Genetic Diversity Testing for Doberman Pinscher

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 Doberman 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 June of 2023, 1205 Doberman Pinschers from the 17 different countries were tested at the VGL to assess genetic diversity in the breed. More information on the geographical distribution of Doberman DNA samples tested for this study can be found on section IIA below.

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 Doberman Pinscher

A. Breed History [1, 2]

Doberman Pinschers were first bred in the town of Apolda, in the German state of Thuringia around 1890 by Karl Friedrich Louis Dobermann. Dobermann served in the dangerous roles of local tax collector, dogcatcher/skinner, and night watchman. Dobermann used local dogs to create what he thought would be the perfect dog to help protect people doing his types of work. There appears to be agreement on this part of the breed's origin, but the story on the type of dogs used to create the Dobermann is somewhat less clear. The best account of the origins and evolution of the Doberman breed in Germany can be found in the writings of Phillip Gruenig, who referred to himself as a founding breeder and judge of Doberman. One story is that Dobermann's first mating involved a black bitch named Bismark (Bissart) and a clever and fearless grey smooth-coated mongrel named Schnupp. An article from 1898 stated the owner of a local gravel pit in Apolda bred his blue-grey bitch with a black "Butcher's dog" and that Dobermann crossed these offspring with German Pinschers to create his breed. Outcrosses to other breeds undoubtedly followed, but the exact breeds vary according to the various historical accounts. The Thueringinn sheepdog, Butcher's dog, German Pinscher and Beauceron existed at the time and in the locality, as did the black and tan terrier. A famous bitch whose dam was a cross between a Greyhound stud and a Doberman bitch was also registered in the early 1900's and brought Greyhound attributes into the breed. Regardless of the original ancestry, Dobermann's goal was to breed dogs that would combine aggressiveness, protective behavior, loyalty, trainability, and physical prowess. He obviously succeeded directly or indirectly in this effort and a standard for the new "breed" was created by the German Kennel Club in 1890.

Dobermann died in 1894 and Otto Goeller christened the "new breed" in his memory. Dobermann's new breed may or may not have been fully developed at the time of Dobermann's death. There is general agreement that further development was left to skilled dog breeders such as Otto Goeller, Karl Doberman, Goswin Tischler and Philip Greunig. The appearance of the breed was standardized and refined, while retaining only the "bravest, toughest, and most loyal dogs". Goeller created the National Dobermann Pinscher Club in Germany in 1899 and was influential in writing the first breed standard. The name Pinscher (terrier in German) was later dropped in 1949 by the Germans and the British, as it was not appropriate for the breed. The Dobermann breed was first registered with the American Kennel Club in 1908 as the Doberman Pinscher, but it was not until 1921 that more than 100 individuals were registered each year. The breed's popularity in the USA increased dramatically after the end of WWII, when soldiers brought back their Dobermanns from Germany.

These original Dobermann were of medium size, compact build, muscular, and extremely loyal and distrustful of unfamiliar people. They became known for their keen ability to hunt and kill vermin. This aggressiveness often extended to other dogs and people, and this behavior has been often referred to as "sharp." However, as Dobermans became more popular in Germany and other parts of Europe, this temperament was throttled back to make them more suitable as pets. Most of this sharpness has been eliminated from contemporary US Doberman Pinschers. This sharp nature was put to good use by the German military in WWI and by all militaries of WWII.

Two major genetic bottlenecks occurred in Germany and Europe as the results of WWI and WWII. The period between 1914 and 1918 saw a great decline in the breed and a small number of dogs played a major role in re-establishing the breed in Germany. One sire, Burschel v. Simmenau, was credited by Gruenig as proving that one individual dog of this stature can redeem an entire breed. The German Dobermann flourished after WWI and many champions were proclaimed, some of which had great genetic influence on subsequent generations. Many champion Dobermanns were exported from Germany during 1920's, including to countries as distant as the USA and the USSR.

The breed in Germany underwent an even more severe genetic bottleneck as the result of WWII and its aftermath, and no litters were registered in West Germany from 1949 to 1958. German Dobermanns were saved by Werner Jung, who searched farms throughout Germany for remaining breeding stock. Preferring to use native dogs, Jung used Dobermanns he found in the countryside of West Germany, four oversized Miniature Pinschers, and a black and red Doberman bitch smuggled from East Germany to re-establish the "original" breed. It is possible that introgressions with other breeds occurred during this time.

The Doberman Pinscher of the USA has its origins firmly in Europe, but geographic isolation and differences in breeding objectives and standards have led to what are essentially two different varieties. The European Doberman Pinscher is larger, more uniform in size, and heavier boned, while the American Doberman Pinscher is much more variable in size. The German Dobermann has been bred more for personal (guard) protection and police/military work, with less emphasis on showing. European breeders adhere more strictly to the original German standards, while standards are more loosely defined in America. A sudden increase in the breed's popularity in the USA in the 1970's resulted in a rapid increase in the number of dogs needed to meet demand, resulting in more indiscriminate breeding and greater variations in size, color and appearance.

B. Appearance [3]

The American Kennel Club (AKC) official breed standard describes the Doberman Pinscher as medium sized with a square, compact, and muscular body. The height at the withers for adult dogs ranges between 26 and 28 inches, and for adult bitches between 24 and 26 inches. Ideally, the height (highest point of the withers) should be equal to the length of the dog (measured horizontally from the forechest to the rear of the upper thigh). The head is long and dry, and widens gradually toward the base of the ears in a continuous line. The top of the skull is flat. The eyes are almond shaped with an iris of uniform color. In black dogs, the eye color ranges from medium to dark brown; in red reds, blues, and fawns the color of the iris blends with that of the markings. The ears are normally cropped and carried erect. Dogs must possess a true scissors bite, with 42 correctly placed teeth: 22 in the lower jaw and 20 in the upper jaw. Overshot bites with more than 3/16 of an inch or undershot bites with more than ⅛ of an inch constitute disqualifications, as well as four or more missing teeth.

The tail is docked at approximately the second joint and is carried only slightly above the horizontal when the dog is alert. The coat is smooth, short, hard, thick and close lying. Colors allowed by the standard are black, red, blue, and fawn (Isabella). Markings allowed: sharply defined rust, appearing above each eye and on muzzle, throat and forechest, on all legs and feet,

and below tail, as well as white patch on chest (not exceeding ½ square inch). Any color besides the ones listed on the breed standard are considered disqualifications.

Temperament [3]

The breed is energetic, watchful, determined, alert, fearless, loyal and obedient. Dogs that are shy or vicious are dismissed from the show ring. Doberman Pinschers are generally known to be affectionate with family members and good with young children.

C. Health

1. Lifespan

The average life expectancy of a Doberman Pinscher is 10-12 years.

2. Diseases [4-22]

1. **Hip dysplasia** and **bloat** (gastric torsion) are disorders shared by many larger breeds of dogs. However, the incidence of both in Doberman Pinschers is low compared to many other breeds.

2. **Dilated cardiomyopathy (DCM)**, a cardiac disorder, is the most important heritable disease of Doberman Pinschers, and is becoming increasingly common among Dobermann in Europe. About one-half of Doberman Pinschers in the USA will develop DCM in their lifetime and the average survival after diagnosis is around two months, although some dogs can survive longer. Sixty percent of DCM is in males and 40% females, with an average age at onset 7.5 years. However, one-fourth of cases occur in dogs over 10 years. This means that most dogs are well past breeding age before the disease is diagnosed. About one quarter of dogs with DCM experience sudden death due to arrhythmias, while the remainder exhibit more classical signs of congestive heart failure such as cough, wheeze, and labored breathing. Two forms of DCM are recognized; an “attenuated wavy fiber type” that is seen in a number of other breeds, and a “fatty infiltration-degenerative type” that appears to be specific to Doberman Pinscher and Boxer. The causes for the disease are largely unknown, although one assumption is that it is an autosomal dominant trait. Mutations in two genes, *PDK4* and *DCM2*, have been associated with DCM in Doberman Pinscher.

3. **Cervical vertebral instability** (cervical spondylomyelopathy, wobbler syndrome) affects 5.5% of Doberman and 4.2% of Great Danes, but also occurs at a lesser incidence in several large (Rottweiller, Weimaraner, German Shepherd, Bernese) and giant (Great Dane, Mastiff) breeds and rarely in small dogs. The usual age at onset in Doberman Pinschers is around 6 years. The syndrome is associated with an instability in the cervical vertebrae due to bony and ligamentous abnormalities that ultimately lead to intervertebral disk slippage, bony malformation, soft tissue hypertrophy and narrowing of the vertebral canal. The C4-5 C5-6 disk regions are most often affected, moving in order of lesion frequency to C3-4, C6-7 and C2-3. The compression damage to the spinal cord and/or nerve roots results in the characteristic clinical signs. The term wobbler syndrome is used to describe the wobbly gait (walk) that is characteristic of the disorder. In addition to the wobbly gait, there may be neck pain and stiffness, difficulty in arising, weakness in the front limbs, atrophy of shoulder muscles, change in gait, and partial or complete paralysis.

