PEER REVIEWED

The Future of Veterinary Genetic Testing

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Genetically based (ie, inherited) diseases are prevalent in dogs. Purebred dogs carry the highest number of disease-causing genetic mutations, but these mutations also occur in mixed-breeds. Breed-specific genetic diseases, which are associated with most canine breeds, result from selective breeding for specific cosmetic and behavioral traits. Inbreeding to achieve desirable traits limits a breed's gene pool and perpetuates genetic mutations, both benign and pathologic, that affect every body system.[1,2] For example, the cardiac and cranial abnormalities seen in many Cavalier King Charles spaniels can be the unintended consequences of selective cosmetic breeding.[1]

Genetic testing, which has been used to identify inherited diseases in humans since the 1950s—beginning with Down syndrome and cystic fibrosis[3]—is becoming an important diagnostic tool in veterinary medicine. Collaborative efforts by the One Health Initiative and the National Institutes of Health, as well as genome-wide studies such as the National Human Genome Research Institute Dog Genome Project[4] and the Broad Institute Dog Genome Project,[5] have greatly advanced veterinary genetics in the past several decades. Efforts to map the canine genome began in the United States in 2003; the results of 2 studies—one of a poodle and one of a purebred boxer—were published in 2004.[2,6,7] Canine genetic research has since expanded to include additional diseases and breeds.

Genetic Mutations

Most mutations occur and recur because of parental genetic influence and environmental adaptation. The mutations influence many characteristics within an offspring's phenotype (eg, coat length and color, behavior, eye color), but some genetic coding errors during development can cause specific disease states.

Genetics 101

- Dogs have 39 chromosome pairs, with each chromosome composed of hundreds to thousands of genes.
- The first 38 nonsex chromosome pairs are referred to as autosomes.
- The 39th sex chromosome pair is called an allosome.
- Genetic diseases are the result of a mutation of a single gene in a chromosome or multiple genes in 1 or more chromosomes.
- Mutation in a gene can result in both benign and pathogenic changes in offspring.

A mutation may then be transferred to offspring through breeding.[1] (See **Genetics 101**, page 25.) A mutation in a single gene (ie, monogenic) is characterized as autosomal recessive, autosomal dominant, or sex-linked. (See **Table 1**.)

- **Autosomal recessive**: Most genetic diseases in humans and dogs are autosomal recessive. (See **Table 2**.) Puppies may be carriers of the genetic defect (ie, ≈50%), be affected by the disease (ie, ≈25%), or be genetically normal (ie, ≈25%).[1,6,8]
- **Autosomal dominant**: These mutations are less prevalent but still common. The disease state is present if this type of mutation is passed to the offspring from only one parent.
- **Sex-linked**: These chromosomal diseases occur because of a mutation on the sex chromosomes, leading to a sex disposition in some inherited diseases.[6,8] Their prevalence is unknown; however, the number of sex-linked testable diseases is much fewer than autosomal recessive and dominant mutations.[2]

TABLE 1 **Patterns of Inheritance & Associated Genetic Diseases**[2,6,19]

Inheritance Type	Description	Most Common Genetic Diseases
Autosomal recessive	Both parents must pass on the recessive gene for offspring to be affected	• Von Willebrand's disease (type I) • Ichthyosis • Juvenile hereditary cataracts (multibreed) • Multidrug resistance
Autosomal dominant	Only one parent needs to pass on the defective gene for the disease to occur	• Juvenile hereditary cataracts (Australian shepherd dog) • Primary hyperparathyroidism • Progressive retinal atrophy (type A)
Sex-linked	Diseases caused by a mutation located on the sex chromosomes (X/Y) that leads to a sex predominance in mutation and potential disease	• Hemophilia B • Hereditary nephritis • Progressive retinal atrophy (X-linked) • Severe combined immune-deficiency

Mutations that occur in multiple genes may result in disease conditions more difficult to identify. Their prevalence is unknown, although research is ongoing. Current known polygenic diseases causing mutations include patent ductus arteriosus in poodles and progressive retinal atrophy in the Welsh corgi.[6,9] These mutations are difficult to identify because they require breeding studies with a large number of participants. Determining the type of inheritance (maternal vs paternal) in polygenic diseases is not specific but can indicate the prevalence of a particular polygenic mutation in a group.[10]

Genetic Testing

Genetic testing refers to the identification of a genetic mutation, which can identify potential diseases or the possibility of offspring carrying the same mutation and disease potential.[11-15]

The ability to identify carriers and affected offspring offers potential benefits to veterinarians, clients, and breeders. For example, dogs suspected of having certain genetic diseases can be identified at a younger age by minimally invasive procedures that require only cheek swabs or blood, urine, or semen samples submitted to reliable laboratories. Preventive and/or advanced care can then be initiated at an earlier age.

