

Genetic Diversity Testing for the Whippet

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 that will assess genetic diversity across the genome and in the Dog Leukocyte Antigen (DLA) class I and II regions. This test panel will be useful to breeders who wish to track and increase genetic diversity of their breed as a long-term goal.

Genetic diversity testing of Whippet is now in the preliminary results phase. During this phase, we continue to test more registered dogs to build genetic data necessary to provide breeders with an accurate assessment of genetic diversity. This report is based on testing of 54 specifically selected Whippet from the USA. This number of dogs is probably sufficient to do a near-final genetic assessment of the breed. Allele and DLA haplotype frequencies will be updated as more Whippets are tested. It is anticipated that new alleles at the 33 STR loci and additional DLA class I and II haplotypes will be identified in the future, but these will tend to be of much lower incidence than those detected in the present population.

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Results reported as:

Short tandem repeat (STR) loci: A total of 33 STR loci from across the genome were used to gauge genetic diversity within an individual and across the breed. The alleles inherited from each parent are displayed graphically to highlight heterozygosity, and breed-wide allele frequency is provided.

DLA haplotypes: STR loci linked to the DLA class I and II genes were used to identify genetic differences in regions regulating immune responses and self/non-self-recognition. Problems with self/non-self-recognition, along with non-genetic factors in the environment, are responsible for autoimmune disease. DLA haplotypes are also useful in studying founder lineages.

Internal Relatedness: The IR value is a measure of genetic diversity within an individual that 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 and cannot be compared between dogs. Two dogs may have identical IR values but with very different genetic makeups.

I. Introduction

A. History [1-5]

The Whippet is a sighthound breed that originated in England, where they descended from Greyhounds brought to Britain with the Romans. The name is derived from an early 17th-century word meaning "to move briskly". There has been a continuum of Greyhound type breeds from the time of ancient Egypt through the Middle ages and ranging from large (greyhound), medium (Whippet), to small (Italian greyhound). A small Greyhound breed became popular as a ratting dog in medieval England and the first written use of the name Whippet for a dog was in 1610. Paintings from the 17th and 18th centuries also show dogs of Whippet type. The Whippet was held in especially high regard in the northern and more rural parts of England and Wales where it was described as "the poor man's racehorse". They are the fastest dog of their weight, capable of achieving speeds of up to 35 miles per hour (56 km/h).

There were originally two varieties of Whippets. A smooth coat was more popular in Lancashire, Yorkshire, and the Midlands of England and evolved into the modern Whippet. A second type had a rough coat from crossbreeding with Bedlington Terriers and was more popular in Durham and Northumberland. The breed achieved world-wide recognition in the late 19th century as did many other English breeds. The modern type Whippet was officially recognized in 1891 by The Kennel Club, making it eligible for competition in dog shows and recording of pedigrees. The Whippet was recognized in 1888 by the American Kennel Club. The Whippet is 61st of 195 most popular breeds according to the American Kennel Club.

Whippets racing appeared in the mid-nineteenth century in a local form of coursing known as 'ragging'. Several dogs would be lined up and released from their collars by handlers at the same time, racing towards their owners standing at the opposite end of the track waving towels. This type of racing was a popular Sunday event in the north and Midlands of England and became a common weekend sport in countries such as Australia. Racing to a cloth evolved to resemble greyhound racing where dogs usually chased after live or mechanical hare. A dichotomy ultimately developed because of those that did not consider pure breeding as important as winning races. The British Whippet Racing Association was established in 1967 to establish race rules and procedures involving non-purebred Whippets. This was viewed as a threat to pure breeders and a Whippet Club Racing Association was established exclusively for purebred animals. Whippets also participate in dog sports such as lure coursing, agility, and flyball.

B. Appearance [2, 4, 6]

Whippets are a medium-sized dog weighing from 15 to 42 pounds (6.8 to 19.1 kg). There are two height ranges for Whippets, depending on whether the dog is being shown in North America. The Fédération Cynologique Internationale and The Kennel Club both call for heights of 18.5 to 20 inches (47 to 51 cm) for males and 17.5 to 18.5 inches (44 to 47 cm) for females. Whippets tend to be somewhat larger in the United States and

Canada as the American Kennel Club and Canadian Kennel Club standards are larger; 18.5 to 22.5 inches (47 to 57 cm) for males, and 17.5 to 21.5 inches (44 to 55 cm) for females. Coat color is considered immaterial in judging of Whippets, and they come in a wide variety of marking patterns and colors ranging from solid black to solid white, with red, fawn, brindle, blue, or cream.[26] The coat is short, smooth and close.

C. Temperament [1-4]

Whippets are quiet but require regular exercise. They are gentle and not prone to anxiety and barking. When not running, they prefer the furniture or the owner’s lap. These attributes make the Whippet an excellent house dog. They are not aggressive to other dogs, but due to their sighthound nature they have been known to chase small pets or animals when the opportunity arises.

II. Genetic diversity studies of the contemporary Whippet

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. Each of these STR loci is known to contain from 7 to 27 different alleles (avg. 15.4 alleles/locus) when tested across many breeds of dogs. Each breed, having evolved from a small number of founders and having been exposed to artificial genetic bottlenecks will end up with only a portion of the total available diversity. Artificial genetic bottlenecks include such things as popular sire effects, geographic isolation, catastrophes, outbreaks of disease, and ups and downs in popularity and resulting increases and decreases in population size. The alleles identified at each of the 33 STR loci and their relative frequencies were determined for 54 Whippets and are listed in Table 1.

