Ho values contribute the least to heterozygosity levels across the breed; they are most likely associated with inherited traits that are important for the breed's phenotypic standard (and thus tend to vary less). Conversely, high Ho values for a particular locus means that it shows greater genetic diversity across the breed, and that these loci can be associated with phenotypic variation among individuals. The values for Ho and He are used to calculate what is known as inbreeding coefficient (or F), which is a measure of how near that locus is to Hardy-Weinberg equilibrium (HWE). An F value of zero signifies that a population is in HWE, or in other words, is randomly breeding (no artificial selection). Positive F values indicate non-random selection (inbreeding), while negative values indicate outbreeding (increased heterozygosity).

Table 3. Standard Genetic Assessment of individual STR loci for 179 American Hairless Terriers. Individual STR loci with high inbreeding coefficients (F > 0.1) are bolded.

Locus	Na	Ne	Ho	He	F
AHT121	10	4.951	0.777	0.798	0.027

AHT137	6	4.522	0.777	0.779	0.003
AHTH130	8	4.122	0.721	0.757	0.048
AHTh171-A	9	3.258	0.732	0.693	-0.06
AHTh260	8	3.298	0.698	0.697	-0
AHTk211	5	2.625	0.631	0.619	-0.02
AHTk253	5	3.277	0.62	0.695	**0.108**
C22.279	6	3.541	0.765	0.718	-0.07
FH2001	7	1.999	0.497	0.5	0.005
FH2054	8	5.753	0.832	0.826	-0.01
FH2848	8	2.163	0.525	0.538	0.023
INRA21	6	4.347	0.743	0.77	0.035
INU005	5	2.077	0.486	0.519	0.063
INU030	6	3.531	0.687	0.717	0.041
INU055	9	3.8	0.709	0.737	0.037
LEI004	5	2.028	0.514	0.507	-0.01
REN105L03	9	3.496	0.704	0.714	0.014
REN162C04	7	3.758	0.687	0.734	0.064
REN169D01	6	1.914	0.441	0.478	0.076
REN169O18	5	2.472	0.62	0.595	-0.04
REN247M23	3	1.743	0.492	0.426	-0.15
REN54P11	6	3.875	0.732	0.742	0.014
REN64E19	9	3.682	0.726	0.728	0.003
VGL0760	12	7.464	0.838	0.866	0.032
VGL0910	14	3.767	0.76	0.735	-0.03
VGL1063	12	3.632	0.687	0.725	0.052
VGL1165	13	3.441	0.709	0.709	0
VGL1828	8	4.355	0.771	0.77	0
VGL2009	7	4.633	0.698	0.784	**0.109**
VGL2409	7	4.302	0.76	0.768	0.01
VGL2918	7	1.289	0.251	0.224	-0.12
VGL3008	8	2.919	0.648	0.657	0.014
VGL3235	7	3.034	0.721	0.67	-0.08

Only two loci (VGL2009 and AHTk253) had high inbreeding coefficients ($F > 0.1$), which suggests that they have been under strong positive selection since breed development and are likely associated with breed-defining phenotypic traits.

D. Differences in population structure as determined by Principal Coordinate Analysis (PCoA)

PCoA measures the genetic relatedness of individuals within a population. The data is computed in a spherical form, but often presented in the two dimensions that most closely represent its multi-dimensional form (coordinates 1 and 2). The closer two individuals cluster together on the plot, the more closely related they are to each other. Overall, the 179 American Hairless Terriers

clustered as expected for a pure dog breed on the PCoA plot using allele frequency data obtained from the 33 or STR marker panel. However, a group of 15 individuals (red circle) clustered separately on the far right of the graph, which indicates that they are more genetically related amongst themselves than to the other individuals from the breed cohort. Pedigree analysis shows that these individuals belong to the same bloodline from the United States (several siblings and their parents), and that this bloodline is remarkably genetically distinguishable from the other lines sampled in this study (**Figure 2**).

