Leonberger Polyneuropathy (LPN): Research Update, September 2011

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Together with our collaborators from the University of Minnesota we continue to search for the genetic mutations underlying hereditary polyneuropathy in Leonbergers (LPN). Last year we identified the LPN1 mutation and subsequently have been offering genetic testing as a service. We have genotyped more than 1800 Leonbergers in Berne for LPN1. We found about 15% LPN1 carriers (D/N) among the submitted samples (see appendix).

According to our data, every dog that is tested “affected” (D/D) in the LPN1 test will develop an early-onset and severe form of LPN. Clinical symptoms will typically become apparent before the dogs reach three years of age, occasionally symptoms may develop later until four years of age. Therefore, matings that could produce D/D puppies should be strictly avoided. There might be a certain risk for LPN1 carriers (D/N) to develop mild symptoms of LPN late in life. However, we don’t have enough data to quantify this risk. Thus, we don’t recommend the categorical exclusion of all D/N dogs from breeding. However, we advise a thorough evaluation of all other characteristics before D/N dogs are used in breeding. D/N dogs should be mated only to tested N/N dogs.

During our research we identified and determined the chromosomal position of a second locus termed „LPN2“ for LPN. At this time we know that there is an LPN2 mutation in a specific region of the genome that harbors about five genes. We do not yet know the causative mutation itself, nor do we know the specific gene(s), which are affected by the LPN2 mutation. Some mutations that lead to hereditary diseases are quite obvious and relatively easy to find. Other mutations are less obvious and consequently much harder to find. We found the LPN1 mutation only weeks after the initial mapping of the LPN1 locus. Unfortunately, LPN2 proves to be more difficult and we have already spent several months in its search.

We think that there is at least one additional locus for LPN (which will become “LPN3”). For the further analysis of LPN2 and LPN3, we recently genotyped 48 LPN-affected dogs that were free of the LPN1 mutation on the 170,000 marker SNP chip. Together with our previous data this will hopefully allow a more precise mapping of LPN2 and an initial mapping of LPN3.

It is essential for our research that we continue to get blood samples and information on the health status of the dogs. Please notify us, if the health status of your dog changes, especially, if we have already a blood sample (e.g. dogs that were submitted for LPN1 testing). If a dog that is not D/D at the LPN1 mutation starts to show clinical symptoms of LPN, please have this dog thoroughly examined. A histopathological examination of a muscle/nerve samples can be done on a biopsy or post mortem and is still considered to be very important for a definitive diagnosis.

We would like to thank all dog owners and breeders as well as our scientific collaborators for their continuing support.

Institut für Genetik

LPN1

UNIVERSITÄT BERN

Land	N/N	D/N	D/D	Total
D	455	82	4	541
CH	256	51	3	310
NL	146	35	7	188
F	118	27	2	147
SF	123	8		131
S	96	5		101
CZ	73	10		83
B	64	9		73
NO	45	6		51
I	42	5		47
DK	33	6		39
UK	26	5	1	32
PL	26	1		27
AT	12	9		21
LV	15	6		21
HU	19	1		20
IR	6	3		9
RUS	7	1		8
BRA	3	3		6
SK	6			6
E	4	1		5
USA	2	1	1	4
EST	2		1	3
UKR		1		1
Total	1579	276	19	1874

31.08.2011