Signs may change with the position of the head and neck. The precise cause of the instability in the cervical vertebrae is unknown, but in giant breeds it has been attributed to too rapid of growth. However, this would not seem to be the situation with Doberman, Rottweilers, and Bassett hounds. The cause is more likely to involve this specific region of the spine and is genetically complex. Chondrodystrophy is genetically complex and even though it is not a normal trait, it is used to varying degrees in creating the desired phenotype in many breeds.

4. **von Willebrand's disease** is the most common genetic disorder among all pure breeds of dogs. About 60% of Doberman carry the causative mutation. The von Willebrand's factor (vWF) is a carrier protein for Factor VIII, the latter being important for blood clotting. vWF is encoded by a large and highly mutable gene and a number of different genetic forms are found among and between dog breeds. Fortunately, most of the vWF mutants in dogs do not severely affect blood clotting and are not of great clinical significance (i.e., resembling human type 1 vWF mutants). Bleeding problems are more likely to be seen during teething, estrus, and surgical procedures (tail dock, ear clip) and are seldom severe enough to require clinical intervention with normal whole blood or plasma.

5. **Prostatic disease** is more common in Doberman Pinschers than among males of any other breed. Prostatic disease can manifest by hyperplasia (benign enlargement), cystic changes, infection, and even cancer. Bacterial infections of the prostate may manifest by recurrent urinary tract infection and abscessation. Bleeding from the penis and hematuria are also common signs of prostate disease. Marked enlargement of the prostate may impinge on the colon and interfere with normal defecation. Prostate cancer can occur, but is uncommon compared to other prostate disorders. The reason why Doberman Pinschers are so prone to prostatic disease is unknown, but there is little doubt that he breed is predisposed, which would suggest heritable factors.

6. **Autoimmune diseases** occur in Doberman Pinschers, just as they do in many other pure breeds. The incidence of autoimmune disorders increases as a breed becomes more inbred and loses genetic diversity. A number of autoimmune disorders of dogs have been associated with specific DLA class I or II haplotypes, although this has not been studied in Doberman Pinschers. The predisposition to autoimmunity is genetically complex and involves less-specific genetic polymorphisms that affect self/non-self-recognition and specific genetic polymorphisms that affect the forms of autoimmunity that occur in a breed. Many autoimmune disorders are shared by many different breeds, in particular chronic thyroiditis leading to hypothyroidism. Doberman Pinschers are one of many breeds that suffer from this disorder. Pemphigus folliaceus is seen in many breeds, but is another autoimmune disorder that is often seen in the Doberman. Systemic lupus erythematosus (SLE) and SLE-like disorders have been described in Doberman. Chronic active hepatitis is a relatively breed specific disease to Dobermans. The condition is usually diagnosed in middle-aged dogs (around 5 years of age), but this can occur in dogs from 2.5 to 10 years. Females are much more likely than males to develop the disorder. The breed specificity and strong predisposition towards females indicate a genetic predisposition Chronic active hepatitis is characterized by inflammation, scarring and destruction of the cells and tissue of the liver, resulting in loss of liver function and ultimately liver failure. Usually, by the time dogs are diagnosed with this condition, the damage to the liver is enough to cause dysfunction, and therefore the survival time and response to treatment is usually poor. There are two theories as to the cause of the disease. The disease has been associated with high levels of copper in the liver and bloodstream,

reminiscent to copper toxicosis in Bedlington terriers. However, there is some indication that high copper may be a result rather than cause of disease. A second theory is that the chronic hepatitis seen in Dobermans is an autoimmune disorder, comparable to a human disease. The histologic appearance of the lesion is compatible with autoimmunity. Studies have linked the disease to specific DLA class II haplotypes.

7. **Color dilution alopecia** (canine follicular dysplasia) occurs in a number of breeds that use the dilute gene to produce shades of black, brown, or red. The dilute gene is a simple recessive that affects the transport of melanin via melanosomes from melanocytes in the base of the hair follicle to the hair shaft. It may be associated with an additional mutation in the basic color gene that further impedes the transport of melanin. An example would be production of grey or silver coat color by combining the gene for black with dilute in certain breeds, e.g., blue coats in Italian Greyhound and Dobermans. Interference with the transport of melanin causes melanin to build up in melanocytes in the hair follicle. The effect of this increased build up is to weaken the hair shaft and make it more apt to break or to be prematurely shed. The disorder leads to a thinning of the hair coat, usually starting around 2-4 years of age and especially over the back-line. It occurs in about 93% of blue-coated Dobermans and 75% of fawns.

8. **Mitral valve disease** or **endocardiosis** is a common problem among all dogs, but the incidence is greater in certain pure breeds. This suggests that the genetic polymorphisms responsible for this disease are complex and ancient and have been concentrated by descent in certain breeds. Although the mitral valve is affected in 60% of cases, 30% of affected dogs will have involvement of both mitral (left atrium to left ventricle) and tricuspid (right atrium to right ventricle) valve and 10% only the tricuspid valve. The valves undergo a slow degeneration that is presumed to be heritable. The valves become thickened and deformed and, with time, the valves cannot form a tight seal preventing backward flow of blood. This blood 'leakage' causes the heart to pump harder and this can eventually lead to congestive heart failure. The disorder is most common in small or miniature breeds such as Poodles, Minature Schnauzers, Chihuhua, Fox terrier, Boston terrier and Cocker Spaniel, but also can affect large dogs, in particular the Doberman Pinscher.

9. **PRA** (progressive retinal atrophy) is a recessive inherited condition in Doberman Pinschers. The disease progresses to complete blindness over months or years. Clinical signs may not become noticeable until 3 years or older. Visual acuity is diminished, first at dusk, later in daylight. A screening test is available and can be performed by a veterinary ophthalmologist. CERF (Canine Eye Registration Foundation) will certify eyes for 12 months from the date of evaluation.

10. **Persistent hyperplastic primary vitreous** (PHPV) or **persistent hyperplastic tunica vasculosa lentis** (PHTVL) is a developmental disorder of the eye. PHPV is essentially a failure of normal separation and regression of the fetal vasculature from the iris and developing lens. The inheritance has been described as autosomal incomplete dominant or complex. The disorder can be detected at 7-8 weeks of age by expert examination but screening is often done at 15-20 months of age, prior to breeding. The severity is graded 1-6, and dogs scoring low (i.e., 1) are sometimes bred. In its severest form, PHPV can lead to glaucoma and loss of the eye. However, because of its strong genetic basis, no affected dogs should be bred, regardless of severity score. Genetic testing led to a decrease in the incidence of the disorder from 19% to 8% in the Netherlands during the period of 1978-1987.

11. **Narcolepsy** is a seizure disorder characterized by transient bouts of seizure activity manifested by rapid transitions between wakefulness and rapid eye movement sleep. Narcoleptic dogs are sleepier than normal, which may go unappreciated. However, more severe attacks may cause cataplexy, a state of generalized and complete muscle relaxation (atonia) with full consciousness but an inability to respond. The disorder is caused by recessive mutations in a gene called hypocretin receptor 2 (*HCRTR2*) in humans and dogs.

12. **Albinism** in Doberman Pinschers is caused by a deletion in a gene known as *SLC45A2*. This mutation traces back to a female, Padula's Queen Sheba or "Sheba", born in 1976. Sheba produced an extensive pedigree as breeders selected for this phenotype. Color-diluted dogs are cream in color with blue-eyes, have little pigmentation around eyes, mouth and nose, and are sensitive to bright light. The trait is considered deleterious with increased risk for skin tumors, in particular melanoma-like cancers.

13. **Cancer.** Doberman Pinschers rank anywhere from fourth to ninth among all breeds for cancer incidence, depending on data from various pet insurance companies and cancer registries. This gives them a higher than normal rate of cancer compared to all dogs. However, a study by Fleming and colleagues found that 26% of Doberman Pinschers in North America will die of neoplasia, placing them on par with most large breed dogs. Osteosarcoma is an important cancer in the breed. Doberman can also suffer other common cancers of dogs such as lymphoma, hemangiosarcoma, Mast cell cancer, and melanoma. There appears to be a predisposition for mammary cancer in intact females and prostate cancer in intact males.

The VGL offers a Doberman Pinscher Health Panel, which bundles together several genetic tests relevant to the breed's health. It includes tests for Deafness with Vestibular Dysfunction (DVD) or DINGS, Degenerative Myelopathy (DM), Dilated Cardiomyopathy (DCM), Narcolepsy, Oculocutaneous Albinism (OCA), and Von Willebrand Disease I (vWD Type 1). For more information, please refer to https://vgl.ucdavis.edu/panel/doberman-pinscher-health-panel.