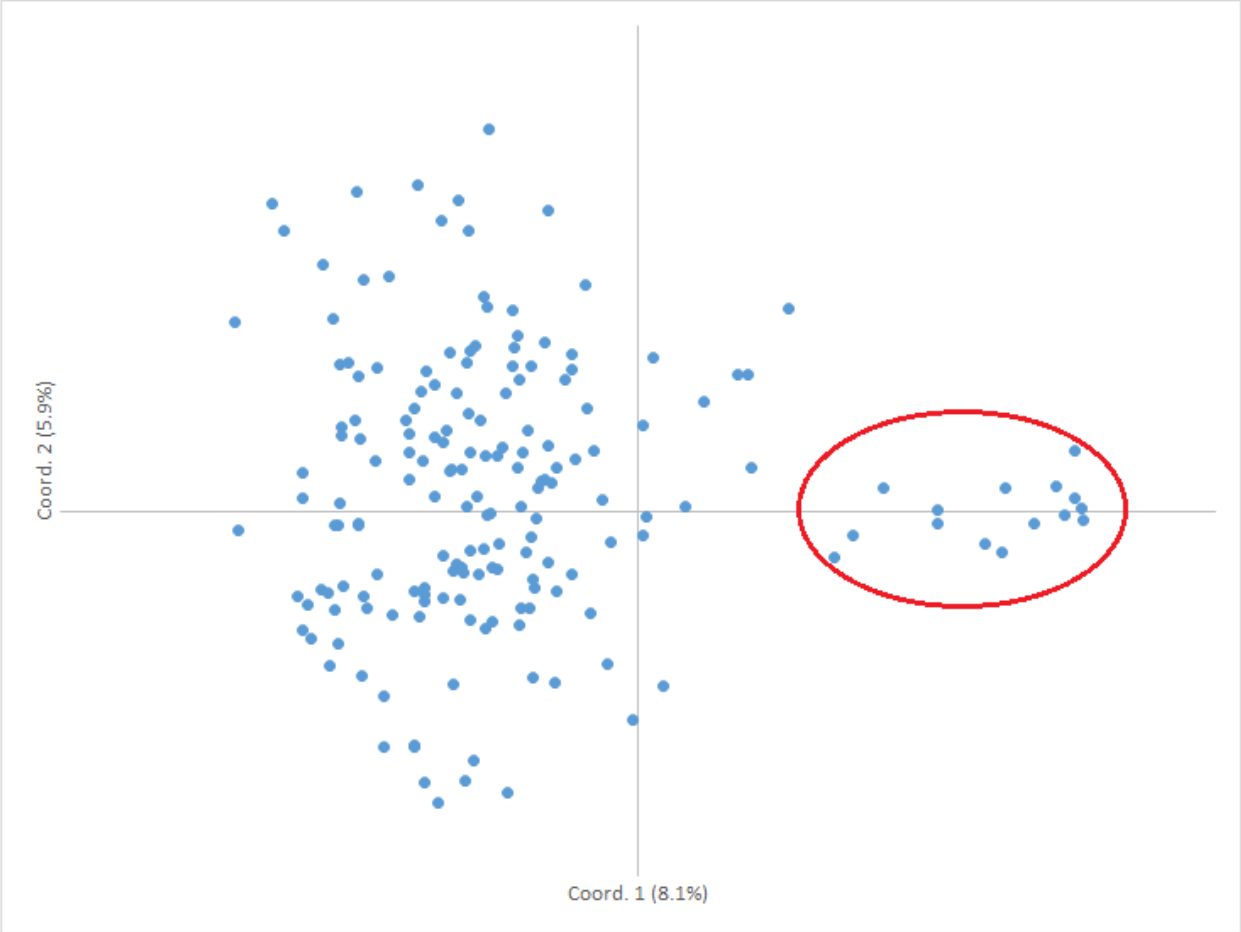


Figure 2. PCoA of American Hairless Terriers (n = 179) based on allele frequencies at 33 autosomal STR loci. A subset of 15 individuals (red circles) clustered separately on the far right of the graph, indicating a genetically distinguishable bloodline when compared to the population-at-large.

Principal coordinate analysis can also be used to determine how two populations have genetically differentiated from each other. **Figure 3** shows a PCoA of the 179 American Hairless Terriers with a closely related breed (Rat Terrier) and a somewhat unrelated breed (Havanese) [7]. American Hairless Terriers (blue dots) and Rat Terriers (gray dots) are clearly related, given their proximity to each other on the plot, but are overall genetically distinguishable. Expectedly given the breed's

history, several American Hairless Terriers bridged the two populations (purple oval); additionally, a few American Hairless Terriers were found among the Rat Terrier population (red circle) (**Figure 3**). These were the same individuals highlighted by the red circle in **Figure 2**, which suggests that their bloodline was a product of outcrossing to Rat Terrier in recent generations. This breeding practice is permitted in the American Hairless Terrier.

Figure 3. PCoA plot of American Hairless Terrier (blue dots; n = 179), Rat Terrier (gray dots; n = 42), and Havanese (orange dots; n = 150).

E. Internal relatedness (IR) scores for American Hairless Terrier

1. IR testing and meaning

Genetic assessments such as those presented in Tables 1-3 are indicators of population-wide heterozygosity and do not reflect the genetic diversity inherited by individuals from their parents.

Internal Relatedness (IR) is a calculation that is used to determine the degree of relatedness of parents of an individual dog. The IR calculation takes into consideration homozygosity at each of the 33 STR loci in this study and gives more weight to rare and uncommon alleles, which would presumably be identified in less related individuals. IR scores of all individuals in a population can be graphed to form a curve ranging from -1.0 to +1.0. A dog with an IR value of -1.0 would have parents that are totally unrelated at all 33 STR loci, while a dog with an IR value of +1.0 has parents that are genetically identical at all loci. IR values above +0.25 occur when the parents of the full sibling parents are themselves highly inbred. *The higher the IR value is above 0.25 for a particular individual, the more closely related are the parents and grandparents of the sibling parents.* **Table 4** summarizes the IR values for the 179 American Hairless Terriers.

Table 4. Internal relatedness (IR) and adjusted IR (IRVD) values calculated using allele numbers and frequencies for 33 STR loci in 179 American Hairless Terriers.

	IR	IRVD
Minimum	-0.3066	-0.1639
1st Quartile	-0.0739	0.0852
Mean	0.0125	0.1880
Median	0.0062	0.1923
3rd Quartile	0.0894	0.2856
Maximum	0.4158	0.6277

The most outbred dog of the study cohort had an estimated IR score of -0.30, while the most inbred dog had an IR score of +0.41, with a mean IR of 0.01 for the cohort. **Table 4** shows that one-half of the dogs had IR values over +0.01, and one quarter over +0.08. Therefore, only a small proportion of American Hairless Terriers sampled in this study (n = 8, data not shown) were equally or more inbred than theoretical offspring of full sibling parents. Finally, the wide range of IR values indicate genetic heterogeneity in the cohort (typical for most pure breeds), and highlight the importance of assessing IR values for individual dogs in order to maintain within-breed diversity by selecting the least related individuals possible for mating purposes.

2. Adjusted IR values (IRVD) as a measure of genetic diversity lost during breed development

The IR values obtained from known STR alleles and their frequencies can be used to approximate the amount of genetic diversity that has been lost as a breed evolves from its oldest common ancestors to the present day. Village dogs that exist throughout the SE Asia, the Middle East and the Island Pacific region are randomly breeding descendants of dogs from which most modern breeds evolved. The known STR alleles and their frequencies of a given breed can be compared with the same alleles and their frequency in modern village dogs to yield an adjusted IR score (IR-village dog or IRVD) (**Table 4** and **Figure 3**, blue line).

