

## **Info from the laboratory for veterinary diagnostics FERAGEN about: DLA genes and genetic diversity - what the practice looks like**

"An apple a day keeps the doctor away!" Even though this saying may apply to many areas of our daily life, it is not that easy, at least in dog breeding. Today's breeder needs at least a basic knowledge of what in addition to intuition and experience concerns about the diseases of his breed and how he can best avoid them in the offspring. Depending on the breed we are talking about, more extensive knowledge may be necessary. Many diseases in our dog breeds today are genetic in nature and for many of these diseases also genetic testing exist. But by no means not for all. All those hereditary problems that can be genetically examined are the least evil because they are easy to test. We know that these genetic tests are usually not very well received by breeders, even if they really should be taken seriously. Why? Because these problems are calculable. If I know the genetic status of the breeding bitch or the male, I can decide exactly whether the two dogs can be mated without causing health problems in the offspring. Things are different with complex diseases. As the name suggests, there are usually several factors here than just a single gene that can lead to diseases. In addition to genetic predisposition, these factors also include environmental influences, environmental toxins, stress, etc. Not every dog that has a genetic predisposition for a disease must actually develop it. And that makes things complicated and unpredictable. Today we know many diseases that are caused by multiple factors. We also include autoimmune diseases, which have been experiencing a trend in recent years. Keywords are hypothyroidism, hemolytic anemia, Addison's disease, diabetes mellitus, polyarthritis, symmetrical lupoid onychodystrophy, or SLO for short. Hardly any breed is not affected by autoimmune diseases and all exceptions can count themselves lucky. Triggers can be harmless infections in themselves or vaccinations. An overreaction of cells of the immune system results that not only viruses or bacteria are fought, but also the destruction of the body's own cells and subsequently autoimmune diseases. This means that an autoimmune disease is nothing more than a fatal immune system defect that, in this case, cannot make a correct distinction between your own body or foreign invaders. Certain genes of the immune system have an important role in immune defense, but also in the development of autoimmune diseases, we call them DLA genes (Dog Leukocyte Antigen). They consist of 3 genes called DLA DRBI, DLA DQAI and DLA DQBI. You can remember the names, but you don't have to. They are also passed on from one generation to the following generation in these three-part packages, the so-called haplotypes. There are numerous different variants of these genes, which experts call alleles. The greatest possible genetic diversity of gene variants is essential for our dogs, because only in this way can our four-legged friends react quickly to a wide variety of infections or changing environmental conditions. Currently, well over 170 gene variants have been found in countless dog breeds, but only very few of these combinations actually still exist in most breeds. On average there are 5 to 7 different haplotypes per breed, mostly one with a high frequency, two with about 20% and one or two with low frequency occur in the dogs of a breed. As already mentioned, these genes are not only important for a functioning immune system but are also related to autoimmune diseases. There are numerous scientific studies that have shown that the presence of certain combinations of these three genes can lead to an increased risk of certain diseases. It is therefore particularly important within a breed to find out how many of these gene variants are still present in order to get an idea of genetic diversity. If there are also problems with certain autoimmune diseases that occur frequently, you can try to find a possible connection between the DLA genes and these diseases. That means, conveniently, two birds can be killed here with one stone.

