

The Skinny on Genes

What You Should Know About Genetic Testing

by Lowell Ackerman, DVM, DACVD, MBA, MPA, CVA, MRCVS

It's a confusing world for veterinary healthcare teams when it comes to genetic testing. There are now panels available that will screen for dozens or even hundreds of different genetic variants and markers. At the same time, most genetic tests today are also available directly to consumers, so clients can request such testing themselves, just as they do with companies like 23andMe and other, similar services.

Genetic Testing and Pet-Specific Care

With pet-specific care, the goal is to be proactive and address potential issues at the earliest possible opportunity, preferably when problems are still subclinical. DNA testing can be very useful for this purpose, as it can be run very early in life, even as early as one day of age.

Genetic testing is a useful tool as long as veterinary teams have realistic expectations. The purpose of genetic tests is not necessarily to confirm a diagnosis but to understand risk factors that could be relevant for an individual pet, even issues that may develop much later in life. So, it is extremely important that veterinary team members understand the difference between association and causation when it comes to such testing.

Genetic testing is just one small piece of the pet-specific care puzzle, but done with the correct motivation, it can help veterinary teams start clients along the path toward a lifetime of appropriate care for their pets.



The vast majority of DNA tests are not absolutely predictive because any one variant detected may not actually be causing the disease in its entirety. Most often they just indicate suspected “risk” based on a statistical association of a variant to clinical disease, and it is up to the veterinary team to put such risks in perspective. For example, the skin condition dermatomyositis is often described as being autosomal dominant with variable expressivity (more on this term later), and confirmation of the diagnosis in affected individuals (usually collies, Shetland sheepdogs, and their crosses) is based on biopsy. It has recently been determined that there are at least three different genetic variants “associated” with dermatomyositis risk, and when considered in aggregate, pets can often be classified as high risk, moderate risk, and low risk for developing dermatomyositis. This can be extremely useful for counseling clients of at-risk pets, even if the predictive ability is not absolute.

In most instances, it is practical to perform genetic screening at about 12 weeks of age. At that time, the pet should be well into vaccination and parasite-control protocols and

hopefully enrolled in pet health insurance. Once again, the goal is not to try to diagnose disease in a healthy little puppy or kitten with such screening but to help prepare a risk profile for the animal so that pet-specific recommendations can be made regarding prevention and early-detection programs. For example, knowing a pet’s multidrug resistant (*mdr1*) genetic status can help inform whether certain medications might be problematic if administered. Knowing the genotypic status for von Willebrand disease can prove very useful if surgical intervention is being considered (including neutering). If veterinary teams consider that the point of genetic testing is to better appreciate potential risk, they will be able to relay more appropriate information to pet owners. The purpose is not to scare pet owners but to provide some peace of mind regarding genetic health and offer some early information for the veterinary team to keep that pet as healthy as possible for as long as possible.

Putting DNA Testing in Perspective

If you have watched any number of crime dramas on television, you’re

probably aware that DNA is an important tool for getting bad guys locked away. Once there is a DNA match, it is hard to make a successful counterargument in court. Similarly, in the news, some incarcerated criminals, some even on death row, have been exonerated through DNA testing. So, is it reasonable to conclude that DNA testing must be beyond reproach when used in health screening?

Whether a practice decides to embrace the concept of genetic testing depends on its strategy for delivering healthcare. There is no doubt that more validation is needed in both human and pet genetic health screening, but that doesn’t negate the real value in providing such a proactive resource for pet owners.

DNA testing is nearly infallible when it comes to matching individuals with a sample of DNA found at a crime scene (or matching paternity or other needs for identification) because depending on the number of data points examined, it can be virtually a statistical certainty (even better than fingerprints). However, when it comes to matching DNA from an individual with the likelihood of

disease development in the future, it very much depends on the specificity of the genetic variant being measured and the individual being tested. That's why it takes a veterinary team to help interpret DNA test results and counsel pet owners accordingly.

Part of the reason that disease detection is not as simple as identification is that disease and traits can be influenced by a variety of different genes as well as environmental factors. Atopic dermatitis (allergies), for example, is a skin condition that tends to run in families, and there are definite breed predispositions, but that doesn't mean that any one DNA test developed will be able to predict onset with any certainty in all pets and all breeds. The body has a lot of redundant systems in place, so even if there is a genetic issue somewhere, it may be possible for the body to compensate through mechanisms elsewhere.

Another important point to consider is that genes themselves don't

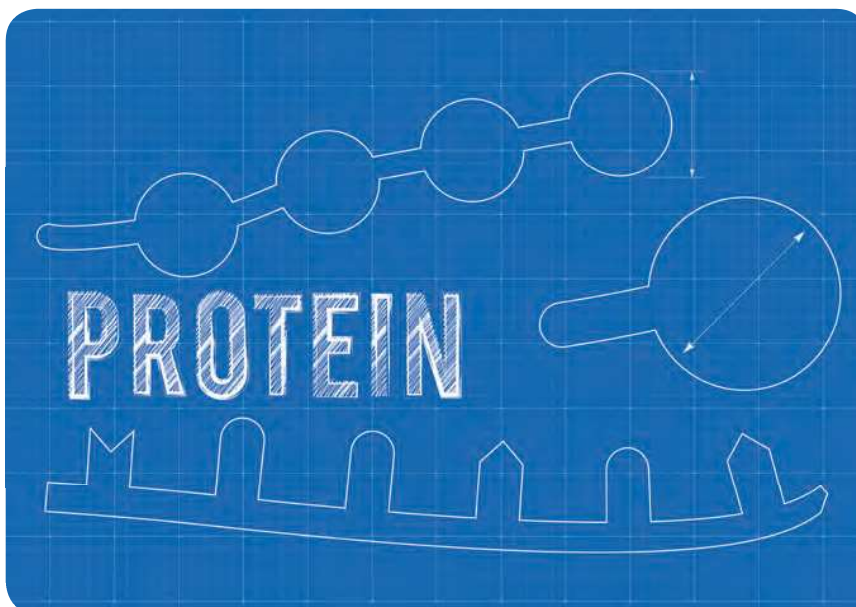
cause diseases. Genes provide the blueprint for creating proteins, and it is typically defective and poorly functional proteins that lead to the clinical picture that we interpret as disease—often with significant environmental influences.