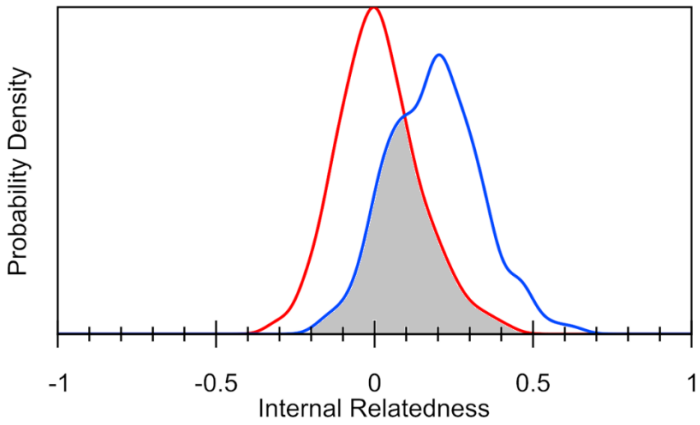


Figure 3. Distribution of IR (red line) and IR-village dog (IRVD) (blue line) values for American Hairless Terrier (n=179). The overlap between the curves (gray area) shows that the breed retains 51.8% of the genetic diversity existing in randomly breeding village dogs.

The mean IRVD value was approximately 0.19 for the population, ranging from -0.16 (most outbred) to +0.63 (most inbred) (**Table 4**). The IRVD curve (**Figure 3**, blue line) is shifted to the right when compared to the IR curve (red line), which is typical for all pure breeds of dogs. The overlapping area of the two curves is an estimate of how much genetic diversity was lost in the creation of a breed. The estimated retention of available canid genetic diversity in American Hairless Terrier was 51.8%, which is greater than the 30% retained genetic diversity calculated from comparisons with known alleles at the 33 STR loci of all canids tested at VGL (**section IIB**). This value reflects the relatively high genetic diversity existing in the breed as identified in **sections IIA**, **IIB**, and **IIC**, and again, is among the highest amount of retained diversity that we have observed at the VGL.

F. DLA class I and II haplotype frequencies and genetic diversity

The DLA consists of four gene-rich regions that make up a small portion of chromosome 12. Two of these regions contain genes that help regulate normal cell- (Class I) and antibody-mediated (Class II) immunity. Polymorphisms in these regions have also been associated with abnormal immune responses, which can cause autoimmune diseases, allergies, and resistance/susceptibility to infectious diseases. Breeds that lack genetic diversity in the DLA region are often more prone to autoimmune disorders.

The Class I region contains several genes, but only one, *DLA88*, is highly polymorphic (i.e., contains many alleles) and is therefore most important for immune regulation. Specific alleles at the four STR loci associated with *DLA88* are linked in various combinations, forming specific haplotypes (**Table 5**).

The class II region also contains several genes, three of which are highly polymorphic: *DLA-DRB1*, *DLA-DQB1* and *DLA-DQA1*. Specific alleles at these three loci associated with the three class II genes are strongly linked, and often inherited as a single haplotype (**Table 6**). An individual inherits one haplotype from each of the parents. It is common for different dog breeds to share common and even rare haplotypes for these loci, depending on common ancestry.

1. DLA class I and II haplotypes existing in the American Hairless Terrier

Loci in the DLA region were genotyped in 177 out of the 179 individuals used in this study. Twenty-one DLA class I and 22 DLA class II haplotypes were identified in American Hairless Terriers (**Table 5**). Compared to other pure dog breeds tested at the VGL, the number of DLA class I and II haplotypes identified in this breed is relatively high and reflects the genetic diversity found at the genome-at-large. The number of DLA class I and II haplotypes found in American Hairless Terriers is among the highest identified in the pure breeds studied to date. Usually, this would be a reflection of many different founders (or founder lines) being involved in the development of the breed; however, this is not the case of American Hairless Terriers given the breed's history. The number of DLA haplotypes identified in this study is more likely a consequence of the relatively high genetic diversity existing in the breed from which the American Hairless Terrier naturally originated: the Rat Terrier. Given the number of dogs tested, it is unlikely that additional haplotypes will be identified, and if they are, they will be at very low incidence.

Most of the class I haplotypes were identified at a low frequency (<10%); however, one DLA class I haplotype (1008) was found in 25% of the individuals tested, whereas another haplotype (1062) was detected in 17% of dogs. Similarly, all DLA class II haplotypes were found at low frequencies except for 2003 which was present in 27% of the individuals tested, and 2021 (15% frequency).

Table 5. DLA class I and II haplotypes identified in American Hairless Terrier (n = 177) and their respective frequencies. Haplotypes with the highest frequency are bolded.

DLA1 haplotype	STR types	Frequency (%)
1002	380 365 281 181	1.4
1008	**386 373 289 182**	**25.1**
1011	376 365 281 180	11.3
1012	388 369 289 188	0.6
1016	382 371 277 178	0.6
1040	380 371 277 186	4.5
1052	380 372 289 184	2.0
1062	**382 371 277 183**	**16.9**
1065	380 371 277 181	1.7
1068	380 373 287 181	11.0
1074	386 383 289 186	0.6
1092	376 379 277 181	1.7
1093	386 379 277 180	4.0
1109	381 379 291 186	0.3
1128	384 376 287 182	5.9
1148	376 375 277 180	0.3
1255	388 371 277 186	4.0
1256	386 365 281 180	1.1
1283	380 379 277 180	5.9
1287	380 373 289 182	0.3