II. Results on Genetic Diversity of Doberman Pinschers

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

A total of 1205 Doberman Pinscher DNA samples from 18 different countries were tested as part of this study. The number of individuals tested per country is listed on **Table 1.**

Table 1. Number of Doberman Pinscher individuals tested per country as part of this study.

Country	Number of individuals
United States	827
Australia	207
Finland	63
Canada	36
Denmark	13
Germany	12
France	12
Sweden	6

Czech Republic	5
Great Britain	4
Netherlands	4
Norway	2
South Africa	2
Brazil	1
Switzerland	1
Mexico	1
Portugal	1
Unknown	8
Total	**1205**

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, 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 1205 Doberman Pinschers are listed on **Table 2**.

Table 2. Alleles and their frequencies for 33 STR markers in Doberman Pinschers (n = 1205). The allele that occurs at the highest frequency at each locus is bolded.

AHT121	**AHT137**	**AHTH130**	**AHTh171-A**	**AHTh260**	**AHTk211**
92 (0.0008)	**131 (0.5046)**	117 (0.0004)	**219 (0.6124)**	**238 (0.8635)**	87 (0.0025)
96 (0.8066)	133 (0.0021)	**119 (0.6967)**	223 (0.0008)	240 (0.0008)	89 (0.1095)
98 (0.1506)	135 (0.0008)	121 (0.0207)	225 (0.0224)	242 (0.0017)	**91 (0.8793)**
100 (0.0270)	137 (0.0793)	123 (0.2411)	227 (0.1743)	244 (0.0278)	93 (0.0079)
102 (0.0108)	143 (0.0004)	125 (0.0008)	229 (0.1191)	246 (0.0921)	95 (0.0004)
104 (0.0012)	145 (0.0017)	127 (0.0012)	233 (0.0606)	248 (0.0108)	97 (0.0004)
108 (0.0012)	147 (0.3436)	129 (0.0357)	241 (0.0104)	252 (0.0025)	
112 (0.0017)	149 (0.0452)	131 (0.0004)		254 (0.0008)	
	151 (0.0083)	133 (0.0029)			
	153 (0.0141)				

AHTk253	**C22.279**	**FH2001**	**FH2054**	**FH2848**	**INRA21**
284 (0.0004)	110 (0.0004)	132 (0.0241)	144 (0.0116)	234 (0.0008)	91 (0.0004)
286 (0.2809)	114 (0.2021)	136 (0.0004)	148 (0.0025)	236 (0.0004)	95 (0.0639)
288 (0.0145)	116 (0.0012)	140 (0.0017)	**152 (0.7058)**	238 (0.0315)	99 (0.0353)
290 (0.7021)	118 (0.2390)	**144 (0.9539)**	156 (0.0303)	240 (0.0095)	**101 (0.8614)**
292 (0.0021)	120 (0.1419)	148 (0.0195)	160 (0.0012)	242 (0.0066)	105 (0.0390)
	124 (0.0091)	152 (0.0004)	164 (0.0017)	**244 (0.9494)**	

	126 (0.3963)		168 (0.2419)	246 (0.0008)	
	128 (0.0095)		172 (0.0050)	248 (0.0008)	
	130 (0.0004)				
INU005	**INU030**	**INU055**	**LEI004**	**REN105L03**	**REN162C04**
110 (0.0029)	144 (0.2660)	208 (0.0012)	**85 (0.6635)**	227 (0.0058)	200 (0.0328)
122 (0.4158)	146 (0.0012)	210 (0.3257)	95 (0.0029)	231 (0.0021)	**202 (0.6033)**
124 (0.3232)	**150 (0.5722)**	212 (0.0058)	97 (0.1440)	233 (0.0008)	204 (0.0025)
126 (0.2427)	152 (0.1606)	216 (0.1680)	103 (0.0017)	**235 (0.9432)**	206 (0.0456)
132 (0.0154)		**218 (0.4859)**	107 (0.1876)	237 (0.0249)	208 (0.0390)
		220 (0.0008)	111 (0.0004)	239 (0.0062)	210 (0.0004)
		222 (0.0124)		241 (0.0166)	212 (0.2448)
				245 (0.0004)	214 (0.0029)
					216 (0.0286)
REN169D01	**REN169O18**	**REN247M23**	**REN54P11**	**REN64E19**	**VGL0760**
202 (0.0618)	158 (0.0515)	268 (0.1187)	220 (0.0004)	139 (0.0008)	**12 (0.3104)**
210 (0.0004)	160 (0.0004)	270 (0.0008)	222 (0.0008)	143 (0.0004)	13 (0.3071)
212 (0.3290)	**162 (0.5054)**	**272 (0.8780)**	**226 (0.5332)**	**145 (0.5714)**	14 (0.0017)
214 (0.1772)	164 (0.0025)	274 (0.0025)	230 (0.0037)	147 (0.2622)	18.2 (0.1714)
216 (0.3166)	166 (0.0025)		232 (0.0021)	149 (0.0174)	19.2 (0.0054)
218 (0.0071)	168 (0.2253)		234 (0.1353)	153 (0.1461)	20.2 (0.1834)
220 (0.1075)	170 (0.1946)		236 (0.0037)	155 (0.0017)	21.2 (0.0120)
224 (0.0004)	172 (0.0178)		238 (0.3174)		22 (0.0004)
			240 (0.0033)		22.2 (0.0041)
					23.2 (0.0033)
					24.2 (0.0004)
					25.2 (0.0004)
VGL0910	**VGL1063**	**VGL1165**	**VGL1828**	**VGL2009**	**VGL2409**
15 (0.0071)	11 (0.0008)	18 (0.0029)	15 (0.0037)	9 (0.0232)	13 (0.0004)
16 (0.0332)	12 (0.0033)	20 (0.0008)	**16 (0.5320)**	**11 (0.5203)**	14 (0.1896)
16.1 (0.0100)	13 (0.0037)	21 (0.0004)	17 (0.3469)	12 (0.0029)	15 (0.0058)
17 (0.0029)	**14 (0.5187)**	22 (0.0290)	18 (0.0050)	13 (0.0245)	16 (0.0037)
17.1 (0.0033)	15 (0.1456)	24 (0.0004)	19 (0.0054)	14 (0.2407)	17 (0.3149)
18.1 (0.0066)	16 (0.2037)	25 (0.0004)	20 (0.0871)	15 (0.1851)	18 (0.0685)
19.1 (0.7037)	17 (0.0154)	26 (0.0008)	21 (0.0195)	16 (0.0033)	**19 (0.3830)**
20.1 (0.1232)	18 (0.0755)	27 (0.0095)	22 (0.0004)		20 (0.0340)
21.1 (0.1017)	19 (0.0228)	28 (0.2975)			
22.1 (0.0079)	20 (0.0100)	**29 (0.5249)**			
23.1 (0.0004)	21 (0.0004)	30 (0.0303)			
		31 (0.1004)			
		32 (0.0025)			

VGL2918	VGL3008	VGL3235
12 (0.0224)	11 (0.0004)	12 (0.0340)
13 (0.0220)	13 (0.1382)	**13 (0.4037)**
14 (0.3734)	14 (0.0270)	14 (0.3622)
15 (0.4556)	**15 (0.6249)**	15 (0.0207)
16 (0.0183)	16 (0.0095)	16 (0.1237)
16.3 (0.0012)	17 (0.0037)	17 (0.0141)
17 (0.0029)	18 (0.1029)	18 (0.0415)
17.3 (0.0091)	19 (0.0838)	
18.3 (0.0046)	20 (0.0079)	
19.3 (0.0266)	21 (0.0017)	
20.3 (0.0577)		
21.3 (0.0062)		

The number of alleles identified for each STR locus in Doberman Pinschers ranged from 4 (INU030 and REN247M23) to 13 (VGL1165) (**Table 2**), with an average number of 7.97 alleles across all loci (**Table 3**). One of the consequences of bottleneck effects that happen during the development and/or along the history of a breed is a disproportionately high frequency estimated for a single allele at most STR loci, as seen in Doberman Pinschers (**Table 2**). These alleles have been inherited from a small number of founding dogs whose phenotypes (and consequently genotypes) were highly valued, and therefore have been positively selected and maintained at high frequency over time. In Doberman Pinschers, a single allele was identified in 50% or more of the population at 25 out of the 33 loci (**Table 2**), which suggests that these alleles were present in the foundation stock and are linked to breed-defining phenotypic traits. Additionally, the high number of STR loci with extremely common alleles reflects a lack of genetic diversity in the breed. Therefore, the goal for Doberman Pinschers breeders should be to re-distribute allele frequencies for the 33 STR markers by conserving and breeding rare lines/families.

