LEMP Genetic Test Result Interpretation
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We have designated the letter D to indicate the mutant form of the LEMP gene and N to indicate the normal form of the gene. A dog's particular combination of N or D forms of the gene is known as its genotype. The three possible genotypes are listed below.

LEMP-N/N: A **clear** dog has no copies of the LEMP gene mutation (this is also referred to as being homozygous normal). LEMP-N/N dogs do not develop leukoencephalomyelopathy caused by the known mutation. However, this result does not rule out the possibility that a dog shows clinical signs of other unrelated neurologic diseases (e.g. polyneuropathy, spinal disc disease, unknown form of LEMP). A LEMP-clear dog cannot produce LEMP-D/D offspring.

LEMP-D/N: A **carrier** dog has one copy of the LEMP gene mutation (this is also referred to as being heterozygous). LEMP-D/N dogs do not develop and are not at risk for leukoencephalomyelopathy caused by the known mutation. However, this result does not rule out the possibility that a dog shows clinical signs of other unrelated neurologic diseases (e.g. polyneuropathy, spinal disc disease, unknown form of leukoencephalomyelopathy). LEMP carriers will, on average, pass the LEMP gene mutation on to half of their offspring.

LEMP-D/D: An **affected** dog has two copies of the LEMP gene mutation (this is also referred to as being homozygous affected). Affected dogs develop the neurological disease on average at 3.4 years of age. Clinical signs are characterized by slowly worsening gait abnormalities, especially spontaneous knuckling, dragging of the paws and hypermetria of the front limbs. LEMP-affected dogs will pass one copy of this mutation on to all of their offspring.

Further Information on LEMP

The LEMP gene test is a so-called direct genetic test. This means that the causal specific DNA segment change in the *NAPEPLD* gene is detected directly. This situation is different from other types of genetic tests that describe only the identification of a DNA marker that could be far away from the true disease gene, and not be as highly reliable as a direct genetic test.

The LEMP mutation is inherited in a partially penetrant autosomal recessive manner meaning that two copies of the mutation are required to show signs of disease. Partially penetrant means that among genetically affected dogs (LEMP-D/D) not all will show obvious clinical signs in their lifetime. We are not able to predict which LEMP-D/D dogs will show signs of LEMP. Those that show signs at a young age often have a rapidly deteriorating disease course resulting in euthanasia by 2 years of age. To produce a puppy with severe, juvenile-onset form of leukoencephalomyelopathy caused by the mutant LEMP gene, it would require that both parents are either LEMP-D/N carriers or LEMP-D/D affected.

Data from our research population indicates that the LEMP-D/D dogs have a life expectancy of at least 3 years less than the average Leonberger. Affected dogs show corresponding gross lesions in the cervical spinal cord white matter that may extend to the thoracic spinal cord, as well as to the brain, while peripheral nerve and muscle biopsies are unremarkable. Spinal reflexes of affected dogs are mostly normal. In the progressive clinical course of the disease, affected dogs may become increasingly immobile within a few months. Like many diseases of the central nervous system, there is no effective treatment for leukoencephalomyelopathy. Since in most cases the dog is not in pain, but is strongly restricted in its quality of life, owners are encouraged to ask a veterinarian for advice.

Breeding Recommendations

LEMP is a recessively inherited form of leukoencephalomyelopathy. **In general, LEMP-D/D dogs should not be used for breeding.** We do not recommend exclusion of LEMP carrier (D/N) dogs from the breeding population. We do recommend avoiding matings that have the potential to produce LEMP-affected (D/D) offspring. In our global biobank of more than 9,000 Leonbergers, ~15% were LEMP-D/N carriers. Immediately eliminating all LEMP-D/N dogs from breeding may have negative consequences for the genetic diversity of the breed. **If a LEMP-D/N puppy is preferred for the breeding program, it should be kept for future breeding and paired with LEMP-N/N dog.**

Within the Leonberger breed LPN1, LPN2, LPPN3, and LEMP genotypes must all be considered when selecting breeding pairs. No affected dogs (LPN1-D/D, LPN2-D/N & LPN2-D/D, LPPN3-D/D, LEMP-D/D) should be bred. Within each mating pair, at least one parent should be LEMP clear (N/N), LPN1 clear (N/N), LPPN3 clear (N/N), and both parents should be LPN2 clear (N/N).

One final word of caution

We were able to identify a causative genetic mutation for one form of LEMP in Leonbergers. While all LEMP-affected Leonbergers to date have tested LEMP-D/D, it is important to remember that this LEMP test is diagnostic for only one form of leukoencephalomyelopathy. Thus, it is still possible that affected offspring with a different genetic form of leukoencephalomyelopathy could occur, even from a mating of two dogs that both have been tested LEMP-N/N. Nonetheless, this LEMP test can reliably detect this severe form of leukoencephalomyelopathy and significantly reduce the incidence of this neurodegenerative disorder in the Leonberger breed. **Finally, we strongly recommend both dogs in a breeding pair to be free of any signs of neurological disease, regardless of genotype.**

Below are the chances any given puppy in a litter from the indicated mating will have the LEMP genotype of N/N, D/N, or D/D. **Matings that produce, or are comprised of a LEMP-affected dog are shown in red and not recommended!**

LEMP genotypes of parents	Average probability **LEMP-N/N** puppies	Average probability **LEMP-D/N** puppies	Average probability **LEMP-D/D** puppies
N/N × N/N	100%	0%	0%
N/N × D/N	50%	50%	0%
N/N × D/D	0%	100%	0%
D/N × D/N	25%	50%	25%
D/N × D/D	0%	50%	50%
D/D × D/D	0%	0%	100%