1288	380 369 289 176	0.8
DLA2 haplotype	**STR types**	**Frequency (%)**
2001	343 324 284	12.1
2003	**343 324 282**	**26.6**
2012	345 322 280	1.7
2014	339 322 284	0.6
2017	343 322 280	0.6
2018	339 324 284	1.1
2021	**339 324 268**	**15.0**
2022	339 327 282	3.4
2024	343 323 280	0.8
2026	351 324 284	0.3
2028	345 327 288	1.1
2032	339 323 280	4.0
2033	339 323 282	0.6
2037	341 327 280	1.7
2040	345 327 280	4.0
2044	343 324 268	1.7
2053	343 324 280	0.6
2067	343 322 284	2.0
2079	343 323 278	5.9
2096	351 322 280	10.5
2137	339 323 288	5.4
2139	351 322 268	0.6

Interestingly, three DLA class I haplotypes appear to be unique to the breed: 1283, 1287, and 1288 (**Table 6**). Two additional DLA1 haplotypes were found to be shared with only one breed: 1148 (shared with Havanese), and 1255 (shared with Rat Terrier) (**Table 6**). DLA class II haplotypes 2137 and 2139 were also found uniquely in American Hairless Terriers (**Table 7**). Finally, many DLA class I and II haplotypes found in American Hairless Terriers were shared with a number of dog breeds, such as Rat Terrier, Havanese, and Poodle (**Tables 6 and 7**).

Table 6. Sharing of DLA class I haplotypes between American Hairless Terrier (highlighted in blue) and other dog breeds/varieties tested at the VGL (n=53).

DLA1 #	STR types	American Hairless Terrier (n=177)	American Eskimo, Standard (n=63)	American Eskimo, Miniature (n=38)	American Eskimo, Toy (n=14)	American Akita (n=158)	Japanese Akita (n=565)	Blend Akita (n=66)	Alaskan Klee Kai (n=634)	Barbet (n=68)	Border Collie (n=63)	Berger Picard (n=139)	Bernese Mountain Dog (n=143)	Black Russian Terrier (n=150)	Biewer (n=128)	Biewer Yorshire Terrier (n=53)	Biewer Terrier (n=201)	Yorkshire Terrier (n=16)	Borzoi (n=149)	Collie (n=49)	Doberman Pinscher (n=1142)	English Bulldog (n=163)	English Mastiff (n=31)	Mastiff (n=21)	Flat Coated Retriever (n=832)	Great Dane (n=56)	Golden Retriever (n=862)	Giant Schnauzer (n=320)	Whippet (n=107)
1002	380 365 281 181	0.014	0.659	0.14	0.11	--	--	--	--	0.066	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.0006	--	0.084
1008	386 373 289 182	0.251	--	--	--	--	--	--	0.0576	--	0.008	--	--	--	0.008	--	--	0.06	--	--	--	0.006	--	--	--	--	0.0012	0.036	0.047
1011	376 365 281 180	0.113	--	0.01	--	--	--	--	0.0552	--	0.071	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.0006	0.009	--
1012	388 369 289 188	0.006	0.024	0.04	--	--	--	--	--	--	0.056	--	--	--	0.207	0.151	0.226	0.28	--	--	0.0009	0.414	--	--	--	--	0.0012	--	0.037
1016	382 371 277 178	0.006	0.008	0.04	0.11	--	--	--	--	--	--	--	0.045	0.01	0.023	0.019	0.012	0.03	--	0.04	0.0206	0.095	0.15	0.14	--	0.188	0.0046	0.047	0.107
1040	380 371 277 186	0.045	--	--	--	0.006	--	--	0.2129	--	--	--	--	--	0.102	0.208	0.077	--	--	--	0.0092	0.04	--	--	--	--	0.0006	--	0.084
1052	380 372 289 184	0.02	--	--	--	--	--	--	--	--	0.008	0.108	--	--	--	--	--	--	--	--	0.0009	--	0.02	--	--	--	--	--	--
1062	382 371 277 183	0.169	--	--	--	--	--	--	0.2279	--	--	--	--	--	--	--	--	--	--	--	--	0.187	--	--	--	--	0.087	--	--
1065	380 371 277 181	0.017	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.0006	--	0.2668	0.002	--
1068	380 373 287 181	0.11	--	--	--	--	--	--	--	--	0.214	--	0.066	--	--	0.009	--	--	--	--	0.0004	--	--	--	0.2837	0.009	0.047	0.053	--
1074	386 383 289 186	0.006	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.037	--	--	--	--	--	--	--
1092	376 379 277 181	0.017	--	--	--	--	0.3115	0.008	--	0.037	0.008	--	--	0.253	--	0.038	--	0.06	--	--	--	0.006	--	--	0.0012	--	--	0.273	--
1093	386 379 277 180	0.04	0.008	0.05	0.07	--	--	--	--	0.162	--	--	--	0.08	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1109	381 379 291 186	0.003	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1128	384 376 287 182	0.059	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.0006	--	--
1148	376 375 277 180	0.003	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1255	388 371 277 186	0.04	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1256	386 365 281 180	0.011	--	--	--	--	--	--	--	--	--	--	0.003	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1283	380 379 277 180	0.059	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1287	380 373 289 182	0.003	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1288	380 369 289 176	0.008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