At this point in time, there are a few hundred genetic variants known to affect the health of pets, but new associations are being uncovered on a regular basis. The important thing to remember with such testing is that the most predictive tests will be for medical conditions controlled by a single gene pair (such as von Willebrand disease type I in the Doberman pinscher, progressive retinal atrophy-rcd1 in the Irish setter, or ichthyosis-A in the golden retriever). The vast majority of diseases seen in pets (such as atopic dermatitis, heart disease, diabetes mellitus, obesity, periodontal disease, and so on), however, actually have a more complicated pattern of inheritance and may involve multiple genes as

well as environmental influences, and genetic tests developed for these types of conditions should be expected to be less predictive even if they still contribute useful information. Even for conditions such as hip dysplasia, heritability is important, but environmental influences have more impact on clinical expression of the disorder than do genetics (heritability ~ 0.25). Genetic variants may also have some association with disease in one breed but not necessarily in others, and this is not a fault of the testing but just a reality of pet-specific care and breed-specific risk.

Because of the complexity of biological systems, just because there is a genetic mutation that leads to a poorly functional protein doesn't mean that the animal will definitely develop disease. We often describe this as penetrance, the likelihood that a given mutation in an animal will result in clinical disease. Not surprisingly, we don't have as much of this information as we would like for many genetic tests, nor for those tests in different breeds. Yet another form of variation is known as expressivity. This refers to the variability in clinical presentation that can be seen in individuals, with some animals with the same genotype being more severely affected and others less so.

Part of the complexity of such testing is also a great opportunity for veterinarians and their teams. If genetic testing didn't require any expertise or interpretation, there would be little reason for pet owners to want to work with veterinary teams to keep their pets healthy. It is this ability to counsel and to coach that makes the veterinary team critical to the success of such programs.



The Financial Aspects of Genetic Testing

Because of changes in both law and technology, it is now possible to run dozens or even hundreds of different genetic tests for only marginally more than the cost of a few individual tests. This has made it cost effective to run genetic profiles or panels rather than individual tests. This provides a lot of information, but it is also important for veterinary teams to realize that not all of these tests are relevant in all pets. Some of these tests may only be associated with disease in certain breeds, so it is critical to be able to differentiate which test results indicate risk in which individuals. In most instances, such information is available from the laboratories performing the testing and may even be flagged on an individual's test report.

An important part of incorporating genetic testing into the veterinary workstream is that well-trained staff can drive such programs. While it is important that veterinarians help develop the framework in which counseling should take place and establish standards of care, most pet-specific care initiatives are driven by well-trained nursing and reception staff.

At present, genetic testing isn't available from the major laboratories to which most veterinary samples are currently being sent. Testing is available from laboratories that specialize in such testing, and most tests that are available can be found on a variety of websites (such as vet.upenn.edu/research/academic-departments/clinical-sciences-advanced-medicine/research-labs-centers/pennngen/tests-worldwide).

The biggest challenge most veterinary hospitals face is how to charge appropriately for such testing. Most veterinary practices have standard markups for their laboratory testing, but such markups must be considered in light of the fact that DNA testing is also available to consumers from virtually all laboratories that perform such testing, including testing done at veterinary schools. It can be a challenge when veterinary practices want to use a standard markup on a laboratory fee that is evident online to the consumer.

Perhaps the best approach to pricing is to realize that DNA testing is not a diagnostic test but rather is a tool to help understand potential risk in otherwise healthy-looking pets. In this way, it is very much like a health-risk assessment questionnaire, preanesthetic profile, or senior panel. Its main purpose is to help veterinary teams plan out a reasonable lifetime of care for pets and their owners based on available information. As such, regardless of what veterinarians charge for the test, whether they use a more conservative markup, treat it as a pass-through expense, have clients purchase the test online and come in for counseling, or even give tests away for free, the financial benefit for the practice actually comes from providing better and more pet-specific care throughout the animal's life.

Conclusion

Genetic testing is an important development in pet-specific care and has a lot to offer if veterinary teams have realistic expectations. Most of the tests are not meant to conclusively deliver a diagnosis,



and they were never intended to do so. Their main contribution is that they inform the veterinary team of potential risk so that teams can be appropriately vigilant. Such testing also serves as an important communication tool with clients, prompting discussions about strategies to keep pets healthy throughout their lives.

When used as a screening test in healthy puppies and kittens, it can be anticipated that most animals will be clear of detectable problems, and this can provide some peace of mind to pet owners that what can be done at this early age is being done. However, even a completely clear genetic profile does not mean that pets are destined for a future without health issues.

Genetic testing is just one small piece of the pet-specific care puzzle, but done with the correct motivation, it can help veterinary teams start clients along the path toward a lifetime of appropriate care for their pets. ✨



Lowell Ackerman, DVM, DACVD, MBA, MPA, CVA, MRCVS, is an independent consultant, author, and lecturer and the editor-in-chief on *Five-Minute Veterinary Practice Management Consult*. Some of this content

has been abstracted from *Pet-Specific Care*, Ackerman, L (Ed), Wiley, currently in production. Visit him online at lowellackerman.com.