B. Assessment of population diversity using standard genetic parameters

Based on the alleles identified for each of the 33 STR loci listed in **Table 2** and their respective frequencies in the study cohort, genetic diversity parameters can be estimated for the population (**Table 3**). Using the 33-marker panel, the 1205 Doberman Pinschers had an average of 7.97 alleles/loci (Na). This number is slightly larger than the last assessment of genetic diversity in the breed, published in 2019, which estimated the Na value at 7.30 (n=521). However, the average number of alleles is less important than the number of alleles that have the greatest effect on heterozygosity, a figure known as average effective alleles/loci or Ne. The Ne in this group of dogs averaged 2.32 effective alleles per locus, again indicating that Doberman Pinschers lack genetic diversity. This number has not changed since the last study in 2019. The observed heterozygosity (Ho) across the study population was 0.47, while the expected heterozygosity (He) was 0.51, yielding a coefficient of inbreeding (F) of +0.07. This value indicates a 7% excess in population-wide homozygosity over what would be expected for a random breeding population.

Table 3. Genetic Assessment of 1205 Doberman Pinschers based on 33 autosomal STR loci. SE = standard error of the mean.

	Na	Ne	Ho	He	F
Mean	7.97	2.32	0.47	0.51	0.07
SE	0.39	0.14	0.03	0.03	0.01

The average number of alleles across STR loci in this breed (Na = 7.97) corresponds to approximately 52% of those identified across dog breeds tested at the VGL (15.4 alleles/locus) (**Table 2**), which means that half of all the known canid diversity has been retained in Doberman Pinschers. However, the average number of effective alleles (Ne) constitutes a more important metric for diversity, since these represent the alleles with the greatest influence on heterozygosity. This number was estimated in Doberman Pinschers at 2.32 (**Table 3**), or only approximately 29% of the total number of alleles segregating in the breed. This is typical for most pure dog breeds, and can be explained by the presence of a high-frequency allele in the majority of STR loci analyzed (**Table 2**). The breed-wide coefficient of inbreeding (F) was estimated at 0.07 (**Table 3**), which indicates a small deficit in heterozygosity from what is expected for a population in Hardy-Weinberg equilibrium (HWE). In other words, this cohort of Doberman Pinschers is 7% more inbred than a random mating 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. **Table 4** lists the average Na, Ne, Ho, He, and F values for each STR locus estimated for this cohort of Doberman Pinschers. Loci with the lowest Ho values contribute the least to heterozygosity levels across the breed, and are likely associated with traits that are important for the breed's phenotypic standard. Conversely, higher Ho values for a particular locus means that it shows greater genetic diversity across the breed, and that these loci might be associated with traits with greater variation among individuals.

Table 4. Standard Genetic Assessment of individual STR loci for 1205 Doberman Pinschers. Individual STR loci with high inbreeding coefficients (F > 0.1) are bolded.

Locus	Na	Ne	Ho	He	F
AHT121	8	1.48	0.31	0.33	0.06
AHT137	10	2.62	0.62	0.62	0.01
AHTH130	9	1.83	0.43	0.46	0.05

AHTh171-A	7	2.36	0.55	0.58	0.05
AHTh260	8	1.33	0.23	0.25	0.05
AHTk211	6	1.27	0.2	0.22	0.07
AHTk253	5	1.75	0.32	0.43	**0.26**
C22.279	9	3.63	0.66	0.73	0.09
FH2001	6	1.1	0.09	0.09	0.02
FH2054	8	1.79	0.43	0.44	0.04
FH2848	8	1.11	0.08	0.1	**0.15**
INRA21	5	1.34	0.25	0.25	0.02
INU005	5	2.97	0.64	0.66	0.03
INU030	4	2.36	0.55	0.58	0.05
INU055	7	2.7	0.56	0.63	**0.12**
LEI004	6	2.02	0.49	0.5	0.03
REN105L03	8	1.12	0.11	0.11	0.02
REN162C04	9	2.33	0.55	0.57	0.03
REN169D01	8	3.92	0.65	0.75	**0.12**
REN169O18	8	2.88	0.61	0.65	0.07
REN247M23	4	1.27	0.21	0.22	0.03
REN54P11	9	2.48	0.56	0.6	0.07
REN64E19	7	2.4	0.54	0.58	0.08
VGL0760	12	3.94	0.69	0.75	0.08
VGL0910	11	1.92	0.46	0.48	0.04
VGL1063	11	2.96	0.62	0.66	0.07
VGL1165	13	2.66	0.57	0.62	0.08
VGL1828	8	2.43	0.58	0.59	0.02
VGL2009	7	2.75	0.6	0.64	0.05
VGL2409	8	3.48	0.64	0.71	**0.1**
VGL2918	12	2.84	0.58	0.65	**0.11**
VGL3008	10	2.34	0.56	0.57	0.03
VGL3235	7	3.2	0.61	0.69	**0.11**

An inbreeding coefficient (F) value of zero means that a population is randomly breeding (no artificial selection). Positive F values indicate non-random selection (inbreeding), while negative values indicate outbreeding (increased heterozygosity). 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. All STR loci had positive F values, and seven STR loci had high inbreeding coefficients (F > 0.1, bolded on **Table 4**). This can only occur if phenotypic traits associated with each locus (i.e., region of the genome) were under a degree of positive rather than random or negative selection. In the last assessment of Doberman Pinscher genetic diversity done at the VGL (2019), 29 of the 33 STR loci had positive F values.

Additionally, the number of effective alleles (Ne) ranged from 1.098 to 3.94 alleles per locus. The fact that one-fourth to one-half of the alleles were contributing to most of the genetic diversity is indicative of the large genetic contribution of a small proportion of founders, which is a reflection

of the bottlenecks that the breed underwent throughout its history. Doberman Pinschers lack genetic diversity, and when coupled with a small pool of widely distributed breeding dogs, breeders may find it difficult to identify and access the most unrelated mates.

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

The degree of genetic relatedness between individuals within a population can be measured with a PCoA. The genetic 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.

The 1205 Doberman Pinschers clustered as expected for a pure dog breed on the PCoA plot using allele frequency data obtained from the 33 STR marker panel (**Figure 1**), with individual dogs reasonably dispersed across all four quadrants of the graph.

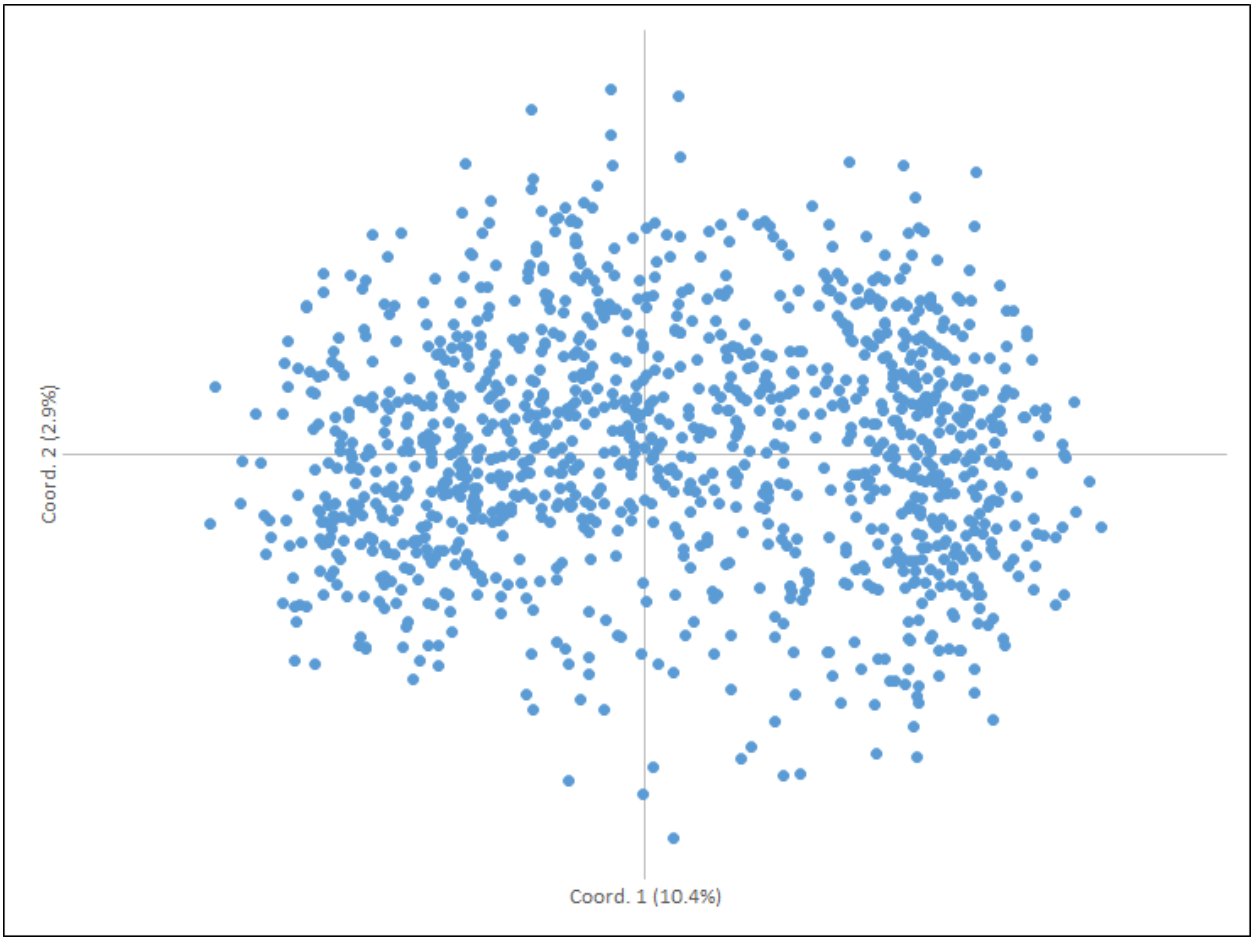


Figure 1. PCoA of Doberman Pinscher (n = 1205) based on allele frequencies at 33 autosomal STR loci.