DLA1 # (cont'd)	STR types	American Hairless Terrier (n=177)	Havana Silk (n=38)	Havanese (n=857)	Italian Greyhound (n=1294)	Irish Setter (n=59)	Irish Red and White Setter (n=75)	Irish Wolfhound (n=78)	Lakeland Terrier (n=132)	Labrador Retriever (n=282)	Llewellin Setter (n=136)	Magyar Agar (n=78)	Newfoundland (n=109)	Polish Lowland Sheepdog (n=74)	Toy Poodle (n=215)	Miniature Poodle (n=403)	Poodle (n=4854)	Rat Terrier (n=42)	Samoyed (n=191)	Saint Bernard (n=89)	Scottish Collie (n=115)	Shiba Inu (n=142)	Shikoku (n=84)	Greater Swiss Mountain Dog (n=57)	Shiloh Shepherd (n=30)	Shiloh Shepherd, ISSA (n=255)	Swedish Vallhund (n=443)	Cardigan Welsh Corgi (n=43)
1002	380 365 281 181	0.014	--	--	--	--	--	--	--	--	--	--	--	--	0.005	0.001	0.1603	0.01	--	--	--	--	--	--	--	--	--	--	--
1008	386 373 289 182	0.251	--	--	0.1209	0.093	0.6	--	--	0.096	0.055	--	--	--	0.021	--	0.0137	0.02	--	--	0.009	--	--	--	--	--	--	--	--
1011	376 365 281 180	0.113	--	0.0012	--	0.085	0.027	--	--	--	--	--	--	--	0.049	0.002	0.0195	0.05	0.272	0.062	--	--	--	--	--	--	--	--	--
1012	388 369 289 188	0.006	--	0.0128	0.0077	--	--	--	0.765	--	--	--	--	--	0.021	0.072	0.0142	0.06	0.013	--	0.009	--	--	0.93	--	--	--	0.23	
1016	382 371 277 178	0.006	0.08	0.1943	0.0626	--	--	--	0.008	0.016	0.029	--	0.321	0.027	0.023	0.029	0.0221	0.05	--	--	0.096	--	--	0.07	--	--	--	--	--
1040	380 371 277 186	0.045	0.01	0.0181	0.0788	--	--	--	0.182	--	--	--	0.289	0.669	0.002	0.005	0.0006	0.17	--	0.011	--	--	--	--	--	--	--	--	--
1052	380 372 289 184	0.02	--	0.0088	0.1866	--	--	0.333	0.011	--	--	0.051	--	--	--	--	0.0003	--	--	--	--	--	--	--	0.27	0.388	--	--	--
1062	382 371 277 183	0.169	--	0.0006	--	--	--	--	--	0.012	--	--	0.005	--	--	--	--	0.07	--	0.062	--	--	--	--	--	--	--	--	--
1065	380 371 277 181	0.017	--	--	0.0004	--	--	--	--	0.378	--	--	--	--	--	--	0.0002	--	--	--	--	--	--	--	--	--	--	--	--
1068	380 373 287 181	0.11	0.25	0.0146	--	0.008	--	0.128	--	0.032	--	--	0.096	0.007	0.009	0.012	--	--	0.042	0.163	--	--	--	--	0.58	0.263	0.374	--	
1074	386 383 289 186	0.006	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.02	--	--	--	--	--	--	--	--	--	--	--
1092	376 379 277 181	0.017	0.2	0.0933	--	--	--	--	--	--	--	--	0.087	--	--	--	0.0002	0.06	--	--	--	--	--	--	--	--	--	--	--
1093	386 379 277 180	0.04	0.04	0.0163	--	--	--	--	--	--	--	--	--	--	--	--	0.0005	--	--	--	--	--	--	--	--	--	--	--	--
1109	381 379 291 186	0.003	--	--	--	--	--	--	--	--	--	--	--	--	0.044	0.019	0.0008	--	--	--	--	0.032	--	--	--	--	--	--	--
1128	384 376 287 182	0.059	--	0.0012	--	--	--	--	--	--	--	--	--	--	--	--	--	0.02	--	0.006	--	--	--	--	--	--	--	--	--
1148	376 375 277 180	0.003	--	0.0029	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1255	388 371 277 186	0.04	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.01	--	--	--	--	--	--	--	--	--	--	--
1256	386 365 281 180	0.011	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.01	--	--	--	--	--	--	--	--	--	--	--
1283	380 379 277 180	0.059	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1287	380 373 289 182	0.003	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1288	380 369 289 176	0.008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

Table 7. Sharing of DLA class II haplotypes between American Hairless Terrier (highlighted in blue) and other dog breeds/varieties tested at the VGL (n=53).

