



The Golden Retriever Club of America, Inc.

An Update on Eye Disease in Golden Retrievers: *prcd*-PRA

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What is Progressive Retinal Atrophy (PRA)?

PRA is the name for a clinical condition of dogs that is characterized by generalized progressive degeneration of the photoreceptor cells of the retina leading to blindness. This disease is NOT retinal dysplasia. There are several different forms of PRA but in most forms the retina will appear normal in young dogs, with retinal degeneration followed by blindness developing with age. Because PRA generally develops in mature dogs, affected dogs are often bred before they either are detected in routine ophthalmologic examination or develop clinical disease.

Several different genetic mutations have recently been shown to cause PRA in dogs and the genetic causes of PRA vary among the breeds (Zangerl et al, 2006; Zangerl et al, 2007, Vilboux et al, 2008). In dogs in general, there are autosomal recessive, autosomal dominant, and sex-linked forms of PRA. However, most forms of PRA are inherited as an autosomal recessive condition – which means that affected dogs need to inherit a defective allele (an allele is one-half of a gene pair, and each parent contributes one allele to its offspring) from each of their parents but that the parents will have normal vision if they have one normal allele. For many dog breeds, there are now genetic tests for the most common forms of PRA affecting that breed. A list of genetics tests is available online from the AKC-Canine Health Foundation and includes tests for genes causing some forms of PRA (<http://www.akcchf.org/canine-health/genetic-tests/>). With regard to breeding considerations, forms of PRA that are presumed to be inherited can be viewed as falling into two very broad categories: 1) PRA where the genetic cause has not yet been identified; and 2) PRA where the genetic cause has been identified and there is a DNA test.

PRA in Golden Retrievers

PRA is rare in the Golden Retriever breed as a whole when compared with other dog breeds. The number of affected Golden Retrievers in this country has been small and stable for many years, with 21 (0.06%) Golden Retrievers affected in CERF examinations conducted from 1990-1999 and 18 (0.05%) Golden Retrievers affected in CERF examinations conducted from 2000-2005 (ACVO, 2007). Nevertheless, PRA is a very serious condition and the frequency of PRA can increase suddenly if a group of Golden Retrievers that carry PRA genes are bred together. This can easily happen when two bloodlines that unknowingly each carry PRA genes are crossed to provide individuals with some success in competition.

Prior to 2007, no genes that cause PRA had been identified in Goldens, and genes that cause PRA in other breeds had not been found in Goldens. In 2007, a Golden Retriever was found to have a specific form of PRA for which there is a genetic test, called progressive rod-cone

degeneration PRA (prcd-PRA). Prcd-PRA is the most common form of PRA in dogs in general (Peterson-Jones, 2007), and affects 18 other breeds, including Labrador Retrievers and Poodles (Goldstein et al, 2006; Zangerl et al, 2006). However, we do not know if it is the most common form of PRA in Golden Retrievers, and we do know that not all PRA in Golden Retrievers is prcd-PRA. The genetic mutation that causes prcd-PRA in dogs also causes one form of retinitis pigmentosa and blindness in humans (Zangerl et al, 2006). A patented commercial genetic test for prcd-PRA is available from Optigen, which provides online information on the prcd-PRA test (http://www.optigen.com/opt9_test_prcd_pra.html), as well as updates on prcd-PRA in Golden Retrievers (http://www.optigen.com/opt9_pra_goldenrtvr.html). This is a genetic test that identifies dogs with the specific mutation which causes prcd-PRA and classifies those dogs with this mutation into dogs with one copy of the mutation (carrier) and dogs with two copies of the mutation (affected). Importantly, the area of the prcd gene that is mutated in prcd-PRA normally shows very little variability between different species, including the dog, mouse and human. The mutation in this critical region of the prcd-PRA gene is able to produce retinal disease in genetic backgrounds as diverse as 18 different dog breeds and an entirely different species, humans. In addition, Golden Retrievers with PRA have been identified who have two copies of the prcd-PRA gene. Thus, the scientific evidence is overwhelming that having two copies of the prcd-PRA can cause PRA in Golden Retrievers.