Table 1: 33 Allele frequencies for 33 STR markers in Whippet (n=54)

AHT121	AHT137	AHTH130	AHTH171-A	AHTH260	AHTk211
94 (0.037)	131 (0.333)	119 (0.019)	219 (0.019)	238 (0.019)	87 (0.722)
96 (0.176)	133 (0.056)	121 (0.167)	225 (0.009)	240 (0.111)	89 (0.120)
98 (0.426)	137 (0.426)	127 (0.269)	227 (0.139)	242 (0.019)	91 (0.130)
100 (0.120)	141 (0.028)	131 (0.481)	229 (0.787)	244 (0.370)	95 (0.028)
104 (0.056)	147 (0.120)	133 (0.056)	237 (0.046)	246 (0.250)	
106 (0.130)	149 (0.019)	135 (0.009)		248 (0.028)	
110 (0.056)	151 (0.019)			250 (0.111)	
				252 (0.083)	
				254 (0.009)	

AHTk253	C22.279	FH2001	FH2054	FH2848	INRA21
286 (0.037)	116 (0.333)	132 (0.130)	148 (0.111)	228 (0.019)	95 (0.509)
288 (0.194)	118 (0.472)	136 (0.019)	152 (0.102)	230 (0.194)	97 (0.009)
290 (0.491)	120 (0.037)	144 (0.620)	156 (0.463)	232 (0.009)	99 (0.231)
292 (0.278)	124 (0.111)	148 (0.231)	160 (0.056)	236 (0.083)	101 (0.250)
	126 (0.019)		164 (0.157)	238 (0.139)	
	130 (0.028)		168 (0.102)	240 (0.278)	
			172 (0.009)	242 (0.157)	
				244 (0.120)	

INU005	INU030	INU055	LEI004	REN105L03	REN162C04
110 (0.019)	144 (0.139)	208 (0.028)	95 (0.583)	229 (0.259)	202 (0.250)
124 (0.481)	148 (0.065)	210 (0.722)	97 (0.009)	233 (0.500)	206 (0.750)
126 (0.306)	150 (0.787)	214 (0.185)	105 (0.028)	235 (0.130)	
130 (0.009)	152 (0.009)	218 (0.065)	107 (0.370)	237 (0.046)	
132 (0.185)			109 (0.009)	239 (0.009)	
				241 (0.028)	
				243 (0.019)	
				245 (0.009)	

REN169D01	REN169O18	REN247M23	REN54P11	REN64E19	VGL0760
202 (0.065)	162 (0.176)	268 (0.546)	222 (0.574)	139 (0.463)	18.2 (0.046)
212 (0.704)	164 (0.148)	270 (0.185)	228 (0.046)	143 (0.009)	19.2 (0.009)
214 (0.028)	166 (0.463)	272 (0.157)	232 (0.046)	145 (0.370)	20.2 (0.296)
216 (0.167)	168 (0.019)	278 (0.111)	234 (0.037)	147 (0.157)	21.2 (0.065)
218 (0.037)	170 (0.194)		236 (0.204)		22.2 (0.204)
			238 (0.093)		23.2 (0.370)
					24.2 (0.009)

VGL0910	VGL1063	VGL1165	VGL1828	VGL2009	VGL2409
13 (0.222)	8 (0.296)	18 (0.148)	15 (0.102)	9 (0.213)	13 (0.093)
15 (0.046)	9 (0.046)	19 (0.028)	16 (0.167)	12 (0.009)	15 (0.306)
16.1 (0.009)	11 (0.426)	20 (0.111)	17 (0.056)	13 (0.324)	17 (0.463)
17.1 (0.352)	12 (0.019)	21 (0.009)	18 (0.037)	14 (0.102)	18 (0.130)
18.1 (0.065)	14 (0.120)	22 (0.046)	19 (0.278)	15 (0.352)	19 (0.009)
19.1 (0.306)	15 (0.065)	25 (0.287)	20 (0.287)		
	16 (0.019)	26 (0.065)	21 (0.019)		
	18 (0.009)	27 (0.028)	22 (0.056)		
		28 (0.019)			
		29 (0.037)			
		30 (0.130)			
		31 (0.083)			

32 (0.009)

VGL2918	VGL3008	VGL3235
12 (0.056)	15 (0.130)	13 (0.074)
13 (0.139)	16 (0.009)	14 (0.583)
14 (0.130)	17 (0.352)	15 (0.019)
15 (0.028)	18 (0.407)	19 (0.037)
16 (0.009)	19 (0.093)	20 (0.046)
17.3 (0.120)	20 (0.009)	21 (0.204)
18.3 (0.019)		22 (0.028)
19.3 (0.167)		23 (0.009)
20.3 (0.231)		
21.3 (0.019)		
22.3 (0.074)		
23.3 (0.009)		

B. Assessment of population diversity using standard genetic parameters

Allele and allele frequencies at each of the 33 STR loci are listed in Table 1 and used to determine basic genetic parameters (Table 2) such as the number of alleles found at each STR locus (N_a); the number of effective alleles (N_e) per locus (i.e., the number of alleles that contribute to heterozygosity in the population); the observed or actual heterozygosity (H_o) that was found in the population; and the heterozygosity that would be expected (H_e) if the existing population was being randomly bred. The value F is a coefficient of inbreeding derived from the H_o and H_e values. A value of +1.0 would occur only if every individual were genetically indistinguishable at each of the 33 STR loci, while a value of -1.0 would be seen when all the dogs were completely different at each of the 33 loci. A value of 0.00 would be seen if the selection of sires and dams were entirely random within the existing gene pool.