DLA2 #	STR types	American Hairless Terrier (n=177)	American Eskimo, Standard (n=63)	American Eskimo, Miniature (n=38)	American Eskimo, Toy (n=14)	American Akita (n=158)	Japanese Akita (n=565)	Blend Akita (n=66)	Alaskan Klee Kai (n=634)	Barbet (n=68)	Border Collie (n=63)	Berger Picard (n=139)	Bernese Mountain Dog (n=143)	Black Russian Terrier (n=150)	Biewer (n=128)	Biewer Yorshire Terrier (n=53)	Biewer Terrier (n=201)	Yorkshire Terrier (n=16)	Borzoi (n=149)	Collie (n=49)	Doberman Pinscher (n=1142)	English Bulldog (n=163)	English Mastiff (n=31)	Mastiff (n=21)	Flat Coated Retriever (n=832)	Great Dane (n=56)	Golden Retriever (n=862)	Giant Schnauzer (n=320)	Whippet (n=107)
2001	343 324 284	0.121	0.659	0.14	0.11	--	--	--	--	0.199	0.143	--	0.01	--	--	--	--	--	--	--	--	--	--	--	--	--	0.1415	0.006	0.098
2003	343 324 282	0.266	0.024	0.04	--	--	--	--	--	0.132	0.056	--	--	--	0.246	0.208	0.249	0.38	--	--	0.0004	0.598	--	--	0.1448	0.009	0.0197	0.03	0.089
2012	345 322 280	0.017	--	--	--	--	0.0009	--	0.0584	--	--	--	0.003	--	--	--	--	--	--	--	--	--	--	--	--	--	0.0006	0.009	--
2014	339 322 284	0.006	0.008	0.03	0.07	--	--	--	0.067	--	--	--	--	--	--	--	--	--	--	--	--	0.092	0.15	0.14	0.0276	0.036	--	0.005	--
2017	343 322 280	0.006	--	--	--	0.009	0.0035	0.015	--	0.029	0.175	0.108	--	--	--	--	--	--	0.007	--	--	0.215	0.21	0.29	0.0006	--	0.0394	0.002	0.238
2018	339 324 284	0.011	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.1412	--	--	--	0.005
2021	339 324 268	0.15	--	--	--	--	--	--	0.224	--	--	--	0.045	--	0.004	--	--	--	--	--	--	--	--	--	--	--	0.087	--	--
2022	339 327 282	0.034	0.024	0.21	0.32	--	--	--	--	--	0.008	--	--	--	--	--	--	--	0.587	--	0.0009	0.015	--	--	0.1166	0.08	0.0006	0.003	--
2024	343 323 280	0.008	--	--	--	--	--	--	--	--	--	--	0.538	--	--	--	--	--	0.01	--	0.0004	0.006	--	--	--	--	--	--	--
2026	351 324 284	0.003	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2028	345 327 288	0.011	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.037	--	--	--	--	--	--	0.084
2032	339 323 280	0.04	--	0.05	0.07	0.003	--	--	--	0.162	--	--	--	0.08	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2033	339 323 282	0.006	0.008	--	--	0.013	--	--	--	--	0.008	--	--	0.507	--	--	--	--	--	--	0.0018	--	--	--	--	0.214	--	0.038	0.103
2037	341 327 280	0.017	0.032	0.26	0.25	0.18	0.2487	0.136	0.3699	--	0.087	--	--	0.287	0.027	0.009	0.06	0.09	--	--	--	--	0.02	--	--	--	0.0145	0.369	--
2040	345 327 280	0.04	--	--	--	--	--	--	--	--	--	--	--	--	0.066	0.085	0.025	0.03	--	--	0.0004	--	--	--	--	--	--	--	--
2044	343 324 268	0.017	--	--	--	--	--	--	--	--	--	--	--	--	--	0.038	--	0.06	--	--	--	0.006	--	--	--	--	--	--	--
2053	343 324 280	0.006	0.222	0.12	0.04	--	--	--	--	--	0.071	--	0.066	--	--	0.009	--	--	--	--	0.0013	--	--	--	0.146	0.009	0.0284	0.063	--
2067	343 322 284	0.02	--	--	--	--	--	--	--	--	0.063	0.892	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2079	343 323 278	0.059	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.0006	--	--
2096	351 322 280	0.105	0.008	0.01	--	--	--	--	--	--	0.032	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2137	339 323 288	0.054	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2139	351 322 268	0.006	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

DLA2 # (cont'd)	STR types	American Hairless Terrier (n=177)	Havana Silk (n=38)	Havanese (n=857)	Italian Greyhound (n=1294)	Irish Setter (n=59)	Irish Red and White Setter (n=75)	Irish Wolfhound (n=78)	Lakeland Terrier (n=132)	Labrador Retriever (n=282)	Llewellin Setter (n=136)	Magyar Agar (n=78)	Newfoundland (n=109)	Polish Lowland Sheepdog (n=74)	Toy Poodle (n=215)	Miniature Poodle (n=403)	Poodle (n=4854)	Rat Terrier (n=42)	Samoyed (n=191)	Saint Bernard (n=89)	Scottish Collie (n=115)	Shiba Inu (n=142)	Shikoku (n=84)	Greater Swiss Mountain Dog (n=57)	Shiloh Shepherd (n=30)	Shiloh Shepherd, ISSA (n=255)	Swedish Vallhund (n=443)	Cardigan Welsh Corgi (n=43)
2001	343 324 284	0.121	0.07	0.0496	--	--	--	--	--	0.002	--	0.071	--	--	0.005	0.015	0.5973	0.01	--	0.017	--	0.014	--	--	--	0.004	--	--
2003	343 324 282	0.266	0.24	0.2165	0.007	--	--	--	0.765	0.023	--	--	0.005	--	0.421	0.507	0.1031	0.13	0.013	--	0.017	--	--	0.93	--	0.01	--	0.23
2012	345 322 280	0.017	--	0.0035	--	0.051	0.2	--	--	--	0.044	0.083	--	--	0.051	0.087	0.0067	0.01	--	--	0.004	--	0.018	--	--	--	--	--
2014	339 322 284	0.006	--	0.0047	0.0015	--	--	--	0.008	0.002	--	--	0.339	0.696	0.021	0.027	0.0205	0.02	--	0.112	--	--	--	--	--	--	--	--
2017	343 322 280	0.006	--	0.0093	0.2133	--	--	--	0.03	--	--	0.449	--	0.284	0.002	0.001	0.0022	0.02	--	--	--	--	--	--	0.27	0.388	--	0.19
2018	339 324 284	0.011	--	0.0204	--	--	--	--	--	--	0.018	--	--	--	--	--	--	--	--	--	--	0.208	0.208	--	--	--	--	--
2021	339 324 268	0.15	--	0.0041	--	--	--	0.295	--	0.012	--	--	0.005	--	0.074	0.052	0.0038	0.02	--	0.062	--	--	--	--	--	--	--	--
2022	339 327 282	0.034	0.08	0.1184	--	0.153	--	0.353	0.174	0.055	0.085	--	--	--	0.007	0.002	0.0005	0.14	0.107	--	--	--	--	--	0.02	0.045	0.058	--
2024	343 323 280	0.008	--	0.0047	--	--	--	--	--	0.089	--	--	--	--	0.072	0.01	0.0003	--	0.016	--	--	--	--	--	--	--	--	--
2026	351 324 284	0.003	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.001	--	--	--	--	--	--	--	--	0.004	--	--
2028	345 327 288	0.011	--	0.0012	--	--	--	--	--	--	--	--	--	--	--	0.005	0.0006	0.1	--	0.011	--	--	--	--	--	--	--	--
2032	339 323 280	0.04	0.04	0.0216	0.0367	--	--	--	--	0.002	--	--	--	--	--	0.009	0.0005	--	--	--	--	0.007	--	--	--	--	--	--
2033	339 323 282	0.006	--	0.0012	0.0054	--	--	--	--	--	--	--	--	--	0.002	--	--	--	--	--	--	--	--	--	--	--	--	--
2037	341 327 280	0.017	--	0.0245	0.0085	0.305	--	--	--	--	--	0.013	--	--	0.009	0.011	0.0005	0.06	--	--	0.004	--	--	--	--	--	--	--
2040	345 327 280	0.04	--	0.0029	0.0012	--	--	--	--	--	--	--	--	--	0.021	0.005	0.0001	0.01	--	--	--	--	--	--	--	--	--	0.06
2044	343 324 268	0.017	--	--	0.0004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2053	343 324 280	0.006	0.26	0.0315	--	0.008	--	0.128	--	0.03	--	--	0.096	0.007	0.012	0.012	--	--	0.56	0.14	--	--	--	--	0.6	0.329	0.524	--
2067	343 322 284	0.02	--	--	0.0004	--	--	--	0.011	--	--	--	--	0.007	--	0.006	--	--	--	--	--	0.211	0.012	--	--	--	--	--
2079	343 323 278	0.059	--	0.0012	--	--	--	--	--	--	--	--	--	--	--	--	--	0.02	--	--	--	--	--	--	--	--	--	--
2096	351 322 280	0.105	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.113	--	--	--	--	--	--	--	--	--
2137	339 323 288	0.054	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2139	351 322 268	0.006	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

