LABOKLIN

LABOR FÜR KLINISCHE DIAGNOSTIK GMBH & CO. KG

NEWSLETTER 2/2010

JUST **NEW** AT LABOKLIN:

Genetic test for polyneuropathy in Greyhounds

Most recently Laboklin acquired permission to perform a genetic test to identify the mutation causing polyneuropathy in Greyhounds. Research on the underlying genetic cause of this disease was done by Prof. C. Drögemüller and colleagues at Vet-Suisse Uni Bern.

Haemophilia B in Rhodesian Ridgeback Dogs-Causative Mutation identified

Haemophilia B is one of the most important inherited disorders of haemostasis in Rhodesian Ridgeback Dogs. The underlying pathomechanism of haemophilia B is a lack or decreased activity of factor IX that plays a critical role in the coagulation cascade. Affected dogs present hemorrhage that can vary from mild to severe depending on the degree of the disease. The clinical signs include haematomas of large sizes, bleeding of the nose, skin, muscles and joints. If the disease is severe and no precautions are taken, affected dogs can bleed to death after surgery or injuries.

Haemophilia B is a sex-linked disorder (x-chromosomal recessive). As a consequence male dogs are affected much more frequently compared to female dogs because they only possess one x-chromosome. If this one chromosome carries the mutation, the dog develops haemophilia B. Heterozygous conductor female dogs occur with a frequency of about 5% within the population of Rhodesian Ridgeback Dogs. These conductor bitches carry the mutation on one of their two x-chromosomes but do not develop the disease. Conductor bitches pass on the mutation to their offspring and about 50% of the male offspring will get the mutation and develop the disease. Female dogs will develop Haemophilia B if they have 2 x-chromosomes that carry the mutation.
Recently, Laboklin and its collaborators Prof. Dr. Mischke from the Veterinary School in Hannover and Prof. Dr. Thomas Dandekar from the University Würzburg were able to identify the mutation responsible for factor IX deficiency. Laboklin submitted the patent for this test and has now the exclusive permission to perform the genetic test for detection of haemophilia B in Rhodesian Ridgeback Dogs. The genetic test allows for the early detection of affected animals and provides important information to dog breeders enabling them to make responsible decisions in order to avoid the occurance of the disease and ultimately decrease the frequency of the mutation within the population of Rhodesian Ridgeback Dogs.

Primary Lens Luxation (PLL) – Genetic test now available in Germany

For more than 75 years, Primary Lens Luxation (PLL), is known to be an inherited disease of the eyes in dogs of several different breeds. Damage to the zonulae fibres lead to a displacement or luxation of the lense in the eyes. As a consequence, painful glaucoma or even blindness can occur. The damage of the zonula fibres can be aquired (trauma) or inherited. The inherited form leads to clinical signs at the early age of 20 months. Changes in the structure of the zonulae fibres occur and luxation of the lense typically takes place at the age of 3 - 8 years. At that time most of the affected dogs will have reproduced.

Recently, Cathryn Mellersh and colleagues (Farias et al., 2010) identified a mutation in the gene ADAMTS17 that is responsible for the development of inherited PLL. Based on their investigations, LABOKLIN developed a genetic test to identify the mutation.

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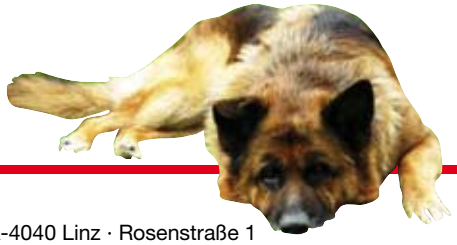

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▶▶▶▶▶▶▶ The mode of inheritance of PLL is autosomal recessive. This means that PLL-affected dogs receive one mutated gene (allel) from the mother as well as from the father. Hence, the parents need to carry at least one mutated allel.

In most cases heterozygous carriers are healthy. However, it is estimated that about 2 - 10 % of the carriers will develop PLL and hence a small risk for carrier animals remains. The mutation responsible for the inherited form of PLL has been detected in the following breeds: Miniature bull Terrier, Tibetan Terrier, Parson and Jack Russell Terrier, German hunt Terrier, Chinese Crested, Lancashire Heelers, Patterdale Terrier, Rat Terrier, Sealyham Terrier, Toy Fox Terrier, Volpino Italiano, and Welsh Terrier. It is possible that the mutation does also occur in other breeds.

Use and uselessness of genetic tests in animals of breeds in which the test has not been validated

We often encounter questions such as: “Do you perform the genetic test for cystinuria developed for Newfoundland Dogs also in Doberman Dogs?“

Any genetic test can be perfomed in any breed because a genetic sequence is analysed that occurs in all animals. However, the specific mutation responsible for the disease in a certain breed does not necessarily occur in animals of a different breed. It is also possible that different mutations are causing the same disease. Von Willebrand disease for example can be the result of 5 different mutations. The appearance of these mutations is breed specific. One of the 5 mutations occurs in several breeds, whereas the other 4 only affect one breed. The breed specificity of the mutations is the result of breeding selection. A mutation can occur spontaneously in one individual animal. This animal will pass on the mutation to its offspring. Since most of the time mating occurs within the same breed, the mutation also will remain and be further distributed among animals of this breed. Mutations that occur in different breeds most likely developed very early during the evolution of the dog before breeding standards were developed and mating restricted to dogs of the same breed. Besides the 5 known mutations, it is very likely that there are more mutations within the same gene leading to von Willebrand disease. In order to verify this statistically it is necessary to examine healthy and affected animals in large numbers.

Does it make sense to run the genetic test for cystinuria that is validated for Newfoundland Dogs in a Doberman dog?
If the test result is positive, it is very likely that the dog carries the mutation and will develop von Willebrand disease and also pass on the mutation to its offspring. Strictly speaking, in order to find out whether the mutation is inherited or not, related animals with a known medical history would need to be tested. If the mutation can not be detected in Doberman Dogs it does not mean that in this breed inherited cystinuria does not occur. It is very possible that a different mutation is causing the same disease in different dog breeds.

In conclusion: Genetic tests that have not been developed for certain dog breeds should not be performed. There are two risks to it: Firstly, a negative result (it will most likely be negative) does not exclude the disease. Secondly, a positive test result without clinical signs of the disease, like in conductor dogs, and without scientific background does not provide sufficient evidence for the disease. Tests like this should be reserved for research purposes only to investigate the occurence of identical mutations in different dog breeds. They must be followed by investigations involving a large number of animals to validate the results. The tests only cost money and the results are unreliable.

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