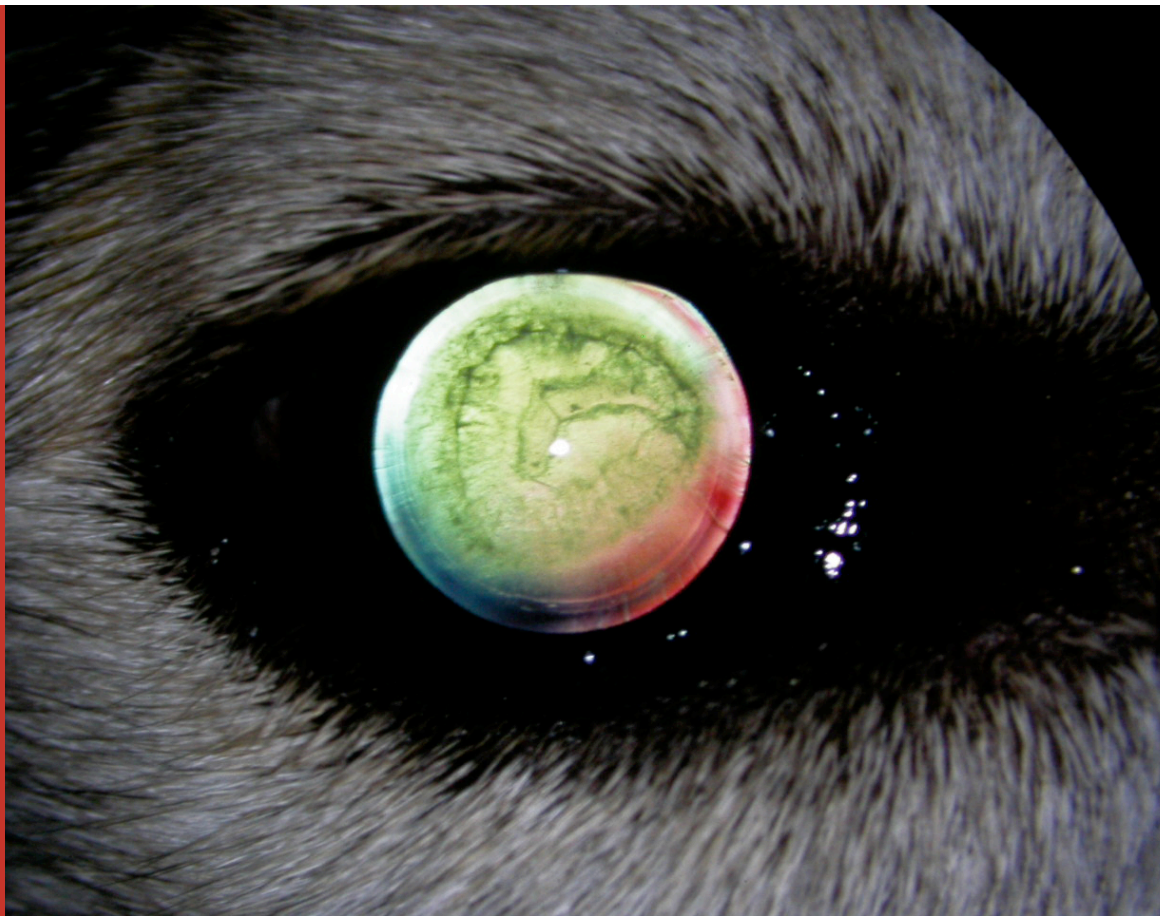


# HEALTH MATTERS

The “Eyes”  
Have It!

This month we learn about two inherited eye diseases in Alaskan malamutes: Juvenile Cataracts and Day Blindness.

Right: Large juvenile cataract in a two-year-old malamute. While small cataracts usually do not significantly impair vision, any dogs affected with juvenile cataracts should not be used for breeding. Photograph courtesy of Stuart Ellis.