The allele frequency data obtained from the 33 STR panel can be used to assess heterozygosity within a population (Table 2). Using the 33-marker panel, the 54 Whippets had an average of 6.09 alleles/locus (N_a). This is higher than for the Shiloh Shepherd ($N_a=4.0$), Lakeland Terrier ($N_a=4.24$), Swedish Vallhund ($N_a=4.91$) and Irish Red and White Setter ($N_a=5.09$); similar to the Llewellyn Setter ($N_a=5.94$) and Flat-coated Retriever ($N_a=5.94$); but lower than large and genetically diverse breeds such as the Labrador Retriever ($N_a=7.33$), Golden Retriever ($N_a=8.39$) and Miniature Poodle ($N_a=8.91$). However, the average number of alleles is less important than the number of alleles that have the greatest genetic influence on heterozygosity, a figure known as average effective alleles/loci or N_e . N_e in this group of dogs averaged 3.18 effective alleles per locus. Therefore, an average of three alleles at each locus contribute to most of the heterozygosity within the breed. The observed (actual) heterozygosity of this group of 54 dogs was 0.63, while the expected heterozygosity (H_e) for a population in a state

resembling Hardy-Weinberg equilibrium (HWE) was 0.64, yielding a coefficient of inbreeding (F) of 0.03 (i.e., only 3% more inbred than predicted for HWE). These standard genetic assessment values indicate that the breed has good genetic diversity, which has been sustained in a relatively random manner across the breeds history.

Ne is also a measure of the number of individuals that are necessary to keep a free-breeding population in a state of HWE from one generation to the next. This number is also known as the effective population size. Pure breeds of dogs have Ne values as low as 2.3-2.6 (Doberman pinscher, Japanese Akita, Swedish Vallhund, Flat coated retriever), 3.3-3.8 (Havanese, Labrador and Golden Retriever, Border Collie, Samoyed, Magyar agar), and as high as 4.2 (Toy Poodle). The effective population size for Whippets from 1980-2000 has been calculated as 56.4 [14], which is just above the theoretical limit of 50 individuals necessary to maintain HWE. For comparison, the effective population size for Toy poodles has been estimated at 136.3 [15]. The low Ne for Whippets suggests the need for breeders to maintain current heterozygosity as vigorously as possible.

Table 2: Standard genetic assessment of 54 Whippets on allele frequencies at 33 genomic STR loci on 25 chromosomes. Values are expressed as means (averages) with one standard error (SE).

	N	Na	Ne	Ho	He	F
Mean	54	6.09	3.18	0.63	0.64	0.03
SE		0.4	0.23	0.03	0.02	0.024

B. Standard genetic assessment values for individual STR loci

The allele frequencies can be also used to do a standard genetic assessment of heterozygosity at each STR locus (Table 3). This provides an estimate of genetic similarities in the specific regions of the genome that are associated with each STR marker. Phenotypic differences equate to genotypic differences. Therefore, alleles that are widely shared across the population are indicators that positive selection is occurring for certain desired traits. The Na values for an individual STR locus for this population of 54 Whippets ranged from a low of 2 to a high of 13 alleles per locus, while the Ne ranged from 1.56 to 7.04 alleles per locus. It is important to remember that each STR locus can have from 7-27 different alleles (avg. 15.4 alleles/locus) when testing across all dogs. The observed heterozygosity (Ho) for an individual STR locus ranged from 0.23 to 0.89, while He ranged from 0.36 to 0.80 (Table 3). Eighteen loci had positive F values and 15 were negative. Nine of the positive loci had F values greater than 0.11, indicating over 10% excess of inbreeding. These loci were under a greater degree of positive selection than those with negative F values and were presumably linked to regions of the genome more strongly associated with current desired breed-specific traits. However, the influences of these various inbred and outbred regions of the genome defined by these 33 STR loci have been kept in balance by breeders as evidenced by a near zero F value for the overall population (Table 2). The degree of inbreeding or outbreeding for individual dogs in this group of 54 will be made apparent from internal relatedness (IR) scores.

Table 3: Standard genetic assessments of individual STR loci of 54 Whippets.

