Genetic testing - for better or worse?

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Molecular genetic studies of various diseases in dogs typically focus on one or a few breeds. When the finding of a mutation is to be implemented to other breeds than those included in the original study, the results are often disappointing. The mutation that causes a particular disease in one breed does not necessarily have the same effect in another breed. For example, the eye disease progressive retinal atrophy (PRA) is a collective term for various forms of atrophy of the retina, caused by diverse mutations. In some breeds, e.g. the Golden Retriever, several forms of PRA are prevalent within the same population. It could be, e.g., that a dog free from one PRA mutation is a carrier of or affected by another form of PRA.

Validation of genetic tests is a complex task. Not only owners and breeders, but also breeding officials and professionals, may have difficulties to find and interpret scientific information needed to assess whether a test can be considered reliable and useful or not. There are currently no regulations to stop laboratories from marketing tests with little or no evidence of efficacy or accuracy. In many cases, more and better information from the suppliers of tests is needed, and should be demanded. Moreover, the international dog community should make additional efforts to support dog breeders and owners in this regard.

NKU/VK would like to stress that a dog showing clinical symptoms of a serious disease should not be used for breeding, regardless of the genetic test result. The dog's clinical health status is in that sense always superior to the genetic status.

Moreover, NKU/VK sees a need for further efforts from the international dog community to support dog breeders and owners with respect to validation and guidance on the use of genetic tests.

The inheritance may be unclear

Many of the genetic tests offered are for diseases inherited in a simple autosomal recessive way. This means that the disease is caused by a single mutation, that in a homozygous genotype (when inherited from both parents) will cause clinical symptoms of the disease. Genetic tests for autosomal recessive conditions will classify dogs as free, carriers or affected. A dog classified as free did not inherit the disease causing mutation from either parent. Hence, it will not be affected by this particular mutation and there is no risk of passing on the mutation to its offspring. A carrier dog has inherited the mutation from one of its parents, i.e. is heterozygous for the mutation. This dog will not itself be clinically affected but may pass on the mutation to its offspring. A genetically affected dog is homozygous for the mutation and will most likely develop clinical symptoms of the disease over time. Thanks to DNA tests for autosomal recessive conditions it is possible to use carrier dogs in breeding, provided that they are mated to a dog free from the mutation. This, of course, requires that the test is validated and accurate. To decrease the prevalence of the mutation over time, carrier dogs should be used cautiously in breeding.

Nevertheless, many of the most prevalent diseases in dogs have a more complex genetic background, being influenced by several genes as well as environmental effects. For these diseases the genetic background is not fully understood. Even though one or several mutation(s) with a large effect on a complex disease may be found, there are also other modifying genes and/ or environmental factors that influence the phenotype. This makes it more complicated to provide and interpret genetic tests for quantitative diseases.

Where a test exists for a complex trait, the mutation (or mutations) tested for may imply an increased risk for a specific condition; however, it is often unclear how high the risk of clinical disease is. Far from all genetically-affected dogs will develop clinical symptoms. Moreover, the test does not provide information on what other genetic risk factors the dog may carry, or to what extent also environmental factors influence the phenotype.

For some of the genetic tests based on mutations influencing a quantitative disease, or a disease with undefined inheritance, the so-called penetrance is only 2-5%. This implies that a dog with the specific mutation has only a 2-5% risk of showing clinical symptoms of the disease.

In some cases, diseases that were initially thought to be inherited in a simple autosomal recessive manner have been shown to have a more complex genetic background.

As a breeder or a dog owner it can be difficult to find information on the inheritance of a specific disease or to assess whether a genetic test is sufficiently validated or not. Information on the laboratory webpage may give some guidance. If the inheritance is described as showing incomplete penetrance, or the test result for genetically affected dogs is said to imply an increased risk of disease, caution is indicated and further investigation, before using the test, is recommended.

An obvious risk with genetic tests for diseases where the inheritance is not yet completely understood is that potential breeding animals are excluded based on uncertain grounds, or that the test incorrectly categorizes individuals free from a disease for which they might have other genetic risk factors. Moreover, if the risk allele tested for is frequent in the population the gene pool may be severely limited.

The general approach of NKU/VK is to advice against the use of genetic tests for conditions where the inheritance is unclear. Tests for diseases that are influenced by many genes should be applied only in cases where evidence based on scientific publications has established that the mutation or mutations cause a significant and defined risk of disease, and provided that the condition is of clinical relevance in the breed concerned.

Combination tests for several diseases

A relatively new phenomenon on the DNA testing market is laboratories offering multi or combination tests for a wide variety of mutations. Several genetic tests for various diseases as well as other traits are combined into one test package, and this is offered to breed groups or in some cases to all breeds. Hence, the owner or breeder will get genotype results for their dog for as many as a dozen to over a hundred different mutations.

This may seem like a convenient and cost-efficient way to get the most information about the dog's genetic makeup. However, the results of these multi-tests are often difficult to interpret and of a limited value, or even misleading, for breeding purposes. It should be emphasized that breeders and owners of stud dogs have to consider the test result in breeding, even if some of the mutations included are not sufficiently validated or of any relevance to the breed concerned. Hence, inaccurate test results or genotype information for irrelevant conditions may imply negative consequences for the gene pool and the development of other traits in the breeding goal. In some breeds, especially numerically small populations, use of these multi-tests risk to pose serious difficulties in finding dogs for mating that match in genotype with respect to all the mutations included.

In light of the above, NKU/VK are reluctant to promote the use of multi-tests and combination test packages currently available. This position is based on the shortcomings in validation and/or relevance for some of the mutations included in these packages, as well as the potential negative consequences on the overall breeding goal that an uncritical use of genetic tests is likely to cause. Instead, NKU/VK recommends breeders and dog owners test for the specific mutation(s) that are relevant in the current breed, provided that these tests are validated.

Moreover, NKU/VK would like to emphasize the importance of breeders and/or dog owners carefully evaluating the usefulness and accuracy of a genetic test before it is performed. Only use tests that are properly evaluated and for conditions that are of clinical relevance in the breed. No dog, or other living creature, is completely free of disease mutations. Uncritical use of DNA tests may in the worst case result in negative effects on the breed's health and gene pool. Please contact your breed club for more information if you are doubtful.

General policy regarding the application of genetic tests in dog breeding

Based on the information above, the Scientific Committee of the Nordic Kennel Union (NKU/VK) would like to make the following general statement regarding the application of genetic tests in dog breeding:

Genetic testing is an excellent tool in breeding for improved dog health, provided that the tests are reliable, relevant and used wisely. Breeders and dog owners should carefully evaluate the benefits and consequences of a genetic test before it is applied. A one-sided or exaggerated focus on DNA test results may result in an increased risk that other important conditions or characteristics are overlooked. The Scientific Committee of NKU would like to emphasize that the breeding program should be based on the prevalence and severity of various health issues, rather than on the availability of genetic tests. If a disease does not constitute a clinical problem in the breed and/ or the DNA test offered is not validated or accurate, it is better to refrain from testing the dog. Otherwise, there is an obvious risk of excluding potential breeding animals, and thus decreasing genetic variation, based on uncertain or false grounds. It is important to keep in mind that dog breeding is about much more than specific diseases and that genetic tests, even though today they are many, do not give the entire picture.