2. Heterozygosity in the DLA region

Due to their physical proximity in canine chromosome 12, the seven loci that define the DLA class I and II haplotypes are in stronger linkage disequilibrium (i.e., have a higher probability of being inherited together) when compared to other parts of the genome. However, the expectation is that these loci have achieved an equilibrium with other loci in the genome over time, and thus will be inherited randomly as well. This assumption can be tested through a standard genetic assessment of each locus (**Table 8**) and averaged across all loci (**Table 9**).

The number of alleles (Na) identified at each DLA locus in American Hairless Terriers ranged from 4 (5ACT) to 10 (DLA I-4ACA). As observed in the 33 STR loci across the genome, the number of effective alleles (Ne) per DLA locus was lower, ranging from 2.56 (5ACT) to 4.73 (5BCA). The observed heterozygosity values for each DLA locus were close to the expected heterozygosity values, yielding inbreeding coefficients (F) around zero similarly to those expected in random breeding populations (**Table 8**). The exception was locus DLA I-4BCT, for which a high inbreeding coefficient ($F > 0.1$) was estimated. The average observed heterozygosity for the DLA region was 0.69 and the expected heterozygosity was estimated at 0.72, yielding an average F value of +0.047 across DLA loci (**Table 9**). This means that the population-wide F value for the DLA STRs was greater than the inbreeding coefficient estimated using 33 autosomal STRs (F = 0.006, **Table 2**). This suggests that the DLA region is not in equilibrium with the genome-at-large, and appears to be undergoing either deliberate or inadvertent positive selection for certain DLA genotypes.

Table 8. Standard genetic assessment for American Hairless Terrier (n=177) using each of the 7 STRs in the DLA class I and II regions.

Locus	Na	Ne	Ho	He	F
DLA I-3CCA	8	4.457	0.743	0.776	0.042
DLA I-4ACA	10	4.058	0.743	0.754	0.014
DLA I-4BCT	5	3.428	0.631	0.708	0.109
DLA1131	9	4.724	0.737	0.788	0.065
5ACA	5	2.773	0.598	0.639	0.065
5ACT	4	2.557	0.615	0.609	-0.01
5BCA	7	4.727	0.754	0.788	0.043

Table 9. Summary of standard genetic assessment for American Hairless Terrier (n=177) using 7 STRs in the DLA class I and II regions. SE = standard error of the mean.

	Na	Ne	Ho	He	F
Mean	6.86	3.818	0.689	0.723	0.047
SE	0.79	0.318	0.025	0.026	0.013

III. What does this assessment of genetic diversity tell us about American Hairless Terriers

American Hairless Terriers originated naturally from Rat Terriers 50 years ago. Not surprisingly, a great deal of genetic similarity was found between these breeds, with some American Hairless Terrier individuals being genetically undistinguishable from the Rat Terrier population. Despite being founded from just a handful of dogs, the American Hairless Terrier possesses one of the highest levels of genetic diversity ever detected in dog breeds tested at the VGL to date. This can be attributed in part by the high levels of genetic diversity existing in the breed it originated from: preliminary STR analysis of 42 Rat Terriers showed high levels of diversity both across the genome (average F = +0.013) and in the DLA region (average F = -0.104). Additionally, American Hairless Terrier breeders have been doing an excellent job maintaining and distributing the genetic diversity existing in the breed through mate selection.

Moreover, the breed has retained a great amount of available canid genetic diversity during its evolution (51.8%) compared to other pure breeds. However, a slight loss of diversity in the DLA region compared to the genome-at-large has been identified in this study, with the DLA having an average 5% excess in homozygosity. This imbalance most likely results from a degree of positive selection for the most common DLA haplotypes.