## She Blinded Me With Science

English geneticist Dr Sally Ricketts brings us up to speed with Hereditary Cataract Research in the Alaskan malamute.

### ***Basics of hereditary cataract in the Alaskan malamute***

Juvenile cataract in the Alaskan malamute is considered to be inherited and typically presents as cataract in both eyes located in the back of the lens, in the posterior polar subcapsular region, much like the hereditary cataract (HC) seen in the Siberian husky and Utonagan. Puppies are born with normal eyes; the age of onset is usually between 9 months to 2 years, but can be older. The cataract may progress slowly outwards with a feathered appearance and with subsequent advancement

into the middle, or cortex, of the lens. HC in the Alaskan malamute can cause some visual impairment, and this can be associated with increased aggression if limitation of vision occurs. Hence it is important for dogs to undergo regular yearly eye examinations throughout life to enable early diagnosis and appropriate management.

### ***Investigation into the genetic causes of HC in the Alaskan malamute***

A collaborative research project is underway at the Kennel Club Genetics Centre in Dr Cathryn Mellersh's group

at the Animal Health Trust (AHT) in the UK and in Professor Hannes Lohi's group at the University of Helsinki and Folkhälsan Research Center in Finland. The researchers aim to identify mutations that contribute to the risk of developing HC in Northern, or Arctic, breeds including the Alaskan malamute and Siberian husky. The purpose of the work is to develop DNA-based tools that can be offered to breeders to help them reduce the risk of producing clinically affected dogs. This work has been funded to date by a grant of \$100,000 from the American

Kennel Club Canine Health Foundation, which expired at the end of 2010. Additional funding is being sought to continue the work.

The studies that are being conducted are called 'genome-wide association studies' or more simply, 'DNA scans', and involve comparing the DNA from a set of HC-affected dogs to the DNA of a set of unaffected dogs to search for regions of the genome involved in the disease. Affected dogs are defined as 'cases' and represent a set of carefully selected dogs that have clinically very similar cataracts. The unaffected dogs are known as 'controls' and are dogs with current clear eye examinations that are older than the typical age of onset for HC, which for the Alaskan malamute has been defined as over four years old, due to insufficient sample numbers of older clear dogs. This age cut-off maximises the number of samples that can be used, while limiting the potential misclassification of young dogs with clear eyes that have been denoted as controls, but that could go on to develop HC and should thus have been classified as cases. Both cases and controls can be a mixture of related and unrelated dogs. The number of dogs required for a DNA scan varies with each disease and breed, but for HC is suggested to be at least 25 cases and 25 controls, as preliminary work in several breeds has shown that HC is a complex condition and is likely to be caused by several different mutations. Sample collection is critical because studies of this type have a much greater chance of success when larger sample sets are used.



### Dog's Eye View?

Each step of the DNA research requires careful labeling and record-keeping.



### DNA samples and analysis

Samples for a DNA scan are collected in the form of cheek swabs, which owners can take themselves, from which DNA is isolated in the laboratory. Investigators can also accept blood samples preserved in EDTA if they are being drawn for a veterinary procedure. Samples are checked for quality and concentration before being sent to a specialised laboratory for genotyping at around 174,000 unique points in the DNA that are variable between individuals. Statistical analyses are then conducted to look for regions of the genome that are associated with HC, for example, a region of DNA that is similar in all cases and different in controls. Once an associated region has been identified, experiments are carried out to narrow down the region and identify the mutation contributing to the risk of developing HC.

### How can you help?

Both the AHT and University of Helsinki are currently collecting samples from Alaskan malamutes for the HC project. If you would like to contribute to the research, scientists are very keen to collect samples from dogs affected with cataract in both eyes, and from dogs with current clear eye examinations and over the age of six years. The AHT provides DNA collection swab kits, free of charge, to individual owners or clinicians—contact Bryan McLaughlin at [bryan.mclaughlin@aht.org.uk](mailto:bryan.mclaughlin@aht.org.uk). If

## Finding Truth in Your Eyes

Working with a cheek swab sent in by a malamute owner, isolation of DNA for the juvenile cataract study begins.