#	Locus	N	Na	Ne	Ho	He	F
1	AHT121	54	7	3.98	0.80	0.75	-0.06
2	AHT137	54	7	3.21	0.61	0.69	0.11
3	AHTH130	54	6	2.98	0.59	0.67	0.11
4	AHTH171-A	54	5	1.56	0.17	0.36	0.54
5	AHTH260	54	9	4.30	0.82	0.77	-0.06
6	AHTk211	54	4	1.81	0.35	0.45	0.21
7	AHTk253	54	4	2.80	0.67	0.64	-0.04
8	C22.279	54	6	2.87	0.72	0.65	-0.11
9	FH2001	54	4	2.20	0.46	0.54	0.15
10	FH2054	54	7	3.63	0.65	0.73	0.11
11	FH2848	54	8	5.53	0.89	0.82	-0.09
12	INRA21	54	4	2.66	0.57	0.62	0.08
13	INU005	54	5	2.78	0.61	0.64	0.05
14	INU030	54	4	1.56	0.33	0.36	0.07
15	INU055	54	4	1.78	0.43	0.44	0.03
16	LEI004	54	5	2.09	0.65	0.52	-0.24
17	REN105L03	54	8	2.96	0.70	0.66	-0.06
18	REN162C04	54	2	1.60	0.43	0.38	-0.14
19	REN169D01	54	5	1.89	0.44	0.47	0.06
20	REN169O18	54	5	3.28	0.61	0.70	0.12
21	REN247M23	54	4	2.70	0.56	0.63	0.12
22	REN54P11	54	6	2.60	0.63	0.62	-0.02
23	REN64E19	54	4	2.66	0.57	0.62	0.08
24	VGL0760	54	7	3.66	0.78	0.73	-0.07
25	VGL0910	54	6	3.66	0.78	0.73	-0.07
26	VGL1063	54	8	3.44	0.54	0.71	0.24
27	VGL1165	54	13	6.66	0.87	0.85	-0.02
28	VGL1828	54	8	4.86	0.78	0.79	0.02
29	VGL2009	54	5	3.51	0.70	0.72	0.02
30	VGL2409	54	5	3.00	0.76	0.67	-0.14
31	VGL2918	54	12	7.04	0.87	0.86	-0.02
32	VGL3008	54	6	3.17	0.69	0.69	-0.00
33	VGL3235	54	8	2.55	0.59	0.61	0.03

On average, the alleles identified in this group of 54 dogs represented 6.09/15.4=39.5% of alleles known to exist in all canids tested at the VGL. This is higher than the Swedish Vallhund (31.9%) and Irish Red and White Setter (34.8%); similar to the Flat-coated Retriever (38.6%), Magyar Agar (40.4%) and Borzoi (40.9%); but lower than breeds such as the Golden Retriever (54.5%), Toy Poodle (55.6%) and Standard Poodle (58%).

D. Differences in population structure as determined by principal coordinate analysis (PCoA)

PCoA measures the genetic relatedness of individuals in a population. The data is computed in a spherical form, but it is often presented in the two dimensions that most closely represent its three-dimensional form (usually coordinates 1 and 2). The more closely individuals cluster together around the XY axis, the more related they are to each other.

The 54 Whippets formed a single population (i.e., breed) divided into four genetically distinguishable subgroups by PCoA (Fig. 1). These subpopulations were comprised of dogs that were more related to each other than to dogs in the rest of the population. This is a common feature of bloodlines within a breed and an indication that the 54 dogs chosen for this analysis were as genetically diverse as possible and likely to be representative of the entire breed.

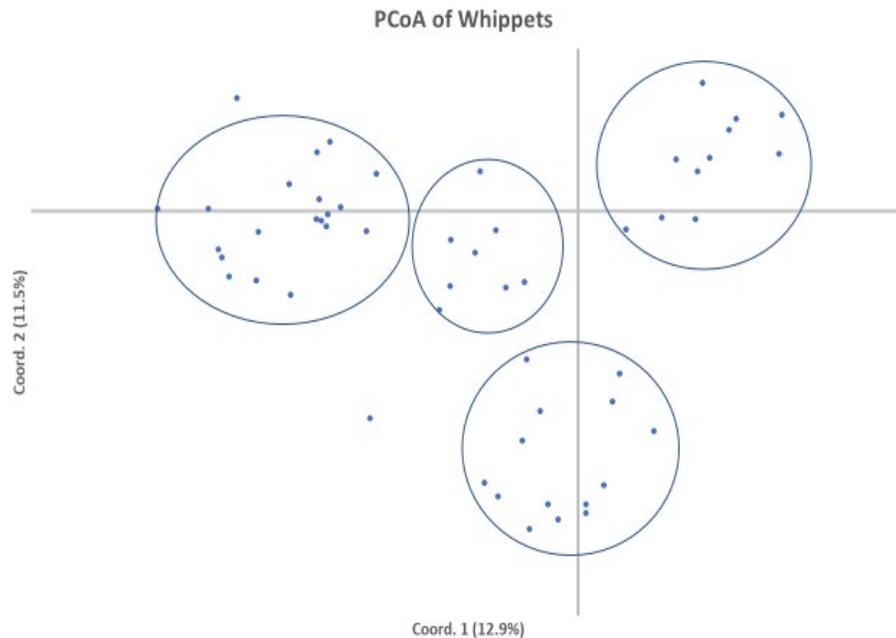


Figure 1. PCoA graph portraying the genetic relatedness of 54 Whippets. The population segregates by degree of relatedness into four subpopulations or bloodlines (circles).

The degree of relatedness of individuals within a breed can be further emphasized by comparing closely and distantly related breeds, such as the Whippet, Italian greyhound, and Samoyed (Fig. 2). Comparing related breeds with a very unrelated breed will enhance the degree of relatedness between related breeds (or varieties/bloodlines). Figure 2 shows that Italian greyhound are composed of two varieties (European and North American) and all Whippets are closely clustered as a single breed and no longer divided into subgroups as in Fig. 1. Samoyeds, being genetically dissimilar are tightly

clustered at a significant distance from the Whippet and Italian greyhound. It is also significant and expected that the Whippet and Italian greyhound are clustered nearest to each other, but it is even more significant that several Italian greyhounds, especially those from Europe, are clustering within or closely adjacent to Whippets. This suggests that some outcrossing has occurred more recently between these two breeds