Principal coordinate analysis can also be used to determine how populations have genetically differentiated from each other over time. **Figure 2** shows a PCoA of 1193 Doberman Pinscher individuals labeled according to region of origin: North America (red circles), Australia (green squares), and Europe (blue triangles). The North American population comprises a single diffuse group. There appears to be relatively frequent introgressions between Doberman Pinschers from different regions of the world, although there is some evidence for genetic isolation as well. From the graph, it can be observed that the Australian and European populations of Doberman Pinschers form somewhat separate clusters, indicating a level of genetic differentiation between these two populations. However, the genetic differences in the Australian and European individuals were not of a magnitude sufficient to create a "variety", such as seen between Japanese and American Akita for example. A more appropriate term would be "bloodline."

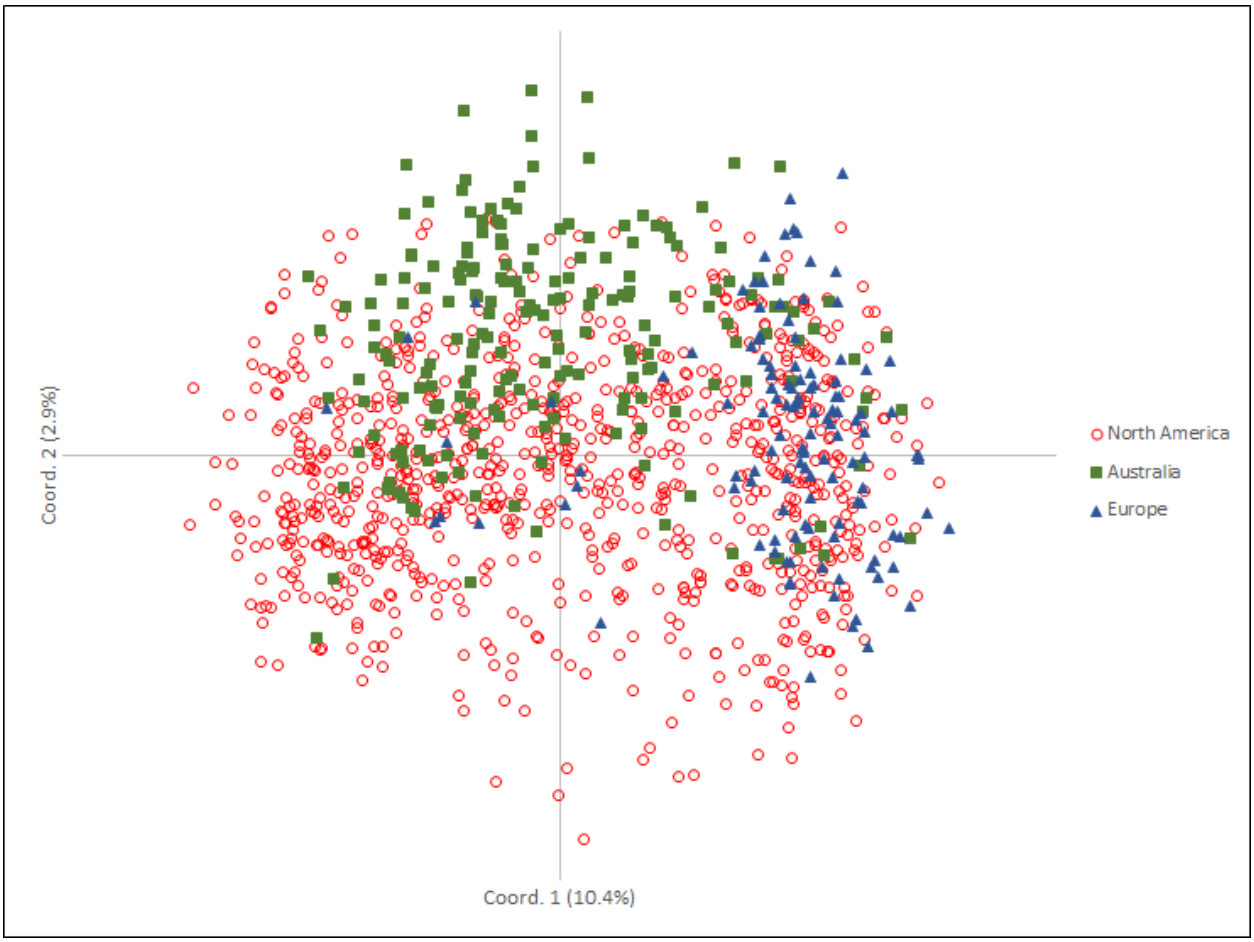


Figure 2. PCoA plot of 1193 Doberman Pinschers, labeled according to their region of origin. Red circles: North America (n=863); green squares: Australia (n=207); blue triangles: Europe (n=123).

E. Internal relatedness (IR) scores for Doberman Pinscher

1. IR testing and meaning

Genetic assessments such as those presented in Tables 2-4 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 5** summarizes the IR values for the 1205 Doberman Pinschers.

Table 5. Internal relatedness (IR) and adjusted IR (IRVD) values calculated using allele numbers and frequencies for 33 STR loci in 1205 Doberman Pinschers.

	IR	IRVD
Minimum	-0.3677	-0.0198
1st Quartile	-0.0442	0.4155
Mean	0.0722	0.4938
Median	0.0722	0.4834
3rd Quartile	0.1796	0.5804
Maximum	0.6196	0.8405

The most outbred dog of the study cohort had an estimated IR score of -0.37, while the most inbred dog had an IR score of +0.62, with a mean IR of +0.07 (**Table 5).** These results show that the population tested varies greatly in the degree of parental relatedness. Roughly 25% of the cohort had IR values between 0.18 and 0.62, suggesting that they are products of closely related parents. The range of IR values estimated in this study has increased since the last assessment of genetic diversity in the breed (2019); then, IR values were estimated between -0.26 and +0.45.

The wide range of IR values indicate genetic heterogeneity in the cohort (typical for most pure breeds): the highly inbred portion of the Doberman Pinscher population tested is balanced out by an equally sized group of outbred dogs, represented by IR values between -0.37 and -0.04 (**Table 5**). *This finding highlights the importance of determining IR values for individual dogs in order to maintain within-breed diversity by selecting the least related individuals possible for mating purposes based on IR values.*

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 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 5** and **Figure 3**, blue line).