**WANTED: Malamute Cheek Swabs! Scientists need more samples for this research; contact them for a free do-it-yourself testing kit, if your dog(s) meet the guidelines in this article.**

you have submitted a sample to the study, it is really important to update scientists with any changes in health that might have occurred since sample submission, as this could have implications for the research. You might also be contacted by the AHT to ask about updated eye examinations, and responses to these queries are really helpful, as it probably means that your dog has already been selected to be part of the study! Also, occasionally a re-sample is requested from a dog that has been selected for the study, simply because the DNA yield is not quite sufficient for genotyping, so if you are able to, please provide one!

### Future prospects and what we hope to accomplish

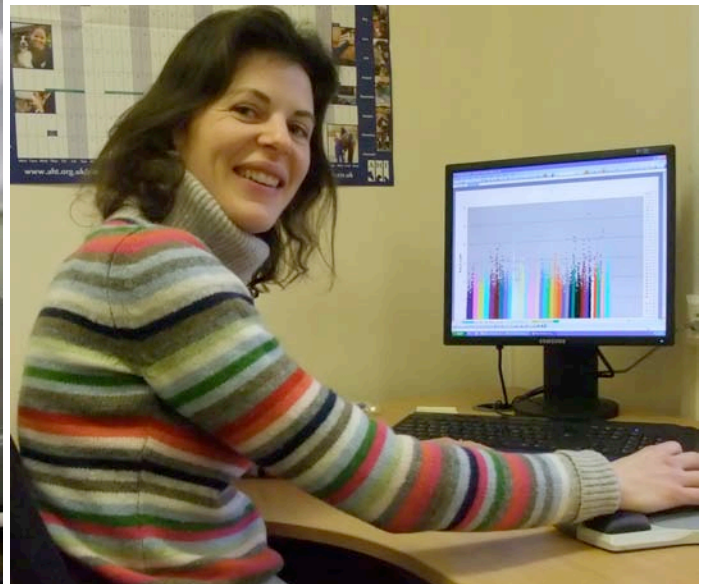
The research described above is active and ongoing and it is hopeful that in the long term at least one or more genetic mutations that contribute to development of HC in the Alaskan malamute will be identified, leading to the subsequent availability of DNA-based tools to help inform breeders of the risk of producing clinically affected dogs when considering two individuals for breeding. Significant advances in technology in the genetics and genomics field over the past five years have made research of this nature much more efficient; however, it is the availability of a large high quality set of samples with accompanying detailed clinical



## I Can See Clearly Now

Left: Dr Sally Ricketts prepares to concentrate DNA samples for the juvenile cataract study.

Below: Analyzing the results of a DNA scan, Sally searches for a region of DNA that is similar in all cases and different in controls.

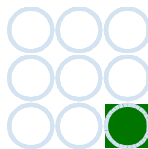


information that is vital to success. The author therefore thanks all Alaskan malamute owners who have submitted samples and information from their dogs, or who have made financial contributions to this project to date.

The author also thanks Dr Cathryn Mellersh and Stuart Ellis (BVSc CertVOphthal MRCVS), and Professor Hannes Lohi and Saija Ahonen, for their valuable research collaboration and contributions to this article.



HELSINGIN YLIOPISTO  
HELSINGFORS UNIVERSITET  
UNIVERSITY OF HELSINKI



## Meet Dr Sally Ricketts of the Kennel Club Genetics Centre, at the Animal Health Trust in the UK

Sally originally entered the field of Genetics when she joined the Animal Health Trust in 1998 working as a research technician within the Genetics Section, which she found both interesting and rewarding. She later completed a PhD at the AHT, in association with the

University of Manchester. Her doctorate studies focused on characterizing the major histocompatibility complex in the dog, an important genetic region involved in the function and regulation of the immune system.

