Genetic testing: what does it mean for breeders?

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The number of genetic tests that can be used to identify heritable disorders is increasing at an astonishing rate. In this article, we discuss what makes a good test, how to use genetic test information and what to do if there is no test available? By getting involved your breed will reap the reward of freedom to use any bloodline.

Direct versus indirect testing

Not all tests offered to help breeders make decisions on their breeding program are equally accurate. Trying to sort them out and know how to use them can by very confusing, even for the most experienced breeder.

The gold-standard for a breeding test is to have a "mutation-based" test. This means that the researcher has identified the exact defect in the gene in the breed where the research was carried out. As a user of these tests, you as a breeder need to know whether the mutation has been observed in your breed. Often, a test that works well in the breed where it was discovered is not at all useful in a second breed.

Ask the test provider: "Is this a mutation-based test and is it validated in my breed?" You should demand the best test for the money or at least know what you are getting.

Indirect testing is where you test a biomarker related to the trait of interest that is not based on a DNA result. Some service providers give people breeding recommendations based on indirect tests. These recommendations should be treated cautiously, since often the disorders that they are making recommendations on are complex traits. Still, if they are all that is available to improve a significant and common disorder then they do have a place in your breeding program. We will discuss complex traits next.

Simple versus complex disorders

Our genes occur in pairs. Every animal receives one gene of each pair from its mother and one from its father, unless the gene lives on the X or Y chromosomes (which are the special chromosomes that decide if we are male or female). In all, we and our dogs have more than 20,000 different pairs of genes. Without exception, we and our dogs all carry some disorder genes. In fact, the average human has been found to carry around 200 of them!

Recessive genetic disorders are seen when there are two copies of the same broken gene (one from each parent). These disorders are known as simple or Mendelian recessive genetic disorders. Dominant Mendelian disorders require only one gene to be abnormal for the disorder to occur. Dominant disorders are less frequently seen because we can readily remove the disorder by not breeding from the affected animal. Sometimes though, the disorder may not show up until the animal has finished its breeding life – and these do tend to persist. An example of this kind of disorder is one which does not affect the dog until it is 9 or 10 years old, and by this time the progeny may have already bred too. These disorders are typically much harder to create a genetic

test for than the recessive disorders because more samples from animals with the disorder are needed to find the gene responsible.

Complex disorders are those that are affected by lots of different genes and the environment. Examples of complex disorders are autoimmune disorders, heart disease, elbow dysplasia, hip dysplasia and cancer. Even when researchers are able to identify some of the genes underlying these conditions, it is difficult to make a firm breeding recommendation based on the genetic testing information. Developing the tests to identify the "risk" genes in these disorders is much more difficult and time consuming. When lots of genes affect risk, it is a bit like playing poker – your pup may be dealt a good hand or a bad hand from the larger deck of genes.

Rather than using a series of DNA based genetic tests, breeding decisions regarding complex disorders are typically based on the dog's own "phenotype", that is, their own radiographic or clinical test result. Usually, having this information for a single breeding dog explains less than 25% of what will be observed in the offspring. However, a lot more understanding of risk of producing pups with the disorder can be obtained by looking at the wider testing results for the whole families of the sire and the dam. There is an international movement afoot to make this kind of analysis more accessible for you as a breeder. We call these family-based scores "estimated breeding values" or EBVs. In the near future, this will be the best option for tackling complex traits. It is most likely that hip scores will be among the first disorders to have estimated breeding values available. You can help gain access to them by encouraging your breed organisation to get involved.

Using genetic test information

Your decision to make use of a test will be affected by many things. If you are part of a breed community, there may be a group decision as to what tests should be applied. The things that should influence your decision should be things like: the efficiency of the test, the severity of the disorder, the age of onset, the frequency of the disorder in the breed, and the cost of the test. The age of onset is a prickly one. I often hear people refer to some lethal genetic disorders that occur around the time of birth as a "breeder problem". If the pup succumbs before 8 weeks this is regarded as less bad than if the pup is sent home with a new family before it becomes ill. While this is true on an emotional level, it is not really justifiable on either animal welfare or economic grounds. Each pup that you lose is costing you the sale price of that pup and this can at times be considerable. While a recessive disorder is expected to affect only ¼ of the pups born to two carrier parents, it may sometimes mean the loss of the entire litter. If at least one parent is clear of the recessive disorder (not a carrier) then no pups will have the disorder.

