

PRA HAS HAD ITS DAY!

Article 1 - Published February 1, 2002

On Feb. 1, OptiGen Laboratory, LLC, a canine genetic testing laboratory began accepting and processing blood tests to determine - with 99% accuracy - if your Toller is clear, a carrier of or affected with Progressive Retinal Atrophy (PRA). This exciting new test, available world wide, is made available through the research of Dr. Gus Aguirre and colleagues of the James A. Baker Institute for Animal Health at Cornell University. It was also made possible by the generous donations of the Van Sloun Fund for Canine Genetics Research to benefit the work of the Inherited Eye Disease Studies Unit; the Morris Animal Foundation; The Seeing Eye Inc., Foundation Fighting Blindness; NEI/NIH grants EY-06855 and 13132, the US and Canadian NSDTR clubs and countless members and Toller owners.



Sue Van Sloun and Dr. Gus Aguirre on the occasion of Sue receiving the Baker Institute's 1998 Arthur F. North, Jr. Canine Service Award

Photo by: Nicola Kountoupes,
Cornell Photography

"The test is as close to perfect as a test can be without actually being a true gene test," said Dr. Aguirre, Alfred H. Caspary Professor of Ophthalmology. Technically referred to as the Toller prcd (progressive rod cone degeneration) test, the new procedure is a gene marker test that can predict with 99 percent accuracy a Pattern A (clear), Pattern B (carrier) or Pattern C (affected) Toller. Unlike other prcd tests offered for other breeds, this marker test is specific for Tollers and results in a greatly reduced chance (0.05 percent or less) of false positive results. The test eliminates the guess work from a breeding program with respect to prcd - the only form of PRA seen in Tollers which results in blindness. Breeders will no longer have to remove affected and carrier stock from their breeding programs. As long as these dogs are bred to clear dogs, they will not produce any affected dogs.

The start of the PRA Toller study was first announced in Quackers (Summer 1994). At that time, founding club members Sue Van Sloun and Marile Waterstraat met with Dr. Aguirre to outline steps necessary in the quest for the answer to PRA. By the Fall 1994 issue of Quackers, six Tollers were featured that were the founding stock for this important research. For the next eight years, the persistence of Dr. Aguirre, Sue Van Sloun and study participants helped define the gene marker which is the basis of the new OptiGen test. Blood samples, fundraising efforts and numerous visits to Dr. Aguirre all made this test a reality. The entire Toller community will benefit from this test, and we thank you all for your efforts and contributions.

Here is information to get started:

For PRA study participants: You need to submit a request form to obtain your test results if any of your dog's blood samples were sent to Dr. Aguirre for developing this test. Please understand that all of the submitted samples were not used to develop this test; therefore, results will not be available for all the research samples from Dr. Aguirre's lab.

Click here to download the study participants form in .pdf file format or **contact one of the following people to get a form:**

Liz Corey Baker Institute
Keith Watamura

To order a prcd Toller blood test: Detailed instructions are available from OptiGen's website that explain how to ship a sample, request a test and information about the Toller prcd test.

Website: www.optigen.com Or contact: **OptiGen**
(607) 257-0301
Email: Genetest@optigen.com

For more information Contact:

Sue Van Sloun, Project Coordinator

Jane Folkman, Education/Communication

Questions and Answers

Q: What type of PRA (Progressive Retinal Atrophy) is seen in Tollers?

A: Tollers have the prcd (progressive rod cone degeneration) form of PRA. It is the only type of PRA known in Tollers at present. Thus, the OptiGen DNA marker test is expected to identify all cases of Toller PRA in tested animals.

Q: What is the usual age at diagnosis?

A: Tollers have been diagnosed with prcd-PRA over a very wide age range - as young as 3 years and as old as 8 years. The typical age of diagnosis is 4 to 6 years. As more dogs are examined, it is likely that even younger and older dogs will be discovered showing first signs of PRA.

Q: What kind of test is the OptiGen prcd-PRA test for in Tollers?