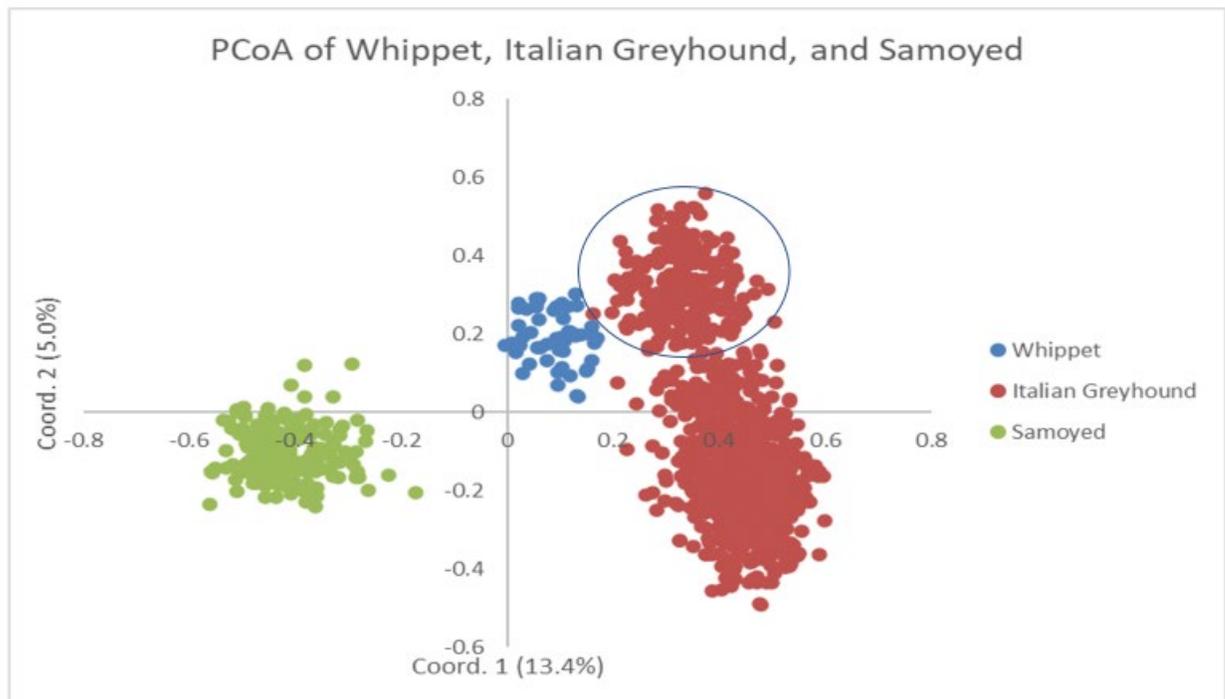


Figure 2. PCoA comparing Whippet, Italian greyhound and Samoyed breeds based on 33 autosomal STRs. European Italian greyhounds are circled.

D. Internal relatedness (IR) of individuals and the population as a whole

1. IR testing

Genetic assessments such as those presented in Tables 1-3 are indicators of population-wide heterozygosity and do not reflect the genetic diversity being provided to individuals by their parents. Internal Relatedness (IR) is a calculation that has been used to determine the degree to which the two parents of an individual dog were related. The IR calculation takes into consideration homozygosity at each locus and gives more importance to rare and uncommon alleles. Rare and uncommon alleles would presumably be present 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 a value of -1.0 would have parents that were totally unrelated at all 33 STR loci, while a dog with an IR value of +1.0 has parents that

were genetically identical at all loci. An IR value of +0.25 would be found among offspring of full sibling parents from a random breeding population. IR values >0.25 occur when the parents of the full sibling parents were themselves highly inbred. The higher the IR value above 0.25 the more closely related were the parents and grandparents of the siblings.

Table 4 lists the IR values for the 54 Whippets that were initially tested. The 25% of most outbred dog in the population had an IR scores of -0.046 to -0.245, while the 25% of most inbred dog in the group had an IR score of 0.093 to 0.247, while the mean (average) IR score for the group was 0.021. Therefore, IR values give a different picture than seen with the population average scores from the standard genetic assessment (Table 2). While the standard genetic assessments indicated a population in HWE, the IR scores showed a population of individuals that ranged from very outbred to very inbred. The most inbred dog in the group was interrelated to the same degree as offspring of full sibling parents. The more inbred dogs are balanced by outbred dogs, making it appear that the overall population was in a state of HWE. This is a common feature of all pure breeds of dogs.

Table 4: Internal relatedness (IR) values calculated using allele numbers and frequencies for 54 Whippet (redline). The IR values can be adjusted to reflect how these same dogs would score if they were to exist in a large population of village dogs (IRVD-blue line).

	IR	IRVD
Min	-0.245	-0.032
1st Qu	-0.046	0.201
Mean	0.021	0.286
Median	0.001	0.278
3rd Qu	0.093	0.376
Max	0.247	0.670