Genetic testing could become part of existing wellness programs to help identify genetic factors that affect the length and quality of a

dog's life. Carriers can be removed from breeding programs or bred more selectively with partners that are genetically normal to decrease the prevalence of genetic diseases.[1,11-13,16]

Genetic testing in dogs is currently limited, however, and caution should be used when recommending testing to clients and breeders. Most tests check only for single gene defects, yet some diseases (eg, canine inherited cataracts) are caused by several different genetic mutations.[17] Many tests identify only the genetic markers for a disease rather than the specific genetic mutation and existence of illness. Genetic markers only identify a series of genes that indicate the possibility of mutation. Testing for genetic markers can be useful, however, as their presence can indicate disease-causing genes, and the affected animal can be monitored more closely for disease signs.[6,15] Clients and breeders must be counseled on the different tests available from veterinary professionals and other advertised sources, and clients must know how best to interpret the results of these tests. (See **Table 3**.)

Conclusion

Canine genetic testing offers a wide range of possible benefits for veterinary medicine. Ongoing research, including clinical trials studying common diseases (eg, progressive retinal atrophy, idiopathic epilepsy, glaucoma, intervertebral disc disease) and continued mapping of the canine genome will help improve diagnostic, preventive, and treatment options for genetic conditions.[18]

Behavioral genetics is an emerging research field that has demonstrated the inheritability of certain behaviors such as flank sucking in Dobermans and the herding ability of some breeds (eg, border collies, German shepherd dogs, Australian cattle dogs).[16] Identifying dogs affected by these mutations may enable them to

TABLE 2

Punnett Square: Autosomal Recessive[a]

		Paternal (Rr)	
		R	r
Maternal (Rr)	R	RR (normal)	Rr (carrier)
	r	Rr (carrier)	rr (disease state)

Abbreviations: R, dominant (normal gene); r, recessive (disease-causing mutation)
[a] Shaded areas indicate possible genotypes of offspring.

TABLE 3

Commonly Performed Genetic Tests[17,18]

Test	Condition Testing For
Uric acid DNA	Diseases characterized by the formation of bladder and/or kidney stones
Degenerative myelopathy in canine breeds	A degenerative disease of the spinal cord that progresses to paraplegia
Hereditary nasal parakeratosis in Labrador retrievers	A disease characterized by dry, rough crusts that develop on the nose tip
Multidrug resistance	Neurologic signs that may develop in dogs as a result of common drugs (eg, ivermectin use in collies)
Exercise-induced collapse	Muscle weakness and collapse after short periods of activity
Pyruvate kinase deficiency in West Highland terriers and basenjis	A red blood cell defect that leads to anemia and liver failure
Von Willebrand's disease	The most common inherited bleeding disorder seen in dogs
Factor VII deficiency	Inherited coagulopathy in some breeds (eg, beagle, Airedale, giant schnauzer, Scottish deerhound)
Juvenile hereditary cataracts	Juvenile cataracts
Progressive retinal atrophy (multigene)	Atrophy of the retina that causes progressive blindness

receive early environmental modification to counter potential negative behaviors. Improved testing accuracy and decreased testing costs will help establish canine genetic testing as a powerful diagnostic tool.

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TAKE ACTION

1. Use caution when recommending canine genetic testing to clients and breeders because the tests themselves—and what they identify—are currently limited.
2. If clients or breeders do elect to test their dogs, counsel them on the different tests available and how the results should be interpreted.
3. Stay up-to-date on canine genetic testing because reduced costs and improvements in accuracy will help establish it as a powerful diagnostic tool that eventually may be included in wellness programs.

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FUN FACT: Colleen currently lives in Atlanta, Georgia, with her husband, Mike, and her 2 cats, Pico de Gato and Hoxton. Her hobbies include reading, weightlifting (her current maximum front squat is 230 lb), and crafting (mainly catnip toys). She loves Elvis Presley and any type of horror movie!