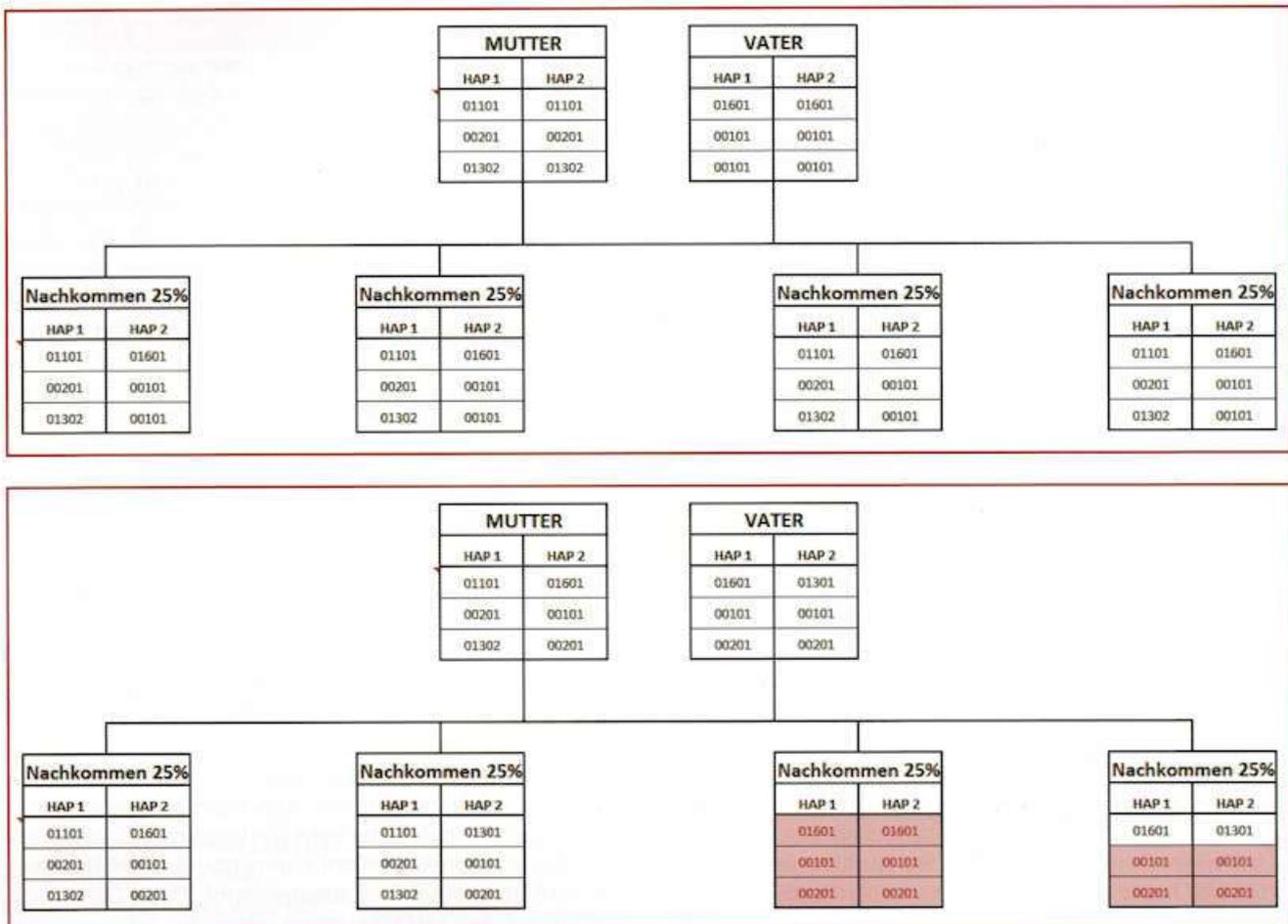
We have been performing DLA typing for the Austrian Leonberger Club since 2016. So far, almost 100 Leonbergers have been examined, not only from Austria, but also from various European countries as well from the USA. These geographically different dogs are of particular interest because we know from experience that other haplotypes can occur there. So far 9 different of these 3 gene combinations have been found in the Leonbergers in the course of our profiling, whereby there are gene combinations that are more similar than others. There are currently 3 haplotypes with a frequency of 20% to 25%. We are talking here of dominant haplotypes because many dogs of one breed have them. But within the tested population there are also quite rare representatives that are certainly worth keeping in the population in the long run. In addition, it can be determined in individual dogs whether they have inherited the same gene variants from the mother or the father or whether they have different ones. In the first case we speak of homozygotes and

in the second we speak of heterozygotes. In order to make the whole thing a bit more demanding, haplotypes of the parent animals can sometimes be the same. This means that of these 3 DLA genes, 1 or 2 genes can have the same variants. In this case we are talking about partially homozygous dogs. A great advantage of this system is the following: If you know the haplotypes of the parents, you can predict which combinations in the offspring are to be expected.