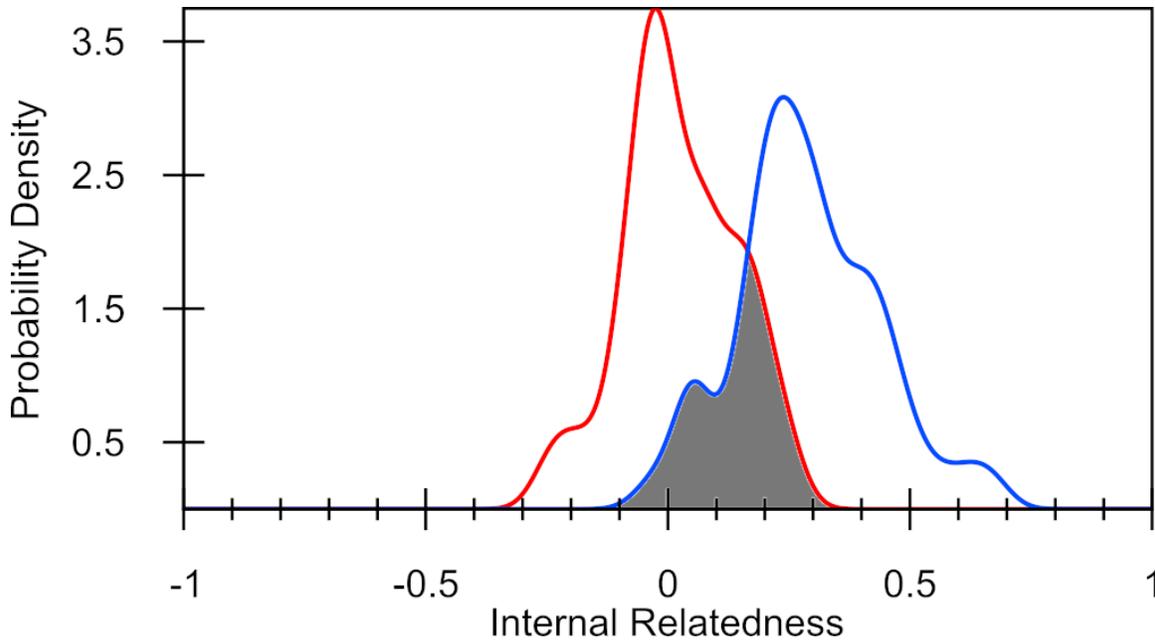


Figure 3. Distribution of IR (red line) and IR-village dog (IRVD) (blue line) values for the Whippet (n=54). The area under the curve (black) represents the degree of allele sharing (32.6%) between Whippets and village dogs.

2. Adjusted IR values (IRVD) as a measure of genetic diversity lost during breed evolution from time of origin to the present time.

It is possible to determine the amount of canid genetic diversity a breed has retained as it evolved to present day. This is done by assuming that individual Whippets were members of the current village dog population found in the Middle East, SE Asia and the Island Pacific nations. The IR values and IR values adjusted to village dogs (IRVD) (Table 4) can then be graphed and the graphs overlaid (Fig. 3). One half of the dogs have IRVD scores from 0.286 to 0.670 and one half with IRVD scores of -0.032 to 0.286. Therefore, if this group of dogs were found among modern village dogs, three-fourths of them would be considered equally or more inbred than offspring of full sibling village dog parents. This degree of inbreeding is seen in many breeds of dogs.

The IRVD curve for the Whippets tested was shifted to the right of the IR curve, and the area of overlap was 32.6% (Fig. 3). This figure is close to the 39.5% of retained genetic diversity calculated from comparison with a somewhat different population, i.e., all canids ever tested at the VGL (Tables 1, 2). This level of retained village dog genetic diversity is lower than the 60% or so retained diversity observed in the Miniature/toy poodle or 54% in Labrador Retriever, and much higher than the 23% for Irish wolfhound, 15% in Doberman Pinchers and 7% in Swedish Vallhund. All pure breeds of dogs have come from relatively small founder populations, which has limited genetic diversity from the time registries were created and closed. Greatly varying amounts of genetic diversity may have been lost subsequently through artificial genetic bottlenecks such as

cataclysmic events (e.g., world wars) or inbreeding for a specific show conformation (e.g., popular sire effects).

E. DLA Class I and II Haplotype frequencies and genetic diversity

The DLA consists of four gene rich regions making up a small part of canine 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 responsible for autoimmune diseases, allergies, and resistance/susceptibility to infectious diseases.

The Class I region contains several genes, but only one, DLA-88, is highly polymorphic (with many allelic forms) and is therefore most important for immune regulation. Specific alleles at the four STR loci associated with the DLA88 are linked together in various combinations, forming specific haplotypes (Table 5). Groups of genes and their alleles inherited as a block, rather than singly, are called haplotypes.

The class II region also contains several genes, three of which are highly polymorphic, DLA-DRB1, DLA-DQB1 and DLA-DQA1. Specific alleles at the three STR loci associated with the three Class II genes are strongly linked and inherited as a single block or haplotype (Table 5). One haplotype comes from each of the parents.

Specific class I and II haplotypes are often linked to each other and inherited as a genetic block. However, there is enough distance between these two regions to allow for a degree of recombination resulting in many class I/II combinations. The STR-based haplotype nomenclature used in this breed diversity analysis is based on numerical ranking with the first haplotypes identified in Standard Poodles being named 1001, 1002, ... for class I haplotypes and 2001, 2002, ... for class II haplotypes. It is common for various dog breeds to share common and even rare haplotypes, depending on common ancestry.

1. DLA class I and II haplotypes existing in Whippets

The 54 Whippets in this study possessed 16 DLA class I and 9 DLA class II haplotypes (Table 5). Three class I (1247-1249) were unique to the breed and the rest shared with several other breeds (Table 5). All class II haplotypes have been recognized in other breeds (Table 6). No class I or II haplotype was dominant in the breed, somewhat different from many other breeds. This indicates that the breed has evolved from a relatively large and diverse founder population. The lower proportion of class II to class I haplotypes was unusual and was previously seen in the Borzoi.