A: The test is a DNA marker test, where markers very close to the disease gene are used to predict the associated normal or affected allele. New markers that are specifically informative for the Toller have been chosen. This test is not a direct mutation or gene test, since the prcd-PRA disease gene in Tollers has not been discovered yet. Results will be reported as Pattern A (clear), Pattern B (carrier) or Pattern C (affected), reflecting the pattern of markers in each dog tested.

Q: Are there any proven cases of false positive alleles in this test similar to other breeds?

A: So far there is no known case of a false positive allele in Tollers. There is no evidence so far that a Pattern B dog might actually be Pattern A, nor that a Pattern C dog might actually be Pattern B or even A. This situation is very different from the initial prcd-PRA test in other breeds where the rate of false positives was substantial. In Tollers, the risk of a false positive result is estimated to be less than 0.05%, based on the theoretical possibility of recombination between the prcd gene and the prcd markers. With more extensive testing of new pedigrees, it is possible that the issue of false positives in Pattern B or C might need to be reconsidered.

Q: Can you please tell me why both "expressivity" and "penetrance" of prcd-PRA play an important role in understanding genetic status in Tollers. What is variable expressivity?

A: Some diseases are very predictable in terms of age of onset and severity of symptoms. Such a disease is typically "expressed" in the same way in each affected individual. But Toller prcd-PRA doesn't fit this description. It can have different ages of onset, different degrees of severity and/or different rates of progression within the same line, pedigree, or even the same litter. One confusing result of reduced or variable expressivity is that a dog can test Pattern C, affected with PRA, yet show no clinical signs of abnormal vision until much later, or show only mild and slowly progressing clinical signs of the disease. This dog must not be confused with a case of false positive.

Q: What is penetrance?

A: The extreme case of reduced expressivity is incomplete penetrance. An inherited disease has incomplete penetrance in

cases where the individual is known to have the affected genotype, but never shows the disease. Even so, the clinical disease shows up again in its offspring. Clearly, the affected genes were present in the parent but the disease didn't "penetrate" to a recognizable state. Again, this case must not be confused with a case of false positive. Toller pedigrees with incomplete penetrance have been documented.

Q: Is there a margin of error for Pattern A?

A: Pattern A Tollers are statistically normal for prcd-PRA and are not expected to develop this disease or pass it to offspring. No known Pattern A Toller has developed PRA or produced PRA-affected offspring, and no known PRA-affected Toller has tested Pattern A. However, there is a low theoretical chance that a Pattern A Toller could have a false negative result and therefore be a carrier (risk is less than 0.5%) or even be affected (risk is less than 0.0025%). False negative results have not yet been observed with the current test.

Q: Is there a margin of error for Pattern B?

A: Pattern B Tollers are not expected to develop PRA and are carriers of PRA with at least 99% certainty. There is a chance (risk is less than 0.5%) of a false negative result, which would make this dog PRA-affected instead of a carrier. Also there is a similar chance (risk is less than 0.5%) of a false positive result in a Pattern B Toller which would make this dog PRA normal. Neither of these possibilities (1 out of 200) has been observed yet.

Q: Is there a margin of error for Pattern C?

A: Pattern C Tollers are homozygous for prcd-PRA markers and are at high risk for developing PRA. There is a small theoretical chance, less than 0.5%, of a false positive result, meaning that a Pattern C Toller could be a carrier, or with even lower chance, less than 0.0025%, could be normal. False positive results have not yet been observed with the current test.

Q: How frequent is prcd-PRA in Tollers?

A: CERF (Canine Eye Registration Foundation) reports that combined frequency of PRA-generalized and PRA-suspicious status in Tollers as 7% of 693 dogs with CERF exam records between 1991-1999. This is a high disease frequency, and might suggest that a large proportion of dogs at risk for PRA are selected for CERF exams. If the CERF frequency is valid, it indicates a high rate of carriers in the Toller populations, possible as high as 40%. However, Dr. Sheryl Krohne, Diplomate of the American College of Veterinary Ophthalmology says "CERF data are rough estimates with an incomplete sample reported." A more accurate prediction of the true incidence of PRA affected, carrier and normal dogs will become clearer as larger numbers of Tollers are OptiGen tested.

