UNIVERSITÄT BERN

Institut für Genetik, Bremgartenstr. 109a, CH-3012 Bern

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Improved testing panel for genetic basis of laryngeal paralysis & polyneuropathy

Over the past 10 years, Leonberger owners and breeders have enthusiastically adopted genetic tests to aid in understanding their dog's condition and designing matings to reduce the incidence of disease. In fact, no Leonbergers with two copies of the LPN1 mutation have been recorded in our biobank with a birthdate later than 2011! At the same time, these tests are being used to similar effect in other breeds where the same or closely related mutations have been found. In this regard, Leonberger owners and organizations have much to be proud of in blazing the trail for genetic improvement of their and other breeds, particularly Saint Bernard. We are extremely honored to be working with you in these endeavors.

Leonbergers, like many other breeds, can suffer from neurological diseases, especially forms of polyneuropathy that often lead to a diagnosis of laryngeal paralysis. Laryngeal paralysis may be the first presenting clinical sign of polyneuropathy, and can appear without gait abnormalities. Two hereditary forms of polyneuropathy/laryngeal paralysis, termed Leonberger polyneuropathy type 1 (LPN1) and type 2 (LPN2), were genetically characterized in 2010 and 2014 by the Universities of Bern and Minnesota, and genetic tests developed. In addition, in 2017 these universities combined to develop and offer a genetic test for another neurological disorder, termed leukoencephalomyelopathy (LEMP), which although not a polyneuropathy, also causes a severe nervous system disease.

The LPN1 and LPN2 forms of polyneuropathy/laryngeal paralysis do not explain all of the apparent cases in Leonbergers, which begs the question of whether other genetic explanations exist.

In this light, we are very pleased to announce **the discovery of a third genetic contributor to polyneuropathy and laryngeal paralysis in Leonbergers**. For convenience and clarity, this form is designated as **LPPN3**. Interestingly, **this newly detected mutation also occurs in affected Saint Bernards, Labrador retrievers, and several other breeds.**

The average age of onset of the clinical signs in dogs with the LPPN3 variant is 3.4 years in Leonbergers, 2.1 years in Saint Bernards, and 7.5 years in Labrador retrievers. In comparison, the LPN1-associated polyneuropathy appears in Leonbergers and Saint Bernards having two copies of the variant (i.e., D/D) with average ages of 2.2 and 1.6 years, respectively. Leonbergers with the LPN2 mutation have an average age of onset of 6.2 years.

The LPN1, LPN2 and LPPN3 mutations combined now account for almost half of all historical Leonberger cases of polyneuropathy/laryngeal paralysis in our biobank. Further, since the discovery of the LPPN3 mutation, we are able to report that 11.5% of a global group of more than 2,700 Leonbergers were LPPN3 mutation carriers. This expanded test panel will enable the community to make even greater strides in controlling the propagation of these devastating disorders and maintaining the health of the population.

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We would like to remind you that the different genetic forms of polyneuropathy have different modes of inheritance. For LPN1, early onset is seen in dogs with two copies of the LPN1 mutation (i.e., D/D), but later onset often, but not always, can be seen with a single copy of the LPN1 mutation (i.e., D/N); for LPN2, onset of disease requires just a single copy of the LPN2 mutation (i.e., D/N); and now, onset of disease due to LPPN3 requires two copies of the LPPN3 mutation (i.e., D/D). **The inheritance of LPPN3 is similar to the LEMP mutation and therefore heterozygous carriers (i.e., D/N) of LPPN3 can be accepted for breeding.**

The Universities of Minnesota and Bern will start offering genetic testing for the newly identified recessively inherited LPPN3 mutation, to accompany our LPN1, LPN2, and LEMP testing, starting Nov 2, 2020. More details are available from our respective websites along with the interpretations of the possible test results.

For the University of Bern:
https://www.genetics.unibe.ch/services/dog/gene_tests_in_the_leonberger/index_eng.html

For the University of Minnesota:
https://z.umn.edu/leonberger

Please note: The Universities of Minnesota and Bern will provide free results to owners of affected dogs that have supplied a neurological exam or laryngoscopy report.

Instructions for ordering the LPPN3 test in Europe

For genetic testing, a 1-5 ml EDTA blood sample of the animal in question is required. Blood samples should be sent in a padded envelope by regular mail without cooling to our laboratory. Order forms can be downloaded on our website.

All four tests for the same dog cost 200 CHF/EUR. A single test (of choice) costs 100 CHF/EUR, two tests (of choice) for the same dog cost 150 CHF/EUR and three tests (of choice) for the same dog cost 175 CHF/EUR. The expected turnaround time is 2-6 weeks.

There is no need for a new blood sample if a sample has already been submitted to the Institute of Genetics of the University of Bern for LPN or LEMP testing, as the LPPN3 test can be performed on this same sample for **55 CHF/EUR** after pre-payment onto the account of the Institute of Genetics (University of Bern):

IBAN: **CH5309000000603151885**, BIC: **POFICHBE** (Postfinance, CH-3030 Bern).

Please mention the lab ID (LB no.) and send an e-mail to cord.droegemueller@vetsuisse.unibe.ch

After the receipt of your payment, we will submit the LPPN3 results by e-mail. The expected turnaround time is 2-6 weeks.

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