Genetic Testing for Breeding and Pet Dogs

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Breeders and veterinarians have been utilizing genetic tests since the beginning of domestic animal breeding. Most genetic tests measure the phenotype of an animal, or what you can see. These include radiographs, blood values, eye examinations, skin biopsies, urinalysis for crystals or metabolites, observations on structure or behavior, and ausculting for heart murmurs. Most tests of the phenotype only identify affected individuals, and not carriers. These may, or may not directly relate to the genotype, or the genes regulating the defect.

It is important to use available genetic testing to maintain the health of pet and breeding dogs. For example, selected breeds should be pre-operatively tested for bleeding disorders or prior to certain drug therapies. Genetic testing can also alter our treatment of certain cancers.

A test of the genotype is one that assesses the DNA of the animal. These tests can be run at any age, regardless of the age of onset of the disorder. Utilizing polymerase chain reaction (PCR) technology, affected, carrier, and normal individuals can be identified. As the majority of genetic disorders are recessive or have a major recessive component, the identification of carriers is important for effective management.

As additional DNA tests are developed for disorders, the role of genetic counseling becomes more important. Without these tests, the number of individuals that can be identified as carriers is low, even though many may be suspect due to having affected relatives. Breeds have closed gene pools; in other words, the diversity of genes in a given breed is fixed. The number of individuals removed from consideration for breeding based on concerns regarding a specific genetic disease is usually low. While this has slowed the management of genetic disease, it has also prevented genetic drift and diversity problems for pure breeds.

History has shown that breeders can be successful in reducing breed-wide genetic disease through testing and making informed breeding choices. However, there are also examples of breeds that have actually experienced more problems as a result of unwarranted culling and restriction of their gene pools. These problems include: reducing the incidence of one disease and increasing the incidence of another by repeated use of males known to be clear of the gene that causes the first condition, creating bottlenecks and diminishing diversity by eliminating all carriers of a gene from the breeding pool, instead of breeding and replacing them, and concentrating on the presence or absence of a single gene and not the quality of the whole animal.

DNA tests have to be developed specifically for each breed (or group of related breeds that share an ancestral mutation). There are two different types of tests of the genotype; direct gene tests and linkage-based tests. Direct gene tests check for a specific mutation in a defective gene. The animal either carries the defective gene, or does not.

Linkage-based DNA tests can be developed even if the defective gene causing a disorder has not been identified. Genome research has identified thousands of genetic markers, or “marker-DNA” that are spread across the chromosomes of the species. A linked-marker is a piece of DNA that lies close to the defective gene on a chromosome.

Breeders can use linkage-based genetic tests the same way direct genetic tests are used. The only difference is that you are not directly testing for the defective gene, only an associated marker; so false-positive and false-negative test results can occur.

A genetic crossover between paired chromosomes mixes the genes that an individual receives from its sire and dam. This occurs on a regular basis during the formation of eggs and sperm. As a defective gene and the linked marker are different areas of DNA that lie close together on a chromosome, it is possible that a genetic crossover can occur between them. This would separate the marker from the defective gene and create false positive (testing for the marker without the defective gene), or false negative (testing as normal, but having the defective gene) results. Depending on the relative distance between the marker and the defective gene on the chromosome, researchers can

predict the frequency of false results for a linkage-based test; for example: 1 in 100.

If an individual's linkage-based test for the defective gene is producing false-positive or false-negative results, all of its descendents that inherit this portion of the chromosome will also have false test results. This has been documented with families of Bedlington Terriers tested for the autosomal recessive copper toxicosis gene. A direct gene test for this gene is now available.

It is obvious that direct gene tests are better than linkage-based tests. However, a test with 90% or 95% confidence is better than no test at all. As genomic research progresses, researchers can identify the defective genes responsible for disorders, and can develop direct gene tests to replace linkage-based tests.

Based on the mode of inheritance of a disorder, and the availability of genotypic or phenotypic genetic tests, breeding management recommendations can be used to prevent or reduce the frequency of carrier or affected offspring.

Once a genetic test is developed, it allows breeders to positively determine if an individual is a carrier of a defective gene. The typical response of a breeder on finding that their animal is a carrier is to remove it from a breeding program. If a majority of breeders do this, it puts the breed's gene pool through a genetic bottleneck that can significantly limit the diversity of the breed. The goal of genetic testing is to allow the superior genes of a breeding individual to be propagated, even if the animal is a carrier. One defective gene that can be identified through a genetic test, out of tens of thousands of genes is not a reason to stop breeding. If an owner would breed an individual if it tested normal for a genetic disease, then a carrier result should not change that decision.

Owners of carrier animals who are of breeding quality in other health, temperament, performance and conformation aspects should be bred to normal testing mates. This prevents the production of affected offspring. The breeder should be counseled to test the offspring prior to placement; to determine whether a pet or breeding home is appropriate. The goal is to replace the carrier parent with a quality, normal testing offspring that carries on the lineage of the breeding program.

If the only quality offspring is also a carrier, then breeders can use that offspring to replace the original carrier. The breeder has improved the quality of the breeding stock, even though the defective gene remains in the next generation. The health of the breed does depend on diminishing the carrier frequency and not increasing it. Breeders should therefore limit the number of carrier-testing offspring placed in breeding homes. It is important to carry on lines. A test that should be used to help maintain breed diversity should not result in limiting it.

By breeding and not selecting against carriers, breeders are selecting for a carrier frequency of fifty-percent; higher than most breed averages. Each breeder must assess the frequency of the defective gene in their own breeding stock and determine their own rate of progress. As each breeder reduces the number of carrier breeding stock, the frequency of the defective gene for the breed will decrease.

We know that most individuals carry some unfavorable recessive genes. The more genetic tests that are developed, the greater chance there is of identifying an undesirable gene. Remember, however, that an animal is not a single gene, an eye, a hip, or a heart. Each individual carries tens of thousands of genes, and each is a part of the breed's gene pool. When considering a mating, breeders must consider all aspects - health issues, conformation, temperament and performance - and weigh the pros and cons.

Without tests, the management of genetic disease involves breeding higher-risk animals to lower-risk animals. Occasionally, a breeding male is determined to not carry a defective gene for which there is no carrier test. The tendency is for everyone to breed to this male, as a guarantee against the disorder. Any major shift in the breeding choices to a limited number of males will restrict genetic diversity, and increase the possibility of propogating additional undetected defective recessive genes in a breeding population. Such genes have become widespread even in populous breeds due to prolific breeding of popular sires.

Breeders are the custodians of their breed's past and future. "Above all, do no harm" is a primary oath of all medical professionals. Genetic tests are powerful tools, and their use can cause significant positive or negative changes. Breeders should be counseled on how to utilize test results for the best interests of the breed.