You may wish to breed into a bloodline that is known to suffer from a genetic disorder. In this case, it is very wise to have a genetic test for the disorder done (if there is one available) because it will enable you to choose safely from within the bloodline that you wish to use.

Our understanding of the frequency of disorder genes in all animals (including ourselves) has changed quite a lot in the past few years. Once upon a time, genetic test providers would tell you that a dog with a "carrier" status for a recessive genetic disorder should not

be bred. We no longer believe that to be the best decision. The modern view is that we should not exclude dogs from the gene pool based on a “carrier” result for a genetic test. Instead, breeders should use the test to make sure that they breed their “carrier” dog with a “clear” or “normal” mate. In this way, dogs can be bred and we need never observe the disorder in their progeny. The breeder can then test potential offspring to try and keep a “clear” or “normal” breeding replacement animal as soon as is practical. In the meantime, the breeder can ensure that one “clear” animal is used for every DNA test in every breeding. The reality is that forcing people to use animals that are “clear” for every test will place unnecessary pressure on the clear animals and may even make them a “popular sire”. The latest research tells us that the damage done to the population by overusing a single popular animal is far worse than the damage done from breeding a carrier animal to a normal mate.

Similarly, to avoid breeding into bloodlines that are known to express a genetic disorder prevents the breed from benefiting from the outstanding qualities and extra genetic diversity that this bloodline may offer. If a test is available, then there is no need to avoid using that bloodline.

Some registries such as the Orthopedic Foundation for Animals in the USA offer “clear by parentage” certification. To get this, both parents in a registered litter need to have certification showing that they have “clear” or “normal” genetic status for a particular disorder. The pup from such a litter will also be awarded “clear by parentage” status for breeding purposes. If a true “clear” result is obtained, and this dog or bitch is only ever bred with other “clear” animals, then a Mendelian disorder should never re-appear. If it does, this implies one of two things, a mistake in a test result, or an inaccuracy in the pedigree.

What do I do when there is no test?

If you are certain that your genetic disorder has a genetic basis, you should first begin discussions with other breeders to determine whether the disorder is common and if it is recessive. If the disorder is recessive and there is no test, the simplest way to avoid the expression of the disorder in the progeny is to outbreed. Outbreeding is trying to locate a mate for your dog or bitch that is as unrelated as possible (within the same breed). This is easier in some breeds than in others. Outbreeding will reduce the risk of simple Mendelian disorders but may not always help as much with complex disorders.

Many breeders fear that by outbreeding they may lose breed-type. This might be true if you outcrossed to a different breed, but so long as you choose an animal that is representative of the type that you desire within your breed, there should be no risk of losing type. This type of outbreeding happens nearly every time a breeder imports a dog for their breeding program.

As a breeder it is your duty to disclose abnormalities that you have observed in your lines to owners of potential mates for your dogs. It is only through being honest and sharing information that the risk of the expression of disorders will be reduced. Likewise, if as a breeder you learn that another breeder has observed a genetic disorder, then it is your duty to be supportive and collaborative for the good of the breed. Every breed has disorders, there is no shame in having a disorder appear if it has not been seen before. If it has been seen before in your lines, then you owe it to the future owners of your pups to do your best to avoid seeing it again.

Making a new test

We can sometimes create a new genetic test for your breed with as few as five affected individuals and a reasonable group of healthy dogs of the same breed. Some disorders look as though they have simple inheritance but are actually complex and these can take more dogs and more time. The cost of this to the university is a minimum of around $1000 per dog for a mutation-based test. To make a test can take a few years before all the pieces come together and we usually rely on small grants from student projects or donations from breed clubs to help them get started.

If your breed group has identified a problem then get involved! Most university veterinary schools will have geneticists who may be able to help. Genetic researchers have an obligation to you to maintain confidentiality. We will not disclose the source of our affected samples in the media or in publications although with your permission we may share the information with other researcher collaborators – who will likewise honour and respect your confidentiality. As researchers, we are here to help the health of the dogs, not to cast blame on the people who are trying their best to do the right thing by the breed by sharing their knowledge and experiences.