This is a summary of the current knowledge of an evolving situation. We do not currently know the frequency of prcd-PRA in Golden Retrievers. However, any Golden Retriever diagnosed with PRA by a board-certified ophthalmologist can be DNA tested for prcd-PRA free of charge (http://www.optigen.com/opt9_research.html), and this testing is the only way to determine whether the dog has prcd-PRA or another form of PRA. Because prcd-PRA is a simple autosomal recessive disease, certain well-defined rules of inheritance apply:

1. A Golden Retriever that is clinically affected with prcd-PRA has inherited a disease allele from each of its parents. Both parents of a clinically affected dog are carriers (or affected), and all siblings of a clinically affected dog are at risk of being carriers or becoming affected. All offspring of a clinically affected dog are carriers, but would only be at risk of becoming clinically affected themselves if the other parent is also a carrier or affected.
2. A Golden Retriever that has one prcd-PRA allele and one normal allele is a prcd-PRA carrier. At least one of its parents is a carrier (possibly both), and all of its siblings are at risk for also being carriers (or affected, if both parents are shown to be carriers).
 - a. Carriers bred to carriers or affecteds can produce affected puppies.
 - b. Carriers bred to DNA tested normal/clears (both alleles are normal) should not produce puppies affected with prcd-PRA but may produce carriers.

The Health and Genetics Committee recommends that close relatives of prcd-PRA affected and carrier Golden Retrievers be DNA tested for prcd-PRA unless they are direct descendants of dogs DNA tested as normal/clear. For example, a sibling to a prcd-PRA carrier or affected should be DNA tested prior to breeding. Carriers should only be bred to Golden Retrievers that have been DNA tested as normal/clear for prcd-PRA, and any offspring sold with full registration should be DNA tested and their status disclosed before ownership transfer. However, if that sibling is DNA tested as prcd-PRA normal/clear and is bred to a dog that is DNA tested as prcd-PRA

normal/clear, there is no need to test the offspring. Importantly, all current data indicates that prcd-PRA carriers are just as likely to be healthy as their normal/clear siblings. If going to a pet home, limited registration with a spay/neuter agreement is particularly important for potential carriers. If going into a potential competition/breeding home, it is essential to have full disclosure of the carrier status and the testing and breeding strategies needed to prevent affected offspring.

In addition to relatives of carriers and affected Golden Retrievers (and their prospective mates), owners may wish to DNA test frequently used stud dogs, although at this time the GRCA Health & Genetics Committee is not recommending widespread or routine testing in the breed. Still, owners may want to test their Golden Retrievers for a variety of reasons, and the test is available at the regular fee for any dog. Discounted testing is available for 1) multiple puppies from the same litter and 2) offspring of DNA tested prcd-PRA normal/clear Golden Retrievers. Details of breeding strategies designed to gradually eliminate the genes for prcd-PRA from an affected line without producing affected puppies are available online at http://www.optigen.com/opt9_test_prcd_pra.html. The GRCA Board of Directors has approved advertising results of the prcd-PRA DNA test, provided that the advertisement is accompanied by a current Canine Eye Registration Foundation (CERF) examination number and a statement that there is another form of PRA in Golden Retrievers. If the findings of a normal prcd-PRA DNA test are submitted to the Orthopedic Foundation for Animals (OFA) with the recording fee, OFA will issue a registry number and a certificate stating the dog is genotypically normal for prcd-PRA. For the offspring of Golden Retrievers tested genotypically normal for prcd-PRA, if DNA identity profiles and parentage verification are submitted for the dog and its parents, OFA will issue a certificate with a suffix CBP, which indicates they are “clear by parentage”). There is also an independent website (<http://www.goldendna.com/>) devoted to providing DNA test information on Golden Retrievers and the prcd-PRA DNA test is the only available DNA test at this time.