Q: What Tollers were used in the research to develop the OptiGen prcd-PRA test?

A: Thirteen families of Tollers, totaling almost 100 dogs, from the US, Canada and Denmark were studied to develop and validate this test. The test can be used on purebred Tollers worldwide.

The Eye Committee

Sue Van Sloun

Project Coordinator

Sue is a founding member of the Nova Scotia Duck Tolling Retriever Club in the US. She initiated the PRA study with Dr. Gus Aguirre, the world's leading expert on PRA, in 1994. Sue has devoted countless time and resources to solving the mystery of PRA in Tollers. Sue currently serves as the Project Coordinator for the Eye Committee.

Jane Folkman

Communication/Education

Jane has a BS degree in Animal Sciences from the University of Vermont and a MS degree in Nutrition from Case Western Reserve University. Jane has previously served as an Associate Editor and freelance writer for several national health publications. Jane will provide education articles and communicate information generated by the Eye Committee.

Liz Corey

Data Coordinator

Liz has a BS degree in Animal Sciences from the University of Vermont and is currently working in genetics research at the James A. Baker Institute for Animal Health in the College of Veterinary Medicine at Cornell University. Liz will serve as the Data Coordinator for the Eye Committee and provide technical review for the Eye Committee education articles.

James A. Baker Institute PRA Study Participants

NSDTRC (USA) Health & Genetics

Article 2; Published March 1, 2002

Congratulations! Without your unwavering devotion and belief in the project we never would have **had our day!**

We started with six dogs, and within a few short years there were almost 100 in the study! Wow! Mind boggling. I can't thank you enough for always being there for me. I began to feel a little like the "Vampire Lady" when I would e-mail for more blood, more blood.

"Thank you," seems so inadequate when compared to the time you gave and the many expenses you incurred when gathering dogs from remote places for yet another eye check. But believe me when I say "Thanks" it comes from the bottom of my heart. Never in a thousand years could I have done it without your fantastic support.

I'd like to give a little extra recognition to some of the people involved in the study.

Foxgrove Kennel - Sue Kish: Sue contributed information on over a dozen dogs and at one time drove down to JAB with dogs, blood and even semen. Thank you Sue.

Kylador Kennel - Lillian Greensides/Karen Wright: Lillian on more than one occasion made arrangements to get dogs down to her so she could do eye checks and gather blood for shipping. I swear some of these dogs were so far north the only form of transportation was by dog sled. Thank you Lillian for always being there for me.

Lennoxlove Kennel - John Hamilton/Marile Waterstraat: John and Marile's Rusty Jones was one of the six. Both made numerous trips with their Tollers as well as other people to Cornell. I know of a couple of times when John gave up training to drive dogs down to Dr. Aguirre while Marile was at work - now that's devotion to a cause. Thanks to both of you.

Springvale Kennel - Sue Dorscheid/Mike Elmergreen: Their Arrow was one of the six. Sue spent lots of time running down Toller owners I couldn't reach and getting them to have eye tests and arranging to have blood sent.

A very special thanks goes to Jody & Michael Petry who traveled many miles to pick up a Toller that was quite important to the study. They arranged for blood tests as well as CERF and then drove the dog back home.

Thanks to your perseverance, Toller breeders now have the availability and results from the new prcd-2/PRA Toller blood test, to safely choose from a wider pool of Toller breeding stock. No longer do we need to avoid a known or suspected carrier of PRA or a pedigree with PRA in its background. Thanks to the 100 dogs that participated in this exciting research and the persistent efforts of researchers, Toller owners and breeders, we have the tool needed to make informed choices.

Of course, it goes without saying that all the Tollers in the study made a significant contribution and we are forever grateful to the many members in the USA and Canada that supported the study program at the J. A. Baker Institute through their financial contributions.

By way of saying "thank you" the PRA Division would like to present you with a Certificate of Appreciation. Instructions for receiving this certificate follow.