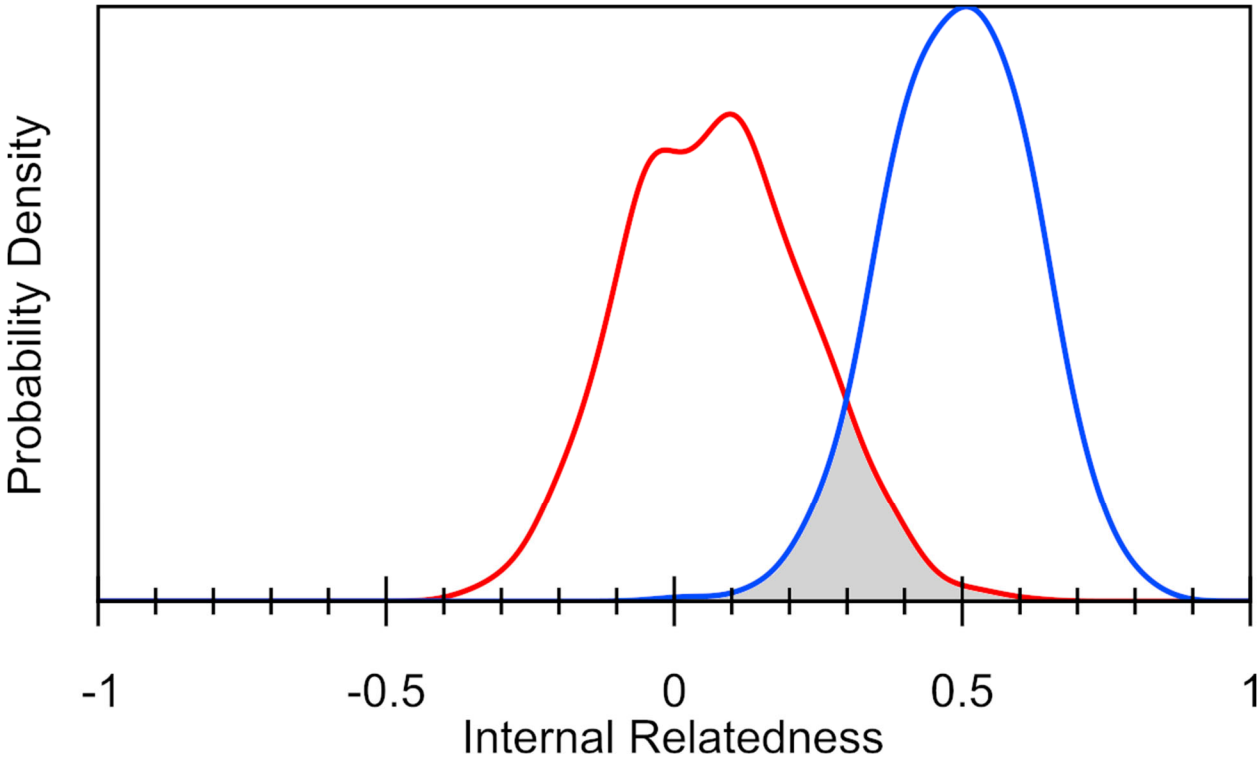


Figure 3. Distribution of IR (red line) and IR-village dog (IRVD) (blue line) values for Doberman Pinscher (n=1205). The overlap between the curves (gray area) shows that the breed retains only 14.1% of the genetic diversity existing in randomly breeding village dogs.

The IR curve for Doberman Pinscher is biphasic (two peaks) with one peak close to 0.07 and a second peak near 0.18. This second peak represents the most inbred dogs in the population, and this group of dogs is most responsible for the positive F values estimated across the breed (**Table 3**) and in individual STR loci (**Table 4**). The mean IRVD value was calculated at 0.49 for Doberman Pinschers, ranging from -0.02 for the most outbred dog to +0.84 for the most inbred individual (**Table 5**). 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 provides an estimate of how much genetic diversity has been lost during breed development. In Doberman Pinschers, the overlap between IR and IRVD curves was only 14.1%, which is almost half of the 30% retained genetic diversity calculated for all canids tested at VGL

(**section IIB**). This value reflects the relatively low genetic diversity existing in the breed as identified in **sections IIA**, **IIB**, and **IIC.**

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 6**).

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. 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 Doberman Pinscher

Twenty-two DLA class I and twenty DLA class II haplotypes were identified in Doberman Pinschers (**Table 6**). These numbers were significantly higher than those identified in 2019, when 12 DLA class I and 12 DLA class II haplotypes were found, and similar to those found in Labrador Retrievers (20 DLA class I and 17 DLA class II haplotypes). 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.

The frequencies of DLA-I haplotype 1094 (74%) and DLA-II haplotype 2089 (77%) were found to be disproportionately high in Doberman Pinschers, which indicates that they were prominent in a founder line and have been retained over the century because of their close association with trait or traits that have strongly defined a highly desirable breed phenotype. Moreover, since they were identified in similar frequencies, it can be inferred that they are in linkage disequilibrium (i.e., inherited together).

Table 6. DLA class I and II haplotypes identified in Doberman Pinscher (n = 1202) and their respective frequencies. Haplotypes with the highest frequency are bolded.

DLA1 haplotype	STR types	Frequency (%)
1012	388 369 289 188	0.08
1016	382 371 277 178	2.12
1017	386 373 289 178	8.11

1030	380 373 293 178	9.65
1040	380 371 277 186	0.92
1045	376 371 277 186	0.04
1052	380 372 289 184	0.08
1068	380 373 287 181	0.04
1091	381 371 277 181	0.21
1094	**395 375 277 176**	**73.92**
1105	382 379 277 178	0.04
1114	380 373 287 183	0.08
1116	380 365 289 186	0.08
1150	395 379 277 176	2.83
1159	395 379 277 181	0.37
1160	386 369 289 176	0.12
1174	399 375 277 176	0.42
1190	386 373 291 178	0.04
1214	397 375 277 176	0.08
1245	395 375 289 178	0.08
1264	391 375 277 176	0.62
1286	394 367 277 184	0.04

DLA2 haplotype	STR types	Frequency (%)
2003	343 324 282	0.04
2006	339 325 280	0.04
2011	345 322 284	0.04
2022	339 327 282	0.08
2023	341 323 282	9.65
2024	343 323 280	0.04
2033	339 323 282	0.17
2039	345 327 276	0.87
2040	345 327 280	0.04
2047	339 331 280	0.04
2053	343 324 280	0.12
2060	343 323 284	0.12
2072	339 325 282	0.08
2087	347 324 280	0.08
2089	**343 331 276**	**77.25**
2090	339 322 278	8.36
2091	343 327 288	2.12
2092	343 331 278	0.29
2094	339 322 276	0.17
2112	341 331 276	0.37

Doberman Pinschers share DLA haplotypes with 54 different breeds/varieties tested at the VGL. Interestingly, DLA-II haplotype 2089 was only found in one other breed, the Scottish Collie, and at an extremely low frequency (0.4%). DLA-I haplotype 1094 occurs at low frequency in Bernese Mountain Dog, Black Russian Terrier, Borzoi, Great Dane, Irish Wolfhound, Newfoundland, and Scottish Collie. A total of seven DLA haplotypes were found to be unique to Doberman Pinschers: DLA-I 1174, 1190, 1214, 1245, 1264, 1286 and DLA-II 2092 and 2112 (**Table 7**).

Table 7. Sharing of DLA class I haplotypes between Doberman Pinschers (highlighted in blue) and other dog breeds/varieties tested at the VGL (n=54).

DLA1 haplotype	STR types	Doberman Pinscher (n=1202)	American Eskimo, Standard (n=65)	American Eskimo, Miniature (n=38)	American Eskimo, Toy (n=14)	American Hairless Terrier (n=186)	American Akita (n=159)	Japanese Akita (n=578)	Blend Akita (n=66)	Alaskan Klee Kai (n=649)	Barbet (n=68)	Border Collie (n=63)	Berger Picard (n=145)	Bernese Mountain Dog (n=147)	Black Russian Terrier (n=150)	Biewer (n=136)	Biewer Yorshire Terrier (n=53)	Biewer Terrier (n=215)	Yorkshire Terrier (n=16)	Borzoi (n=149)	Collie (n=49)	English Bulldog (n=163)	Bulldog (n=1)	English Mastiff (n=31)	Mastiff (n=21)	Flat Coated Retriever (n=855)	Great Dane (n=65)	Golden Retriever (n=871)	Giant Schnauzer (n=325)
1012	388 369 289 188	0.0008	0.023	0.04	--	0.005	--	--	--	--	--	0.056	--	--	--	0.228	0.151	0.221	0.28	--	--	0.414	--	--	--	--	--	0.0011	--
1016	382 371 277 178	0.0212	0.008	0.04	0.11	0.005	--	--	--	--	--	--	--	0.044	0.01	0.022	0.019	0.012	0.03	--	0.04	0.095	0.5	0.15	0.14	--	0.2	0.0046	0.046
1017	386 373 289 178	0.0811	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.4427	--	--	0.083
1030	380 373 293 178	0.0965	0.008	0.03	--	--	--	--	--	--	0.029	0.008	--	0.01	--	0.445	0.349	0.495	0.31	--	--	--	--	0.08	--	--	0.246	0.0011	--
1040	380 371 277 186	0.0092	--	--	--	0.043	0.006	--	--	0.2126	--	--	--	--	--	0.096	0.208	0.079	--	--	--	0.04	--	--	--	--	--	0.0006	--
1045	376 371 277 186	0.0004	--	--	--	--	0.003	--	--	--	--	0.159	--	--	--	--	--	--	--	--	0.96	--	--	--	--	--	--	--	--
1052	380 372 289 184	0.0008	--	--	--	0.022	--	--	--	--	--	0.008	0.103	--	--	--	--	--	--	--	--	--	--	0.02	--	--	--	--	--
1068	380 373 287 181	0.0004	--	--	--	0.11	--	--	--	--	--	0.214	--	0.065	--	--	0.009	--	--	--	--	--	--	--	--	0.2731	0.008	0.0465	0.055
1091	381 371 277 181	0.0021	--	--	--	--	--	--	--	--	--	--	--	--	0.503	--	--	--	--	--	--	--	--	--	--	--	0.054	--	0.035
1094	395 375 277 176	0.7392	--	--	--	--	--	--	--	--	--	--	--	0.143	0.013	--	--	--	--	0.01	--	--	--	--	--	--	0.038	--	--
1105	382 379 277 178	0.0004	--	--	--	--	--	--	--	--	--	--	--	--	--	0.004	--	--	--	--	--	--	--	--	--	--	--	--	--
1114	380 373 287 183	0.0008	--	--	--	--	--	0.0009	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1116	380 365 289 186	0.0008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1150	395 379 277 176	0.0283	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1159	395 379 277 181	0.0037	--	--	--	--	--	--	--	--	0.103	--	--	--	--	--	--	--	--	0.047	--	--	--	--	--	--	--	--	0.166
1160	386 369 289 176	0.0012	--	--	--	--	0.003	--	--	--	--	--	--	0.537	0.03	--	--	--	--	0.581	--	--	--	--	--	--	--	--	--
1174	399 375 277 176	0.0042	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1190	386 373 291 178	0.0004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1214	397 375 277 176	0.0008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1245	395 375 289 178	0.0008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1264	391 375 277 176	0.0062	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1286	394 367 277 184	0.0004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