If a certain gene combination is now also linked to a possible risk of disease, as is actually the case with some breeds, skillful mating can ensure that both parents do not pass on these genetic dispositions to the offspring.

A comparison of the parental haplotypes is shown in the following figures. Always 3 consecutive numerical values result in a gene combination. Don't let numbers confuse you. What is really relevant is that the numerical values in the left column differ from those in the right column of each parent. All those combinations that are white in the offspring are optimal, since these offspring have received different combinations from the parents. You can also see this from the different numerical values. All those areas that are shown in red are overlapping, because bitch and male had the same two gene variants.

What few people consider is that even from animals that are homozygous, i.e. have the same numbers on the left and right in the column, heterozygous offspring with different numerical values can arise. This can be seen in Figure 1. Both parents are homozygous (same numerical values), but all offspring are heterozygous (different offspring).



The Austrian Leonberger Club already has a handsome and constantly growing collection of genotypes that make a significant contribution to breeding monitoring. In order to make this breeding monitoring even more precise and extensive, the genetic diversity of the DLA genes was extended to the entire DNA of the dog. How it works? Relatively easy by determining over 230,000 genetic markers from each dog. Thanks to this large number of measuring points, a wide variety of evaluations can be carried out, for example how different or similar two dogs of a breed are. This information can provide important information especially for upcoming matings, since virtual matings based on the DNA can be used to calculate which male compared to a bitch shows the greatest genetic variance. The same data can also be used to determine how

high the inbreeding coefficient is in the offspring from two dogs. This means that breeding pairs can be chosen so that the maximum genetic diversity in the puppies is achieved and the inbreeding level can be reduced from generation to generation. The current procedure for calculating inbreeding coefficients, as currently used in breeding, is based on written pedigree data and is therefore limited to the number of generations that are fully available and assumes that the pedigree information is correct. Genetic data can also be used to calculate inbreeding coefficients, so-called genomic IKS. This is possible up to 50 generations retrospectively and no written pedigrees are necessary. The diversity test with all of its evaluations is also interesting if a breeder is planning, for example, a mating with a foreign male or has frozen semen sent from abroad. Both involve effort and cost.

The basic idea is usually to bring new genetic material into the breeding. If one bears in mind such efforts, the genetic material of these foreign males should actually differ and be an added value for breeding. Whether this is the case can also be found by testing genetic diversity.

Especially for clubs, this represents an innovative and extensive way of performing breeding monitoring on a genetic basis. The Austrian Leonberger Club has already successfully put all of this into practice, laying the cornerstone for working out a connection between the genetic data and the development of the dogs thanks to these possibilities. The aim in breeding dogs should be to keep the genetic material as long as possible.

### **What is the practical process like?**

The dogs are currently being tested by the Austrian Leonberger Club, which also manages the data from the evaluations. Setting up such a database only makes sense if as many dogs as possible are tested and the data is available within the participating community. This means that the data is shared in a closed community and the ticket to this community are the test results of the respective dog. It should be clearly mentioned here that it is not about degrading certain dogs or emphasizing others. There is a lid for every pot and if a bitch and a male do not fit so well together, another partner will find be found. The fear that a male dog might not fit at all is unfounded.

The order forms for participation in the diversity project can be requested from the breeding department of the Austrian Leonberger Club. (Mrs. Sissy Fessler, ÖCLH-breed referee): [sissy.fessler@a1.net](mailto:sissy.fessler@a1.net)

After paying the fee for the testing, it is released by the club and the data analysis begins. After completion of all analysis results, the evaluations of the existing dogs and those of the newly added dogs are updated so that the latest results are available with each new round of analysis. These results are shared and discussed within a closed group.

The aim of this project should be to build a comprehensive genetic international database of Leonbergers, which is available to the Leonberger community and / or its members. This database is based on the actual genetic information of individual dogs and thus represents the genetic status of the breed. The focus is on preserving genetic diversity, and every dog that is included in this database makes a valuable contribution to the maintenance of this wonderful breed.

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