I would greatly appreciate it, if you would fill out the listing form and send to the Eye Registry. This particular form is only for the Study group dogs. The results for the Study dogs are listed only with James A. Baker Institute and not OptiGen. We

don't want to see these results just disappear. So, believe it or not, once again you have the opportunity to be a ground-breaker - the first to register.

NSDTRC (USA) Health & Genetics has developed an Eye Registry. This was done to keep track of and use wherever possible, all test results relating to the Toller Eye. The first step is the formation of a PRA test results database. Your help would really be appreciated by me. Please consider listing in the open section. I feel if those Toller owners whose dogs come back with a "B" or "C" see that some of the top breeders list their dogs, that it will give them the courage to follow suit. There is comfort in numbers.

Before I close good friends, let me say once more how proud I am of all of you who have given so much to see this dream come true. Thank you

Sue Van Sloun, PRA Study Coordinator

INSTRUCTIONS

For PRA study participants:

1. You need to submit a request form to James A. Baker Inst. to obtain your test results for any of your dog, whose blood samples were sent to Dr. Aguirre for developing this test.

** Please understand that all of the submitted samples were not used to develop this test. In that case a letter will be sent by the J.A. Baker Institute notifying you that results are not available for those samples not used.

2. The form is available .pdf format.

3. Or to receive a form via mail, please contact:

Liz Corey
Keith Watamura, Baker Institute

(4) Lisiting Form:

Available in .pdf format. Or contact:
Liz Corey

Dear Toller Owners,

By now all of you have read or heard of the new DNA test for PRA in Tollers made available through Dr. Aguirre's research at the James A. Baker Institute. Now, we are embarking on a new way of doing things with entirely different thought processes in how we choose to breed our dogs. Our gene pool is small and we must always remember that it is the "whole" Toller that is of importance to the health and welfare of the breed, not the results of this one test. We will be spending a lot of time learning how to think in this new way over the next several months and how to use this new tool in our breeding decisions.

I'm so encouraged by all the 20/20 Clinics that are being planned and the support for the test so many of you are giving by having your dogs tested. A number of you have emailed me your individual results. We believe that the most effective way to serve the entire Toller community is to be able to share the results with anyone making an inquiry. We are in the process of developing a voluntary open registry, but while you are receiving your results and they are fresh in your mind we ask that you send us the results by following the procedures outlined on the [**EYE REGISTRY RELEASE & LISTING FORM**](#). We want a successful program, and we can only do that with your participation and support.

OptiGen will forward all US owned Pattern A dogs for listing in the US Toller registry. As soon as the reciprocal agreement between the US Toller Club and the Canadian Toller Club is registered with OptiGen these listings can be shared between countries.

For all of you who have reports of Pattern B and Pattern C dogs, please fill out the Release/Listing form so that in time there will be the most comprehensive collection of data possible with regard to prcd-DNA in our breed. Optigen will not send any B or C results to a club registry, so we have to use this secondary form. We strongly believe that for our database to be accurate and without question as to the validity of the information, we need your signature of authorization, a copy of the test results, and a copy of your dog's registration papers so that we can verify ownership. We will not report any Pattern B or C results without receiving this information. In addition, Pattern A results may be sent with the completed form and documentation if you want your results included in the database before the quarterly Pattern A report from Optigen is sent to Liz Corey.

Before closing, I want to take just a moment to thank every one of you for your generous financial support of this study over the past eight years. I'm so glad you never lost faith in the vision of the program. We have now moved into this new phase of the program and our vision continues. It goes without saying that the program will have greater success if support continues through shared information. Thank you for continuing your support.

You're the Greatest!
Sue Van Sloun, Chair
NSDTRC (USA) PRA Sub-Committee

The NSDTRC (USA) Health & Genetics Eye Registry accepts PRA-DNA results from anyone wishing to submit them. We do, however, recommend and encourage the owners of dogs registered outside the US to also submit results with the appropriate registry within their country of origin.

In Canada, contact:
Cheryl Tomayer
NSDTRC of Canada Hip/Eye/Heart Registrar

Other countries, contact your parent breed club for information.