



UNIVERSITY OF MINNESOTA

VETERINARY DIAGNOSTIC LAB



^b
UNIVERSITÄT
BERN

June 2010

Genetic Testing for Inherited Polyneuropathy in Leonbergers

Leonbergers may suffer from a hereditary neurological disease, which has frequently been termed “inherited polyneuropathy (IPN)” or “Leonberger polyneuropathy (LPN)” by veterinarians and breeders. Affected dogs suffer from slowly worsening exercise intolerance and may develop gait abnormalities, such as an exaggerated hitched step, especially in the hind limbs. There is often wasting of the hind limb muscles as well. Additionally, these dogs may have noisy breathing, a change in their bark, or even difficulty breathing due to involvement of the larynx and laryngeal folds in the throat. Eventually the disease may progress to the point where the dog can no longer support its own weight.

Genetic research carried out at the University of Minnesota, the University of Bern, and the University of California-San Diego, indicates that polyneuropathy is likely a group of several genetically distinct, but clinically similar diseases. We have mapped two major genetic risk loci and identified the causative mutation in one of these loci that we now term LPN1. Dogs being homozygous mutant (two copies of the mutation) for this mutation will typically develop neuropathy before they reach 3 years of age. At this time we do not know whether heterozygous carriers of this mutation (one copy of the mutation) might also develop mild clinical signs late in life, but they will most likely not develop severe disease. The identified mutation is responsible for approximately one third of the cases of polyneuropathy in Leonbergers. The other two thirds of cases are apparently caused by different genetic mutations.

The University of Minnesota and the University of Bern will offer genetic testing for the identified LPN1 mutation starting July 1st, 2010. At this time we recommend that all breeding dogs should be tested. We also recommend avoiding breeding homozygous mutant dogs as well as matings that could produce homozygous mutant dogs. We do not recommend excluding heterozygous mutant dogs from breeding as this would significantly constrict the gene pool of the Leonberger population and might lead to an increase in the other forms of disease. However, heterozygous carriers of the LPN1 mutation should only be mated to tested dogs which are free of the mutation. This will ensure that no homozygous mutant offspring affected with the severe form of the disease will be born.

At this time the implementation of genetic testing cannot completely eliminate polyneuropathy from the Leonberger population. This LPN1 test diagnoses only one of possibly several genetic risk factors. Thus, it is still possible that affected offspring with a different genetic form of polyneuropathy will result even from a mating of two dogs that both have been tested free for this mutation. However, the current LPN1 test can reliably eliminate one severe early-onset form of disease and significantly reduce the overall frequency of polyneuropathy in Leonbergers.

Dog owners who submitted blood samples for the research projects in either Minnesota or Bern before 15-June-2010 will receive the results of this LPN1 genetic test at no cost within the next weeks. We are continuing to search for the other genetic risk factors and blood samples from additional dogs affected by apparent neurological disease will enhance this research. Dog owners who submit a blood sample from an affected dog, together with neurological exam or biopsy results, may receive the LPN1 test for free.

In **North America**, muscle and peripheral nerve biopsy specimens should be submitted to:
Comparative Neuromuscular Laboratory Phone: (858) 534-1537
University of California, San Diego Website <http://vetneuromuscular.ucsd.edu>
Basic Science Building Room 2095 Questions email musclelab@ucsd.edu
9500 Gilman Drive
La Jolla, CA 92093-0705

In **Europe**, muscle and peripheral nerve biopsy specimens should be submitted to:
Institut für Neuropathologie Phone: +49 (0)211-8118658
Neuroimmunologisches Labor Mobile: +49 (0)173-5449500
Prof. Dr. Thomas Bilzer Fax: +49(0)211-8117804
Geb. 14.79, Ebene III E-Mail: bilzer@uni-duesseldorf.de
Moorenstraße 5 <http://www.leonbergerunion.com/health/healthd.htm>
D-40225 Düsseldorf

Instructions for ordering the LPN1 test:

North America. Genetic testing will be performed at the University of Minnesota Veterinary Diagnostic Laboratory. The preferred sample is 2 – 3 ml of fresh blood collected in EDTA tubes.

Further information on sample submission, as well as the required submission forms is available at:
<http://www.cvm.umn.edu/vdl/ourservices/canineneuromuscular/home.html>

The samples, packaged in a padded, leak-proof container, accompanied by a submission form for each dog, should be sent by regular mail without coolant to the Veterinary Diagnostic Laboratory:

Veterinary Diagnostic Laboratory Phone: (612) 625-8787 or (800) 624-8787
College of Veterinary Medicine Website: www.vdl.umn.edu
University of Minnesota LPN-specific questions email: lpninfo@umn.edu
1333 Gortner Avenue
St Paul, MN 55108-1098

The price per test is \$85 and the expected turnaround time is 3 – 4 weeks.

Europe. For genetic testing a 2-5 ml EDTA blood sample of the animal in question is required. The use of plastic tubes is recommended. Blood samples should be sent in a padded envelope by regular mail without coolant to our laboratory. They have to arrive within 3-4 days of sample taking. Order forms can be downloaded from:

http://www.vetsuisse.unibe.ch/genetic/content/service/dog/index_eng.html

Please send the samples together with a signed order form to:

Institut für Genetik
Stichwort „Leonberger“
Bremgartenstrasse 109A
CH-3001 Bern

The direct genetic test costs 110.-- CHF or 75.-- EUR plus VAT. Initially, we will run the test once a month. As we cannot run the complete procedure for single individual samples it may take 1-2 months until the result is communicated to the owners.