Following completion of her PhD studies in 2005, Sally sought to broaden her experience in the field of genetics, and moved to the Department of Public Health and Primary Care at the University of Cambridge in the UK, taking a role within the field of human genetics.

Throughout this period she followed the exciting progress being made in the field of canine genetics, with the development of new technologies that have been so crucial to progress in understanding human disease.

Sally was therefore very pleased to return to the Genetics team at the AHT in late 2009 to work in Dr Cathryn Mellersh's group on several fascinating studies aiming to uncover the causes of inherited diseases in dogs. Sally chose this field of work in order to conduct research that directly impacts the health and welfare of the dog population, through the prevention of suffering and disease.

For more information, visit [www.aht.org.uk](http://www.aht.org.uk).

## Blinded by the Light

Does this song refer to Day Blindness, where affected dogs cannot see in bright light? AMCA Health Committee member Julie Edwards reviews the history of this genetic disorder, as well as breaking news in diagnosis and treatment.

### ***What is day blindness?***

Degeneration of the “cones” in the retina of the eye as a result of a mutation of gene CNGB3 causes Cone Degeneration Disease (CD) or hemeralopia, commonly known as day blindness. Cones are specialized photoreceptor cells that enable an animal to see in bright light.

### ***What are the signs and symptoms?***

Once retinal development is completed, usually around 7 weeks of age, signs will first appear. Affected pups become almost blind in daylight and afraid of light, because exposure to bright light appears irritating and possibly even painful. As a result they shy away from brightly-lit areas. Affected puppies may bump into objects that unaffected puppies easily avoid. Other signs and symptoms include reluctance to come out of shadows and dark dog houses during the daytime, and aggressiveness and fearfulness in unfamiliar settings. As the affected dog gets older, symptoms do not increase, and vision in the dark remains normal.

**The discovery that day blindness is an inherited disease is credited to malamute breeder Dr Kenneth Bourns, working in conjunction with Dr Lord and the Ontario Veterinary College in the 1960's. Recently a DNA test was developed, and gene therapy trials are also in progress.**

### ***How long has it affected the breed?***

Day blindness was discovered in the early to mid-1960s. Earlier anecdotal references to “night dogs” in the north exist, which are suspected cases of Cone Degeneration Disease.

Dr Kenneth Bourns of Boru Kennels first discovered CD in his kennel in 1960 when 3 out of 10 pups in a litter exhibited difficulty seeing during the daytime, but not at night. When he came forward, many people suggested he spay and neuter the sire and dam and the entire litter and move on. Fortunately for breeders today, he wanted answers. He and Dr Lord at the Ontario Veterinary College conducted test breedings, and identified the condition as an autosomal recessive disease, which means both parents must carry the gene to produce affected offspring (see chart).

### **The Future's So Bright....I Gotta Wear Shades**

Did you know.... sunglasses have been tried as a treatment for dogs with Day Blindness?

Uber-cool mals Tyler and Willow do not have day blindness; they are professional models! Photos courtesy of Stacey Moore and Beth Ortensi.



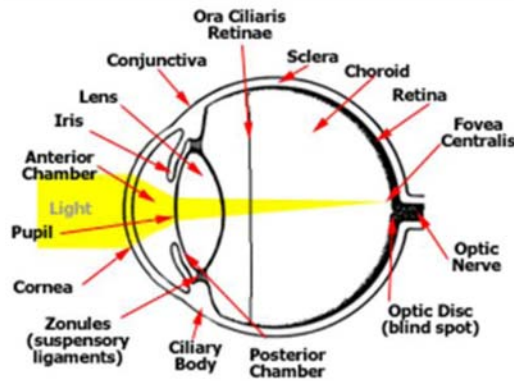
Sire	Dam	Offspring
dd	dd	100% dd
dd	Dd	50% dd, 50% Dd
dd	DD	100% Dd
Dd	dd	50% dd, 50% Dd
Dd	Dd	25% DD, 50% Dd, 25% dd
Dd	DD	50% DD, 50% Dd
DD	dd	100% Dd
DD	Dd	50% DD, 50% Dd
DD	DD	100% DD