DLA1 haplotype	STR types	Doberman Pinscher (n=1202)	Havana Silk (n=42)	Havanese (n=960)	Italian Greyhound (n=1355)	Irish Setter (n=59)	Irish Red and White Setter (n=79)	Irish Wolfhound (n=78)	Lakeland Terrier (n=135)	Labrador Retriever (n=291)	Llewellin Setter (n=151)	Magyar Agar (n=78)	Newfoundland (n=137)	Polish Lowland Sheepdog (n=80)	Toy Poodle (n=227)	Miniature Poodle (n=410)	Poodle (n=5054)	Rat Terrier (n=44)	Samoyed (n=192)	Saint Bernard (n=89)	Scottish Collie (n=117)	Shiba Inu (n=153)	Shikoku (n=84)	Greater Swiss Mountain Dog (n=57)	Shiloh Shepherd (n=54)	Shiloh Shepherd, ISSA (n=267)	Swedish Vallhund (n=474)	Cardigan Welsh Corgi (n=43)	Whippet (n=108)
1012	388 369 289 188	0.0008	--	0.0125	0.0077	--	--	--	0.763	--	--	--	--	--	0.022	0.073	0.01464	0.06	0.013	--	0.009	--	--	0.93	--	--	--	0.23	0.037
1016	382 371 277 178	0.0212	0.08	0.1953	0.0635	--	--	--	0.007	0.015	0.026	--	0.328	0.025	0.024	0.028	0.02196	0.05	--	--	0.094	--	--	0.07	--	--	--	--	0.106
1017	386 373 289 178	0.0811	--	--	--	--	--	--	--	0.04	--	--	--	--	--	--	0.00267	--	--	0.112	--	--	--	--	--	--	--	--	--	--
1030	380 373 293 178	0.0965	0.05	0.0031	0.0306	--	--	--	--	0.041	0.02	--	--	--	--	--	0.00218	0.02	--	--	--	--	--	--	--	--	--	--	--	--
1040	380 371 277 186	0.0092	0.01	0.0161	0.0775	--	--	--	0.181	--	--	--	0.281	0.675	0.002	0.005	0.00059	0.17	--	0.011	--	--	--	--	--	--	--	--	--	0.088
1045	376 371 277 186	0.0004	--	--	--	--	--	--	--	0.005	0.003	--	--	--	0.02	0.005	0.00069	--	--	--	0.722	--	--	--	--	0.002	--	0.33	0.005
1052	380 372 289 184	0.0008	--	0.0109	0.186	--	--	0.333	0.011	--	--	0.051	--	--	--	--	0.0003	--	--	--	--	--	--	--	0.333	0.384	--	--	--
1068	380 373 287 181	0.0004	0.25	0.013	--	0.008	--	0.128	--	0.033	--	--	0.106	0.006	0.009	0.012	--	--	0.042	0.163	--	--	--	--	0.5	0.264	0.365	--	--
1091	381 371 277 181	0.0021	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.219	0.012	--	--	--	--	--	--
1094	395 375 277 176	0.7392	--	--	--	--	--	0.192	--	--	--	--	0.015	--	--	--	--	--	--	--	0.004	--	--	--	--	--	--	--	--
1105	382 379 277 178	0.0004	--	0.0005	--	--	--	0.321	--	0.089	--	--	--	--	0.07	0.051	0.00366	0.02	--	--	--	--	--	--	--	--	--	--	--
1114	380 373 287 183	0.0008	--	0.0172	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1116	380 365 289 186	0.0008	0.05	0.1031	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1150	395 379 277 176	0.0283	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1159	395 379 277 181	0.0037	--	--	--	--	--	--	0.004	--	--	--	0.004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1160	386 369 289 176	0.0012	--	--	--	--	--	--	--	--	--	--	0.004	--	--	--	--	--	0.016	0.09	0.009	0.013	--	--	--	--	--	--	--
1174	399 375 277 176	0.0042	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1190	386 373 291 178	0.0004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1214	397 375 277 176	0.0008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1245	395 375 289 178	0.0008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1264	391 375 277 176	0.0062	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1286	394 367 277 184	0.0004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

DLA2 haplotype	STR types	Doberman Pinscher (n=1202)	American Eskimo, Standard (n=65)	American Eskimo, Miniature (n=38)	American Eskimo, Toy (n=14)	American Hairless Terrier (n=186)	American Akita (n=159)	Japanese Akita (n=578)	Blend Akita (n=66)	Alaskan Klee Kai (n=649)	Barbet (n=68)	Border Collie (n=63)	Berger Picard (n=145)	Bernese Mountain Dog (n=147)	Black Russian Terrier (n=150)	Biewer (n=136)	Biewer Yorshire Terrier (n=53)	Biewer Terrier (n=215)	Yorkshire Terrier (n=16)	Borzoi (n=149)	Collie (n=49)	English Bulldog (n=163)	Bulldog (n=1)	English Mastiff (n=31)	Mastiff (n=21)	Flat Coated Retriever (n=855)	Great Dane (n=65)	Golden Retriever (n=871)	Giant Schnauzer (n=325)
2003	343 324 282	0.0004	0.023	0.04	--	0.263	--	--	--	--	0.132	0.056	--	--	--	0.265	0.208	0.242	0.38	--	--	0.598	--	--	--	0.1462	0.008	0.0195	0.029
2006	339 325 280	0.0004	--	--	--	--	--	--	--	--	0.007	--	--	--	--	--	--	--	--	0.087	--	--	--	--	--	--	--	--	0.151
2011	345 322 284	0.0004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2022	339 327 282	0.0008	0.023	0.21	0.32	0.032	--	--	--	--	--	0.008	--	--	--	--	--	--	--	0.587	--	0.015	--	--	--	0.1152	0.092	0.0006	0.003
2023	341 323 282	0.0965	0.008	0.03	--	--	--	--	--	--	0.029	0.008	--	--	0.003	0.445	0.349	0.498	0.31	--	--	--	--	0.08	--	--	0.246	0.0011	--
2024	343 323 280	0.0004	--	--	--	0.008	--	--	--	--	--	--	--	0.527	--	--	--	--	--	0.01	--	0.006	--	--	--	--	--	--	--
2033	339 323 282	0.0017	0.008	--	--	0.005	0.013	--	--	--	--	0.008	--	--	0.507	--	--	--	--	--	--	--	--	--	--	--	0.185	--	0.038
2039	345 327 276	0.0087	--	--	--	--	0.091	0.1029	0.273	--	--	0.151	--	--	--	--	--	--	--	--	0.95	--	--	--	--	--	--	--	--
2040	345 327 280	0.0004	--	--	--	0.038	--	--	--	--	--	--	--	--	--	0.063	0.085	0.023	0.03	--	--	--	--	--	--	--	--	--	--
2047	339 331 280	0.0004	--	--	--	--	--	--	--	--	0.103	--	--	--	--	--	--	--	--	0.013	--	--	--	--	--	--	--	0.0098	--
2053	343 324 280	0.0012	0.223	0.12	0.04	0.005	--	--	--	--	--	0.071	--	0.065	--	--	0.009	--	--	--	--	--	--	--	--	0.1474	0.008	0.0281	0.065
2060	343 323 284	0.0012	--	--	--	--	0.003	--	--	--	--	--	--	--	0.03	--	--	--	--	--	--	--	--	--	--	--	--	--	0.003
2072	339 325 282	0.0008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.02	--	--	--	--	--	--	--	--	--
2087	347 324 280	0.0008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2089	343 331 276	0.7725	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2090	339 322 278	0.0836	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.083
2091	343 327 288	0.0212	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.04	--	--	--	--	--	--	--	--
2092	343 331 278	0.0029	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2094	339 322 276	0.0017	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2112	341 331 276	0.0037	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

