

## Lupoid Dermatitis Linked Marker DNA Test – FAQ

Q1: What is a linked marker?

A: A marker is a DNA sequence that can differ between individuals of a species. It is referred to as “linked” when it is known to be on the same chromosome and close to some other DNA feature, such as another marker, or gene. In this case, the Lupoid Dermatitis (LD) linked marker DNA test assays a DNA sequence variation or “marker”, that is on the same chromosome and very close to the gene that is mutated to cause LD (let’s call it the LD gene). Geneticists refer to alternative forms of genes or markers as alleles. When the disease-causing allele/version of the LD gene, sometimes referred to as the “mutant” allele, is present, we see allele “2” at the LD marker. When a normal allele of the LD gene is present, we see allele “1” at the LD marker.

Q2: How does the LD linked marker DNA test work?

A: We assay the sequence variation at the LD linked marker. When a dog has the test result 1-1, both copies of the marker are allele 1, and there is a very high probability that the dog is normal/clear, meaning that both copies of the LD gene in that dog are normal alleles. When a dog is 1-2, that dog is likely to have one normal and one mutant allele, making it a probable carrier of the disease-causing allele (carriers show NO signs of LD). Dogs that have the test result 2-2 are very likely to be affected with LD.

Q3: Why isn’t the test 100% accurate?

A: Because the marker variation is NOT the actual LD gene mutation that causes the disease, it is possible, but unlikely, that the test results could, in a very few cases, be incorrect. There are two different reasons for this.

One source of error occurs when there was an exchange of DNA between the two copies of the chromosome that contains the LD gene in a carrier parent or other ancestor of the dog being tested. This exchange or swapping of DNA, referred to as recombination, changes the chromosomes so that allele 2 is located on a chromosome containing the normal allele, and allele 1 is on the chromosome containing the mutant allele.

The second source of error is what Optigen has termed a “false allele”. This refers to the situation when there are copies of the chromosome with allele 2 that do NOT have the LD-causing mutation in the PWD population.

Q4: Is there a false allele?

A: We have observed one false allele to date. In our research, we have examined 35 affected dogs and 40 parents of affected dogs (obligate carriers), and have observed a false allele in a dog of which we have no history or pedigree. In addition, this dog appeared to have a slightly different form of the disease, therefore it is possible that it was caused by a different gene. We also examined about 250 additional dogs. There were no 2-2 (predicted affected) dogs, and all of the 1-2 (predicted carrier) dogs had at least one grandparent that had been known to produce one or more LD pups (obligate carrier). This does not mean that there is no false allele, just that we haven’t seen one yet, so we do not expect it to be common.

Q5: How often have you observed recombination between the marker and the LD locus?

A: We have never observed recombination between the LD gene and the marker to date. Research done by other laboratories has detected an approximately 4% recombination rate between markers that are beyond the ends of the part of the chromosome that must contain the LD gene. From this data generated in other laboratories, we would expect a recombination frequency between 0 and 4%. That is, the test could be wrong up to 4% of the time, although we have NOT observed any recombination events to date in our research. We believe the recombination rate is close to 0% as the marker lies within the gene that we suspect causes the disease.

Q6: What can be done about the possible inaccuracies?

A: There are two things that can be done. We need you to report to us when you have evidence that the test was wrong. For example, we need to know if any 2-2 dogs (probable affected) live beyond six months of age. We also need to know if affected dogs are produced by matings between 1-1 dogs or from matings between a 1-1 and a 1-2 dog. Also, please let us know if, as a result of this test, you discover that in the past you have performed a mating between two 1-2 dogs. In this case, we would like to know how many puppies were produced, and if there were any deaths before age 6 months. The second thing is for us to do. We need to continue our research to examine this chromosome region to find the LD gene and mutation. Any proceeds from the LD linked marker test will go directly to support this research.

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