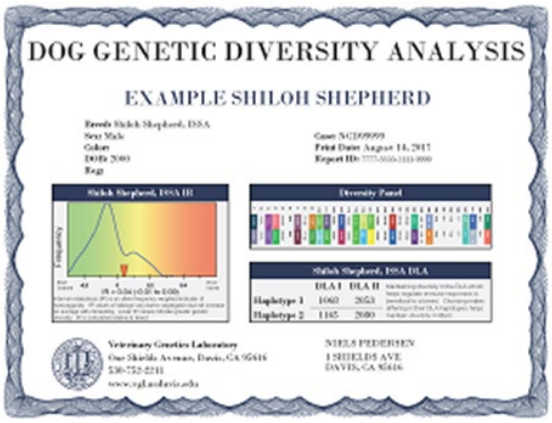
Given that outcrossing with the Rat Terrier is permitted, this practice can be used if the need to introduce new alleles into the American Hairless Terrier population is needed. This has been demonstrated in this study by the discovery of a bloodline that is more closely related to Rat Terriers, and thus genetically distinguishable from the overall population. Although breed-wide standard genetic assessments indicate that the American Hairless Terrier is very heterogeneous, internal relatedness (IR) scores indicate that there are individuals whose parents are quite related, sometimes to the equivalent level of full siblings. It is important to identify such individuals or bloodlines prior to breeding to find mates that will produce puppies that have lower IR scores. This should not be a problem as the breed has great genetic diversity from which to select the best mates. It is also possible by proper selection among existing dogs to correct specific genetic imbalances such as in the DLA region.

IV. Results of VGL Canine Diversity Testing

A. How will you be given the results of DNA-based genetic diversity testing on your dog?

After a sample is submitted for genetic testing, the identity of the dog and owner will be replaced by a laboratory barcode identifier. This identifier will be used for all subsequent activities and each owner will be provided with a certificate that reports the internal relatedness, genomic STR genotypes and DLA class I and II haplotypes for the dog(s) tested. The internal relatedness value for the dog being tested is reported in relation to others in the population. The alleles at each of the 33 STR loci are presented as numbers that correspond to those found in Table 1. Each locus will have two alleles, which can be different (heterozygous) or the same (homozygous). Each allele is inherited from one of the parents. Dogs from closely related parents will be homozygous for more alleles at each locus, or in regions of the genome that are under strong positive selection for phenotypic trait or traits mostly favored in the breed. Dogs with a predominance of rare (i.e., low frequency) alleles will be more distantly related to the bulk of the population than dogs that have

a predominance of common (i.e., high frequency) alleles. A sample genetic diversity report is shown below.


DOG GENETIC DIVERSITY ANALYSIS

EXAMPLE SHILOH SHEPHERD

B. What should you do with this information?

The goal for breeders should be to continue to produce puppies with IR scores close to zero, and as informed breeding decisions are made, even lower scores. Mates should be preferably selected to avoid homozygosity at any genomic loci or DLA class I and II haplotype; moreover, mating of dogs with less frequent genomic alleles or DLA haplotypes is encouraged. Maintaining existing genomic diversity will require using IR values of potential mates based on the 33 STR loci to assure puppies of equal or greater overall diversity. However, because IR values reflect the unique genetics of individuals, they cannot be used as the primary criterion for selecting ideal mates. Mates with identical IR values may produce puppies significantly more or less diverse than their parents. Conversely, breeding dogs with high IR values (providing they are genetically different) may produce puppies with much lower IR scores than either parent. A mating between a dog with a high IR value and one with low IR value, providing the latter has few alleles and DLA haplotypes in common, will produce puppies much more diverse than the highly inbred parent. Breeders should also realize that a litter of puppies could have a wide range of IR values, depending on the comparative contributions of each of the parents. The more genetically diverse and different the parents, the greater the range of IR values in their offspring.

The next step is to compare the DLA class I and II haplotypes of the mates. You want to avoid breeding dogs that will produce puppies homozygous for the same haplotypes; once again, less common haplotypes may increase breed diversity in relation to common ones.

Breeders who would like to predict the genetic outcome of puppies of certain sires and dams should screen them for genetic differences in alleles and allele frequencies for the 33 genomic STR loci. Rare alleles should be favored over common ones. This information is included on all certificates and on the breed-wide data found on the VGL website.

Finally, this study will also contribute the genetic information from American Hairless Terriers to a web repository. This information could be used in a mate selection online service that will allow

a breeder to identify, among all the dogs tested, potential mates that would be most suitable to increase genetic diversity in their litters.

V. References

1. Wikipedia. American Hairless Terrier. https://en.wikipedia.org/wiki/American_Hairless_Terrier.
2. American Kennel Club – American Hairless Terrier. https://www.akc.org/dog-breeds/american-hairless-terrier/.
3. American Hairless Terrier Club of America. https://ahtca.info/index.html.
4. OFA – The Canine Health Information Center. American Hairless Terrier. https://ofa.org/chic-programs/browse-by-breed/?breed=AHT.
5. Pedersen NC, Liu H, Leonard A, Griffioen L. A search for genetic diversity among Italian Greyhounds from Continental Europe and the USA and the effect of inbreeding on susceptibility to autoimmune disease. Canine Genet Epidemiol. 2015, 2:17.
6. Pedersen NC, Brucker L, Tessier NG, Liu H, Penedo MC, Hughes S, Oberbauer A, Sacks B. The effect of genetic bottlenecks and inbreeding on the incidence of two major autoimmune diseases in standard poodles, sebaceous adenitis and Addison's disease. Canine Genet Epidemiol. 2015, 2:14.
7. Parker HG, Dreger DL, Rimbault M, Davis BW, Mullen AB, Carpintero-Ramirez G, Ostrander EA. Genomic Analyses Reveal the Influence of Geographic Origin, Migration, and Hybridization on Modern Dog Breed Development. *Cell Rep.* 2017; 19(4):697-708. doi: 10.1016/j.celrep.2017.03.079.

This report was generated by Felipe Avila and Shayne Hughes on 12/05/2022.