DLA2 haplotype	STR types	Doberman Pinscher (n=1202)	Havana Silk (n=42)	Havanese (n=960)	Italian Greyhound (n=1355)	Irish Setter (n=59)	Irish Red and White Setter (n=79)	Irish Wolfhound (n=78)	Lakeland Terrier (n=135)	Labrador Retriever (n=291)	Llewellin Setter (n=151)	Magyar Agar (n=78)	Newfoundland (n=137)	Polish Lowland Sheepdog (n=80)	Toy Poodle (n=227)	Miniature Poodle (n=410)	Poodle (n=5054)	Rat Terrier (n=44)	Samoyed (n=192)	Saint Bernard (n=89)	Scottish Collie (n=117)	Shiba Inu (n=153)	Shikoku (n=84)	Greater Swiss Mountain Dog (n=57)	Shiloh Shepherd (n=54)	Shiloh Shepherd, ISSA (n=267)	Swedish Vallhund (n=474)	Cardigan Welsh Corgi (n=43)	Whippet (n=108)
2003	343 324 282	0.0004	0.25	0.2125	0.007	--	--	--	0.763	0.022	--	--	0.004	--	0.43	0.51	0.10388	0.13	0.013	--	0.017	--	--	0.93	--	0.009	--	0.23	0.088
2006	339 325 280	0.0004	--	0.0016	--	--	--	--	--	--	--	0.192	--	--	0.002	--	0.03393	--	--	--	--	0.003	--	--	--	--	--	--	0.051
2011	345 322 284	0.0004	--	0.0005	--	--	--	--	--	--	--	--	--	--	0.051	0.002	0.02028	0.06	--	--	--	--	--	--	--	--	--	--	--
2022	339 327 282	0.0008	0.07	0.1146	--	0.153	--	0.353	0.174	0.058	0.089	--	--	--	0.007	0.002	0.00049	0.14	0.107	--	--	--	--	--	0.028	0.043	0.057	--	--
2023	341 323 282	0.0965	0.05	0.0031	0.0306	--	--	--	--	0.041	0.013	--	--	--	--	--	0.00218	0.02	--	0.399	--	--	--	--	--	--	--	--	--	--
2024	343 323 280	0.0004	--	0.0047	--	--	--	--	--	0.086	--	--	--	--	0.075	0.01	0.00059	--	0.016	--	--	--	--	--	--	--	--	--	--	--
2033	339 323 282	0.0017	--	0.001	0.0052	--	--	--	--	--	--	--	--	--	0.004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.106
2039	345 327 276	0.0087	--	--	0.0804	--	--	--	--	0.005	--	--	0.288	--	--	--	0.00059	--	--	--	0.714	--	--	--	--	0.002	--	0.31	--
2040	345 327 280	0.0004	--	0.0026	0.0011	--	--	--	--	--	--	--	--	--	0.02	0.005	0.0001	0.01	--	--	--	--	--	--	--	--	--	0.06	--
2047	339 331 280	0.0004	--	--	--	--	--	--	--	--	--	0.096	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2053	343 324 280	0.0012	0.26	0.0286	--	0.008	--	0.128	--	0.031	--	--	0.106	0.006	0.011	0.012	--	--	0.56	0.14	--	--	--	--	0.519	0.337	0.527	--	--
2060	343 323 284	0.0012	--	--	--	--	--	--	--	--	--	--	0.004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2072	339 325 282	0.0008	--	0.0172	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2087	347 324 280	0.0008	--	0.0005	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2089	343 331 276	0.7725	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.004	--	--	--	--	--	--	--	--
2090	339 322 278	0.0836	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2091	343 327 288	0.0212	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	0.056	--	--	--	--	--	--	--	--
2092	343 331 278	0.0029	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2094	339 322 276	0.0017	--	--	--	--	--	--	--	--	--	--	--	--	0.002	--	--	--	--	--	--	--	--	--	--	--	--	--	--
2112	341 331 276	0.0037	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1214	397 375 277 176	0.0008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1245	395 375 289 178	0.0008	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1264	391 375 277 176	0.0062	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
1286	394 367 277 184	0.0004	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

2. Heterozygosity in the DLA region

Due to their physical proximity on chromosome 12, the seven loci that define the DLA class I and II haplotypes are in strong linkage disequilibrium (i.e., have a higher probability of being inherited together) when compared to the genome-at-large. 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. This assumption can be tested through a standard genetic assessment of each locus (**Table 8**) as well as averaged across all DLA loci (**Table 9**).

The highest number of alleles (Na) identified at each DLA locus for Doberman Pinschers was 11 (DLA I-3CCA) whereas the lowest was 5 (DLA I-4BCT and 5ACA). However, the number of effective alleles (Ne) per DLA locus was even lower than that estimated for the genome-at-large, ranging from 1.47 (DLA I-4BCT) to 1.67 (DLA I-4ACA). Inbreeding coefficients estimated for each DLA locus were close to zero (0.02 to 0.07) (**Table 8**). Also according to the expectation that the DLA region has achieved an equilibrium with other regions of the genome, we can observe that the average inbreeding coefficient estimated for this region (F=0.05, **Table 9**) is similar to that estimated across the 33 STR loci (F=0.07, **Table 3**). This suggests that only a small subpopulation (around 5%) of Doberman Pinschers are more inbred than the population as a whole based on DLA haplotypes. This corroborates the hypothesis that the over-representation of the linked 1094 /2089 DLA haplotypes (**Table 6**) occurred during the earliest origins of the breed, followed by a longer period of somewhat random breeding.

Table 8. Standard genetic assessment for Doberman Pinscher (n=1205) using each of the 7 STRs in the DLA class I and II regions.

Locus	Na	Ne	Ho	He	F
DLA I-3CCA	11	1.63	0.37	0.39	0.04
DLA I-4ACA	8	1.67	0.37	0.4	0.07
DLA I-4BCT	5	1.47	0.31	0.32	0.04
DLA1131	7	1.54	0.33	0.35	0.06
5ACA	5	1.52	0.33	0.34	0.02
5ACT	7	1.6	0.36	0.38	0.04
5BCA	6	1.57	0.34	0.36	0.06

Table 9. Summary of standard genetic assessment for Doberman Pinscher (n=1205) using 7 STRs in the DLA class I and II regions. SE = standard error of the mean.

	Na	Ne	Ho	He	F
Mean	7	1.57	0.35	0.36	0.05
SE	0.73	0.02	0.01	0.01	0.01

III. What does this assessment of genetic diversity tell us about Doberman Pinschers

Low levels of genetic diversity were identified in the Doberman Pinscher. Additionally, there is evidence that founders or founder lines have had a disproportionately high genetic influence on the breed, and that the genetic imbalance originating from that phenomenon is being maintained

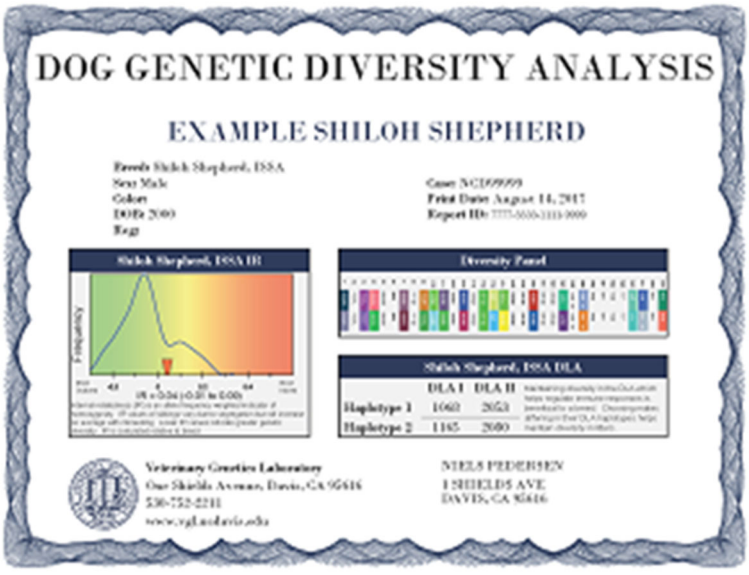
to some degree by artificial selection (breeding practices). These conclusions are supported by results from both the 33 autosomal STR markers and the DLA loci analyzed. However, our results also show that a fraction of the Doberman Pinscher population is outbred based on IR values. This should be taken in to consideration in the efforts to re-distribute the existing genetic diversity by choosing sires and dams that are as unrelated as possible.

In summary, the goal for Doberman Pinscher breeders is to re-distribute the existing genetic diversity by breeding the least related parents possible based on genotypes for the 33 STR markers and the DLA loci, as well as IR values.

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.



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 Doberman Pinschers 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.

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