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Short Communication

Researcher responsibilities and genetic counseling for pure-bred dog populations

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ABSTRACT

Breeders of dogs have ethical responsibilities regarding the testing and management of genetic disease. Molecular genetics researchers have their own responsibilities, highlighted in this article. Laboratories offering commercial genetic testing should have proper sample identification and quality control, official test result certificates, clear explanations of test results and reasonably priced testing fees. Providing test results to a publicly-accessible genetic health registry allows breeders and the public to search for health-tested parents to reduce the risk of producing or purchasing affected offspring. Counseling on the testing and elimination of defective genes must consider the effects of genetic selection on the population. Recommendations to breed quality carriers to normal-testing dogs and replacing them with quality normal-testing offspring will help to preserve breeding lines and breed genetic diversity.

Breeders of dogs are becoming educated about their obligations and ethical responsibilities regarding the testing and management of genetic disease. Genetic testing is health quality control. In many cases, it is no longer ethical to breed dogs without pre-breeding genetic testing. Genetic tests may include breed-specific genotypic tests or phenotypic examinations of, for example, eyes, hips, elbows, patellas and heart or thyroid function. Breeders need to be aware of how their breeding choices affect the gene pool of their breeds. They should utilize breeding choices that improve the quality of the breed with respect to conformation, temperament and ability, improve the health of the breed and maintain gene-pool diversity.

Veterinarians should provide information on breed-specific genetic testing requirements to prospective owners prior to purchasing pets, as well as to breeders. These requirements can be found at the Canine Health Information Center (CHIC),[1] established by the not-for-profit American Kennel Club Canine Health Foundation and Orthopedic Foundation for Animals (OFA). In this way, health-conscious breeding and purchasing can become the standard to improve the genetic health of dogs.

Molecular genetics researchers who discover defective genes have their own responsibilities to dog breeders and owners. The discovery of a disease-causing gene in a breed population is only the first step in assisting breeds. Many molecular genetics researchers find themselves in the business of providing a genetic testing service. This service to breeders, owners, breeds and the general public brings with it several responsibilities:

1. Prior to offering a commercial genetic test to the public, proof of causality should be published in a peer-reviewed scientific publication. This raises secondary issues that the industry also needs to consider, including patent protection, trade secrets and the unlicensed offering of genetic tests by commercial laboratories.
2. Established laboratory quality control measures should be strictly adhered to in the receiving, processing, recording, laboratory procedures and reporting of results of genetic testing.
3. Application forms should properly identify the animal with its registered name and numbers and should have owner signature certification. While it is expected that some pet animals may not have this information available, all breeding animals should.
4. Official test result certificates should be generated that contain all identifying animal information, the test result and interpretation of the result. These result certificates are important for the owner to present to prospective breeders and prospective pet owners to certify that genetic testing has been performed.
5. Results and limitations for different types of genetic tests should be clearly explained to breeders and owners. Linked marker-based DNA tests should include statements about the possibility of false positive or false negative results due to genetic crossovers. Abnormal test results for susceptibility genes of complex diseases should be labeled '*At Risk*' instead of '*Affected*', so as to not imply a wholly causative effect. Test results should be accompanied by clear statements of the mode of inheritance of the disorder, penetrance and expressivity, sensitivity and specificity of the genetic test for clinical disease and percentage of genetic variation of disease represented by the testable loci.

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[1] See: www.caninehealthinfo.org.

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6. Genetic testing fees should be reasonably priced. The commercial service of genetic testing is a public service to breeders and owners. Genetic testing fees are not an alternative to research funding, holding breeders and owners as hostage benefactors. The commercial cost of a typical animal genotypic test should not be more than US$35-75.[2] This should provide a reasonable profit and license fee for the testing facility and discovering researcher. If the mutation-discovering research laboratory is not interested in commercial testing, then their discovery can be licensed to a commercial testing laboratory for a per-test license fee.
7. Test results should be provided to a publicly-accessible genetic health registry. This allows veterinarians, breeders and the public to search for health-tested parents, to be able to identify health-conscious breeders and thus to reduce the risk of producing or purchasing affected offspring. Test results can be reported in an open (all results published), or semi-open (only normal results published) manner; there is a trend towards open reporting of all results. An example is the centralized genetic registry database of the OFA.[3]
8. Determining the prevalence, distribution and changing frequencies of defective genes in breed populations can be used to assist breeds with genetic improvement. These studies require valid statistical sampling from the breadth of the gene pool. The initial collection of data pertaining to a disease provides a bias towards affected individuals and their close relatives. Early genetic testing, once a commercial test is offered, also tends to be skewed towards carriers, since breeders with close relatives identified as 'affected' or 'carrier' tend to submit samples for testing more readily than those who do not know of related carriers. Different within-breed populations worldwide tend to have different population dynamics that can produce different defective gene frequencies.

Genetics researchers are looked to for genetic counseling advice to manage genetic disease. Breeding recommendations should be offered that are specific to the disease-related gene and the breed. The effect of genetic selection on the population must be taken into consideration to preserve breeding lines and breed genetic diversity.

A genetic test should enhance and not limit breeding choices. Using a direct DNA test, carriers of fully-penetrant, disease-causing recessive genes that are otherwise desirable should be bred to homozygous normal individuals and replaced with desirable homozygous normal offspring. This maintains breed lines while eliminating the defective gene. The use of carrier breeding stock primarily should be to produce homozygous normal replacement individuals. The continued propagation of known carriers in the population should be avoided. Otherwise, as more testable disorders emerge, the mating choices of quality animals (to prevent carrier to carrier matings) could be unnecessarily limited.

The emotional aspects of carrier test results must be recognized. The emotional response to receiving a carrier test result can be overwhelming and it must be reemphasized continually that the correct action is to breed quality carriers and not to discard them from the gene pool.

For dominant disease-causing genes, the recommendation is to replace the affected breeding individual with a normal-testing first degree relative. While a breeder's first choice may be excluded, the line can be continued with closely related individuals. For X-linked diseases, the use of normal male relatives maintains breeding lines. Females at high carrier risk should not be used, since carrier females produce approximately 50% affected males.

For complexly inherited disorders with testable liability genes, knowledge of the test results or affected status of close relatives allows the breeder to recognize the risk of producing the genetic disorder. Selection can be based on estimated breeding values, or breadth and depth of pedigree normalcy, which can be visualized on a dog's vertical pedigree on the OFA website (Keller et al., 2011).

Conflict of interest statement

The author is a volunteer member of the Board of Directors of the not-for-profit Orthopedic Foundation for Animals.

Reference

Keller, G.G., Dziuk, E., Bell, J.S., 2011. How the Orthopedic Foundation for Animals (OFA) is tackling inherited disorders in the USA: Using hip and elbow dysplasia as examples. The Veterinary Journal 189, 197–202.

[2] US$1 = approx. UK£0.60, €0.68 at 27 April 2011.
[3] See: www.offa.org.