The number of DLA class I and II haplotypes found in these 54 Whippets was average compared to many other breeds studied to date. The numbers of DLA class I (n=16) and II (n=9) haplotypes found in Whippets were higher than the Swedish Vallhund (6, 4) and Shiloh Shepherd (7, 6); similar to the Giant Schnauzer (14, 15), Samoyed (13, 12) and Shiba Inu (16, 15); and much lower than Golden Retriever (26, 23) and Miniature Poodle (33, 23).

Table 5: DLA class I and Class II haplotypes and their frequencies in Whippets (n=54). Updated May 14, 2020

DLA1 #	STR types	Frequency
1002	380 365 281 181	0.046
1008	386 373 289 182	0.074
1012	388 369 289 188	0.037
1016	382 371 277 178	0.102
1040	380 371 277 186	0.056
1045	376 371 277 186	0.009
1056	386 373 289 190	0.083
1058	387 378 287 186	0.148
1066	376 375 277 178	0.194
1104	386 373 289 186	0.130
1162	386 373 289 181	0.009
1208	386 373 277 181	0.037
1209	386 378 287 186	0.028
1247	376 373 289 190	0.009
1248	386 365 281 181	0.028
1249	388 379 289 190	0.009
DLA2 #	STR types	Frequency
2001	343 324 284	0.074
2003	343 324 282	0.120
2006	339 325 280	0.028
2017	343 322 280	0.250
2028	345 327 288	0.056
2031	339 322 282	0.102
2033	339 323 282	0.167
2048	339 331 282	0.194
2062	345 327 282	0.009

2. DLA haplotype sharing with other dog breeds

DLA haplotypes are much more conserved than most other regions of the genome and each DLA region inherited as a block of linked genes from each parent and passed on by descent. Therefore, the number and incidence of DLA haplotypes found in a breed can be used to estimate the founder/founder lines that were used to create a breed and the importance of the various lines in subsequent breed evolution. The DLA class I and II regions are frequently shared between breeds, reflecting common distant ancestry and inheritance by descent (Table 6). As might be expected, the greatest sharing of DLA haplotypes was with the Italian Greyhound. However, a great deal of haplotype sharing was observed with European breeds such as Poodles, Golden and Labrador Retrievers,

Table 8. Standard genetic assessment of 54 Whippets on allele frequencies at 7 STR loci within the DLA class I and II region on canine autosome 12. Values are expressed as means (averages) with one standard error (SE).

	N	Na	Ne	Ho	He	F
Mean	54	5.14	3.51	0.65	0.69	0.07
SE		0.51	0.33	0.04	0.03	0.03

III. Health [7-11]

Whippets have been bred for coursing, work, and race, which requires sound bodies free of physical exaggerations that might affect heart, breathing, muscles, ligaments, or skeleton. Therefore, disorders like Hip dysplasia are uncommon in Whippets [8,9]. They are also relatively free of the ear infections, skin allergies, or digestive problems afflicting many other pure breeds.

A. Lifespan

The lifespan of Whippets is reportedly 10-15 years with a median of 10 years [3, 9]. A small number of dogs have lived to 16 and 17 years [9].

B. General health problems

A Kennel Club health survey done in 2004 found the major causes of death in Whippets in the UK to be heart failure of some type (14%), cancer (10%), urological problems (6.4%), followed by cerebral vascular (stroke), neurologic (seizures), spinal disease, immune mediated thrombocytopaenia (IMTP) and autoimmune hemolytic anemia (AIHA), gastrointestinal problems (enteritis, pancreatitis), musculoskeletal problems (arthritis, brittle bones, joint pain), endocrine disorders (Cushing’s disease, Type I diabetes, Addison’s disease), and liver failure [7].

The American Whippet Club recommends three test procedures for all dogs prior to breeding [12]. The first is a BAER test for normal hearing in both ears. Two different studies have found 0.4-1.3% of dogs tested to be bilaterally deaf [8, 13]. Deafness has been associated with several coat color and pattern mutations in various dog breeds, including Piebald and Merle coats [13]. The second recommendation is a normal OFA approved eye exam at least one year prior to mating. The third test is an OFA advanced cardia exam with echocardiogram performed by a Board-certified Cardiologist at least two years of a mating. The most common cardiac problem is chronic valvular degeneration in older dogs. However, there is concern about an increased incidence of dilated cardiomyopathy (DCM) possibly associated with grain-free diets [16, 17].

C. Heritable disease problems

Genetic eye defects such as hereditary cataracts, primary lens luxation and progressive retinal atrophy are uncommon in the breed. Nevertheless, the American Whippet Club

recommends that breeding stock be given a complete eye examination and certified free of problems. Whippets are, like other sighthounds, more sensitive to barbiturate anesthetics. This is in part due to their low concentration of body fat and their liver's inability to metabolize anesthetics.

Genetic tests for the following disorders are available for the breed depending on need: Degenerative Myelopathy (DM), Glycogen Storage Disease V11, Muscular Hypertrophy, Dilute coat color Alopecia, Multi Drug Resistance, Phosphofructokinase Deficiency (PKF), Primary Lens Luxation (PLL), L2 Hydroxyglutaric Aciduria (L2-HGA), and Hyperuricosuria (HUU) [11].

A myostatin mutation causing a muscular hypertrophy was identified in Whippets in 2007 [10]. Whippets with a single copy of this mutation are largely unaffected, although there is an unsubstantiated claim that they may be faster but prone to cramping and overheating on exercise. Dogs that are homozygous for the mutation are known as Bully whippets and can suffer a range of disorders. Homozygotes often die within the first few days of life from a wobbler type syndrome and/or failure to nurse because of an extreme undershot lower jaw. Dogs that survive into adulthood can suffer painful muscle cramping, jaw anomalies, abnormal dentition, and deficient cognition. Genetic testing has greatly reduced the numbers of Bully whippets.

