Progressive Retinal Atrophy in Miniature Long-Haired and Smooth Haired Dachshunds

Progressive retinal atrophy (PRA) is a term for retinal degenerations occuring in many breeds of dog. Many forms of PRA exist, each form being confined to one or a few breeds only. The disease results in a degeneration of the light-sensitive membrane at the back of the eye - the retina - resulting in loss of vision, and often leading to blindness.

The disease is caused by a change to a gene involved in sight. This change, or mutation, occurred spontaneously, but once in the population has been inherited from generation to generation like any other gene. The mutation upsets the delicate processes involved in vision and causes the long-term degeneration seen.

There is currently no treatment for the disease. Breeding stock are regularly checked by eye examination, although this can only pick up affected dogs after symptoms have developed and will never detect the symptomless carriers.

Research at the Animal Health Trust has identified a genetic change underlying pra in Miniature Long-haired Dachshunds. The mutation has been designated *cord1* and is a cone-rod degeneration affecting both these types of cells which are crucial to vision in the retina. This mutation has now also been identified in Miniature Smooth-haired Dachshunds and we are extending the DNA test to include this breed as well as Miniature Long-haired Dachshunds.

This form of PRA has been documented in scientific literature and was believed to have an age of onset of around 2 years. However, our research has shown that some dogs with the cord1 mutation are not diagnosed until much later in life, sometimes as late as 10 years of age, and the average age of diagnosis of the Miniature Long-haired Dachshunds in our study was 4.98 years. It is possible that the factors causing this variation could delay the onset of obvious clinical signs beyond the lifespan of the dog, so owners may never see behavioural changes and never recognise that their dog has a problem. However, the dog will still be genetically-affected by the disease and have two copies of the cord1 mutation. Genetically-affected dogs will always pass a copy of the cord1 mutation on to all their offspring, unlike carriers who pass the disease gene to only half their offspring. Undiagnosed genetically-affected dogs are therefore a particular danger for the breed and it is likely that the very high frequency of the cord1 mutation in Miniature Long-haired Dachshunds sent in for DNA testing has arisen because of the use of undiagnosed genetically-affected dogs in breeding programmes. These 'late onset' pups may develop PRA earlier in life than their parents. We are currently investigating the variation in age of onset, which could be genetic or environmental in origin. Until this research is completed, the factors determining the age at which breeders will begin to see signs of the disease will remain unknown.

Clearly, no blame can be attached to breeders who have unwittingly bred from undiagnosed genetically-affected dogs in the past. However, the DNA test now provides the means to avoid breeding further affected animals, and to eventually eradicate PRA caused by the cord1 mutation from miniature dachshunds.

The test is available now and information on submitting samples is given below.

Breeders will be sent results identifying their dog as belonging to one of three categories:

This dog is CLEAR of the cord1 mutation:

: This dog has 2 copies of the normal gene and will neither develop PRA caused by the cord1 mutation, nor pass this mutation to its offspring. This mutation has been shown to be sufficient to cause PRA in the lines originating from UK breeding stock used in our research. However, other factors may delay the effects of the cord1 mutation in some dogs.

This dog is a CARRIER of the cord1 mutation

: This dog has one copy of the normal gene and one copy of the cord1 mutation. It will not develop PRA but will, if bred from, pass on the cord1 mutation to 50% of its offspring, on average. This mutation has been shown to be sufficient to cause PRA in the lines originating from UK breeding stock used in our research. However, other factors may delay the effects of the cord1 mutation in some dogs.

This dog has TWO COPIES of the cord1 mutation

: This dog has 2 copies of the cord1 mutation. This mutation has been shown to be sufficient to cause PRA in the lines originating from UK breeding stock used in our research. There may however be additional genes in the population which can delay the effects of the cord1 mutation in some dogs

Because of the very high frequency of the cord1 mutation, we would advise breeders to take a gradual approach to eliminating the mutation from their stock to avoid restricting the gene pool available. Both carriers and affected dogs can be used to breed - but only when crossed with DNA tested clear dogs. For carrier x clear crosses, half the offspring (on average) will be clear and half will be carriers. Litters from these crosses should be DNA tested to distinguish clears from carriers. Genetically-affected x clear crosses will only produce carriers; there is therefore no need to DNA test these litters.

There may be other forms of PRA in the miniature dachshund population that are caused by a different mutation to cord1. The current DNA test is specific for the cord1 mutation and will not therefore detect dogs affected by alternative forms of PRA. During the course of our research we did see some evidence of another, late-onset form of the disease, in a restricted number of lines.

Many breeders of Miniature Smooth-haired Dachshunds have generously contributed samples to the research leading to our identification of the cord1 mutation in this breed and we would like to thank them for their co-operation. Without these samples we could not have validated the test for the Smooth-haired variety. For those samples which were used in the research, owners are offered a certificate for a cost of £5 administration fee. For those samples submitted for research but not used in the research programme, owners are offered one test at the discount price of £35. To check whether your sample was used as part of the research programme, please contact the address given below.

The research leading to the development of this test has been published as:

Mellersh,C.S., Boursnell,M.E.G., Pettitt,L., Ryder,E.J., Holmes,N.G., Grafham,D., Forman,O.P.

Sampson,J., Barnett,K.C., Blanton,S., Binns,M.M., Vaudin,M. (2006) Canine *RPGRIP1* mutation establishes cone-rod dystrophy in miniature longhaired dachshunds as a homologue of human Leber congenital amaurosis. *Genomics* **88** 293-301

Samples submitted should be cheek swabs (a non-invasive sampling method) obtainable from the Animal Health Trust. Samples should be sent together with a completed DNA Testing form and payment for each sample to Genetic Services, Animal Health Trust, Lanwades Park, Kentford, Newmarket, Suffolk CB8 7UU. Kits for taking cheek swabs are available by phoning 08700 509144 or via e-mail to swab.request@aht.org.uk. Further information can be obtained by e-mailing dna.testing@aht.org.uk.The price of the test is £50, which includes the cost of the sampling kit and £7.45 VAT.