dd= Dayblind

Dd= Carrier, normal vision

DD= Non-carrier, normal vision

Although relatively rare, cases of day blindness still appear from time to time, indicating the gene continues in the current population of Alaskan malamutes. Breeders should remain vigilant to prevent future cases and ensure the disorder does not become more common in the breed.



### The Canine Eye

Day Blindness is an inherited disorder of cone cells, which are located in the retina.

Image courtesy of <http://www.peteducation.com>

### Can I test my dog for Cone Degeneration?

A veterinary ophthalmologist can perform an electroretinogram (ERG) and look for the distinct characteristic cone, to confirm a suspected case of day blindness. The ERG procedure requires sedation to keep the dog still during the exam.

OptiGen Labs in New York now offers a DNA test for CD. Developed by Drs Acland and Aguirre, the development of this test is a major breakthrough for Alaskan Malamutes and German Shorthaired Pointers (another breed affected by the disorder). It can determine non-carrier, carrier, or affected DNA status of tested animals.

OptiGen offers the test for the regular price of \$160. They also hold discount periods once a year and a 25% discount for 20/20 clinics, if through a scheduled event and if 20 or more samples are submitted at one time.

Please contact OptiGen at [genetest@optigen.com](mailto:genetest@optigen.com) if you want to schedule an event to take advantage of this discount.

OptiGen also extends free DNA testing for any CD affected pedigreed dogs that have been diagnosed by a veterinary ophthalmologist.

### How should the DNA test be used?

Due to the relative rarity of the disorder, it is especially important to test dogs if they have any known or suspected relatives with day blindness. If an animal is found to be a carrier, it can be bred to a confirmed non-carrier, and the offspring tested. Breeding in this manner prevents affected puppies from being born, while helping to keep the genetic pool of the breed more diverse, by not excluding all carrier animals from breeding.

### Is treatment available?

In the beginning, some people actually tried sunglasses, with mixed results. But obviously, having any malamute wear sunglasses may not be a realistic solution! Tinted contact lenses have also been tried.

Currently, Dr Andras Komaromy at the University of Pennsylvania is conducting successful pre-clinical trials of gene therapy. The lab administers a correct copy of the CNGB3 gene directly into the retina of CD affected dogs and so far, treated dogs show signs of improvement. If the success of the trials continues, the treatment should soon be available to the public.

Another victory in the ongoing quest for the best possible health of the Alaskan malamute, the Cone Degeneration DNA test provides hope that DNA tests for other inherited diseases will also be developed. If your Alaskan malamute may be at risk of being a carrier for Cone Degeneration, please consider testing your dog.

### Sources and More Information

**OptiGen Website-** [http://www.optigen.com/opt9\\_test\\_cd.html](http://www.optigen.com/opt9_test_cd.html)

**Minnesota Malamute Club Website-** <http://www.minnesotamalamuteclub.com/brdprobs/dayblind.htm>

**Malamute Health Website-** [http://www.malamutehealth.org/articles/eye\\_dayblindness.htm](http://www.malamutehealth.org/articles/eye_dayblindness.htm)

### About the Author

AMCA Health Committee member Julie Edwards holds a Bachelors degree in Biology, is a nationally certified (AMT) Medical Technologist, and the Laboratory Director at the hospital where she works. She also writes for other national canine publications. She and her husband, Ric, are loved and owned by their malamutes at Ghost Dance ([www.ghostdance.biz](http://www.ghostdance.biz)). She would love to hear from you at [ghostdance@bigbend.net](mailto:ghostdance@bigbend.net).