Thoughts for Consideration Regarding Genetic Testing

It is very likely that all dogs carry several deleterious recessive genes. The prcd-PRA test allows us to see the dogs that carry the prcd-PRA mutation. The test also allows us to breed those carriers responsibly, so that the chance of a PRA-affected puppy is greatly reduced, while gradually reducing the prevalence of the gene in Golden Retrievers. For our breed, this is a first. It is important to remember that “for a dog to have a lasting influence on the breed, it must be an extraordinarily successful individual” and to avoid the knee-jerk reaction of inappropriately removing excellent dogs from the gene pool just because we now have a way to identify their carrier status for this disease. Also, rapid elimination of carriers can narrow the gene pool so that other harmful recessive genes are concentrated, thus potentially causing more harm than good. Therefore, some breeders working with affected lines will choose to breed carriers to normal/clear individual and test the offspring that may be used for breeding while others will only breed normal/clear to normal/clear and will not need to test the offspring. Both approaches are responsible.

Goals for achieving a healthier breed over the long term as more genetic tests become available include: honesty; open communication of genetic problems; rational use of the prcd-PRA test

and other emerging DNA tests to prevent producing affected Golden Retrievers; tolerance of those with different breeding strategies that still produce healthy puppies; acceptance that many dogs will carry abnormal genes, but that carriers should not be bred to carriers because we must avoid producing homozygous affected puppies; and an understanding that genetic tests allow us an opportunity to produce homozygous normal individuals gradually without loss of quality. A rational informed approach to genetic testing will pave the way for the extraordinarily successful individual of the future to be as good or better in their performance/conformation as we could have ever envisioned in the past, but increases the likelihood that the descendants from successful lines also contribute good health to the Golden Retrievers' future.

Prcd-PRA Health Clinics

Optigen offers a 20% price discount for 20 or more samples in a group mailing. There is an additional 5% discount when the orders are entered online. An additional 5% discount may be negotiated for 75 or more samples in a group mailing where online orders are completed. Thus, clubs can offer prcd-PRA health clinics that benefit multiple owners. Information is available online at http://www.optigen.com/opt9_clinicinfo.html. Clubs interested in sponsoring health clinics can email the Optigen 20/20 coordinator for additional information (2020clinic@optigen.com).

The Importance of CERF Exams

Yearly eye examinations are critical to detecting cases of clinical PRA because prcd-PRA is not the only cause of PRA in Golden Retrievers. Guidelines from the American College of Veterinary Ophthalmologists on PRA are clear: "Breeding is not advised for any animal demonstrating bilaterally symmetric retinal degeneration (considered to be PRA unless proven otherwise)" (ACVO, 2007). For Golden Retrievers that have ever been bred, breeders should continue yearly examinations throughout their lives, and those examinations should be recorded by the ophthalmologist on original CERF forms (don't use a photocopy) and registered with CERF if the dogs are clear. Whether or not the owner chooses to register with CERF, if the CERF form is used, the frequency of eye diseases is recorded by ACVO. Because this does not disclose the identity of affected dogs unless owners chose to do so and enables GRCA to follow trends in eye disease in the breed, this is particularly important. In addition, if dogs with clinically normal eyes are registered with CERF, breeders can check to be sure that ancestors of their puppies had clinically normal eyes into late adulthood. GRCA member clubs offering eye clinics are encouraged to require use of the CERF forms so we can track the frequency of inherited eye diseases in Golden Retrievers.

PRA Research

From the increasing number of publications identifying genes causing PRA in dogs, it appears that many different research groups are studying PRA in dogs. Owners with PRA affected dogs (any form) can submit blood or cheek swabs to the Canine Health Information Center (CHIC) DNA repository at no charge, which will make DNA from those dogs available to approved research studies. Information on the CHIC DNA repository is available online at <http://www.caninehealthinfo.org/dnabankfaq.html>, although to submit affected dogs at no

charge, please email Eddie Dzuik directly at EDziuk@OFFA.org. In addition, Optigen will test dogs diagnosed by a veterinary ophthalmologist with PRA for known causes of PRA on a research basis at no cost to the owners, provided the owners receive pre-approval from Optigen. (This is how prcd-PRA was identified as a cause of PRA in Golden Retrievers.) Information on research at Optigen is available online at http://www.optigen.com/opt9_research.html). The GRCA Health and Genetics committee encourages owners of PRA-affected Golden Retrievers and their first degree relatives to submit samples to both the Optigen research program and the CHIC DNA repository.

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