IV. What does this assessment of genetic diversity tell us about the contemporary Whippet

The Whippets tested constituted a single breed, albeit with some intra-breed variation to the level of bloodline. The breed originated from dogs that shared many of their genomic alleles with village dogs currently found in the Middle East, SE Asia, and Island Pacific nations. Their DLA haplotypes are also shared with many other breeds that evolved mainly in England.

The anticipation is that the 54 dogs tested will define 90% or more of the known autosomal alleles and DLA class I and II haplotypes for the breed. This is sufficient to provide a reasonable assessment of genetic diversity in the breed. Nevertheless, it is important to screen more Whippets, especially from parts of the world outside of the USA. Genetic diversity for the breed appears below average for pure breeds, and it is important to identify any additional diversity that might exist.

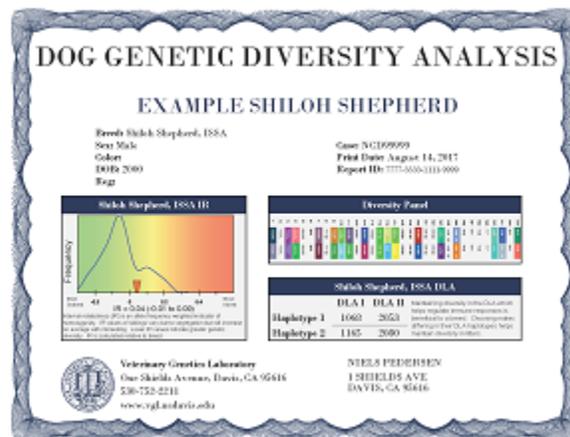
Whippets have maintained a below average level of genetic diversity since founding. This knowledge is impetus for breeders to be as diligent as possible in maintaining existing diversity through the following generations. A lack of genetic diversity is not in itself bad, providing the founder population was relatively free of deleterious genetic traits and breeders have been judicious in avoiding any artificial genetic bottlenecks that may cause either a loss or imbalance of original diversity. The breed is surprisingly clear of breed-specific heritable disease traits and enjoys a good lifespan. Breeds that lack genetic diversity must be managed much more closely to avoid further loss of genetic diversity and have less leeway in dealing with simple recessive or complex polygenic

disorders that might arise. Elimination of deleterious traits may result in loss of genetic diversity, especially when diversity is already low.

V. Results of 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 related to the entire 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 are either different (heterozygous) or the same (homozygous). Each allele is inherited from each of the parents. More of the alleles at each locus will be homozygous in dogs from closely related parents or that in regions of the genome that are under strong positive selection for some favored phenotypic trait or traits. Dogs with a predominance of rarer (i.e., low incidence) alleles will be more distantly related to the bulk of the population than dogs that have a predominance of common (i.e., high incidence) alleles.



B. What should you do with this information?

The use of DNA for testing genetic diversity in the Whippet has confirmed that the breed lacks genetic diversity genome-wide and in the DLA region, most likely from a small number of founder individuals/lines. It is more important, therefore, to closely monitor existing diversity into the future. We believe that this can be most accurately done with DNA testing as a supplement to in-depth pedigrees. If the breed were to consider increasing genetic diversity by further genetic introgressions, DNA testing of dogs intended for such introgressions would also be essential.

The goal for breeders should be to continue to produce puppies with IR scores less than 0, and with time, even lower scores. Although most of the individuals tested were randomly bred, there were small subpopulations of dogs that were much more inbred or outbred than the rest of the population. Therefore, there is a possibility to better balance genetic diversity in the breed. Mates should be selected to avoid homozygosity at any genomic loci or DLA class I and II haplotype and encourage the use of dogs with less common genomic alleles or DLA haplotypes. 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, like what is being done by many Standard Poodle breeders. However, IR values, because they reflect the unique genetics of individuals, cannot be used as the criteria for selecting ideal mates. Mates with identical IR values may produce puppies significantly more or less diverse than their parents. Conversely, a mating between dogs with high IR values, providing they are genetically different, may produce puppies having much lower IR scores than either parent. A mating between a dog with a high IR value and a 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 may 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. You want to avoid breeding pairs that will produce puppies that will be homozygous for the same haplotypes, and once again, less common haplotypes may offer more diversity than common ones.

Breeders who do not have access to computer programs to predict the outcome of pairings based on IR values of sire and dam can also compare values by manual screening. Potential sires and dams should be first screened for genetic differences in alleles and allele frequencies for the 33 genomic STR loci. Some extra weight should be given to rare vs common alleles. This information is included on all certificates and on the breed-wide data on the VGL website.

Puppies, once born, should be tested for their actual IR values, which will reflect the actual genetic impact of each parent on internal diversity. Considerations of mate choices for genetic diversity should be balanced with other breeding goals but maintaining and/or improving genetic diversity in puppies should be paramount.

A more effective use of this study is to contribute the genetic information to a web repository. The best format for such a repository and testing has been provided by Standard Poodle breeders. This information could be incorporated into a mate selection service that will allow a breeder to identify, among all the dogs tested, potential mates that would be most ideal for increasing genetic diversity in their litters-
<https://www.betterbred.com/>.

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