Recent Advances in Hereditary Diseases and Genetic Testing – Dr Carla O'Donnell PhD, CPDT

Next to humans, the largest number of naturally occurring hereditary disorders and genetic tendencies to disease has been reported in dogs. The number of reported hereditary diseases in dogs is rapidly growing. At present, dogs are susceptible to more than 900 hereditary diseases and every year over a dozen new defects are being reported, some serious, some mild and some inconsequential. Amongst breeders it is often heard, "There is nothing wrong with the mother and father, they are perfectly healthy. I do not need to do genetic testing." Unfortunately, carriers of genetic problems are often invisible and without testing; you cannot predict whether your litter will be at risk for disease.

Some people will say, "I have never seen any issues in the puppies I produce. I do not need to do genetic testing." Many genetic issues do not get diagnosed as a genetic issue or may develop years after that dog was bred. Health and genetic screening on the parents is important to minimise the chance that these issues will occur. Health issues are often heartbreaking and expensive. Every measure possible should be taken to avoid health issues especially when genetic testing is cost effective and readily available today.

So, what is Genetic testing?

Genetic testing involves examining an individual's Deoxyribonucleic acid (DNA). Genetic testing can reveal changes (mutations) in DNA that may cause illness or disease. DNA molecules are made of two twisting, paired strands, often referred to as a double helix. Each strand is composed of a sequence of substances known as nucleotides. There are four different types of nucleotides sometimes called bases: The bases are adenine (A), thymine (T), guanine (G), and cytosine (C). Bases on opposite strands pair specifically: An A always pairs with a T; a C always pairs with a G. The order of the As, Ts, Cs and Gs determines the meaning of the information encoded in that part of the DNA molecule just as the order of letters determines the meaning of a word. It acts like a recipe holding the instructions telling our bodies how to develop and function.

Genes are sections of our DNA sequence that contain the code for a specific protein, normally linked to a specific function or physical characteristic. In dogs, for example, a stretch of DNA known as 'CFA28' has a strong influence on the number of coat hairs a dog has. Variations in these parts of the DNA lead to the differences we see in dog's coats. For example, whether they are double- or single-coated. Dogs with double coats have different DNA at 'CFA28' than dogs with single coats. A common misconception about genes is that one gene is responsible for one characteristic, which is highly unusual. More commonly, physical characteristics result from a combination of many genes. Dogs have about 20,000 to 25,000 genes that are located along 39 pairs of chromosomes (compared to 23 pairs in humans).

In the past two decades, much progress has been made in identifying the mutations causing some of the genetic diseases in dogs. Thus far, most of the DNA tests available involve genetic disorders with single gene defects with simple Mendelian inheritance and are mostly breed specific. Most

laboratories can screen for multiple genetic diseases with simple cheek swabs, this testing is easily done on puppies at relatively early ages.

All living creatures carry gene mutations and a lot of these are recessive, in that the dog carries a normal copy and a mutated copy of the gene and if a normal copy of the gene is present the dog is clinically healthy. However, these recessive non-working genes have the potential to be an issue if they are bred with another animal also carrying a mutated copy of the gene. From a health perspective, carriers show no symptoms (they don't have the disease) and will make great pets. However, they may not be suitable for breeding to other carriers. But being identified as a carrier of a recessive disorder in no way affects the health of the dog.

There is a potential risk of genetic disease that comes with reproduction. This risk is why every expectant couple says "We want a boy (or "we want a girl)... but we do not care as long as the baby is healthy". All puppies have a risk for genetic disease. By breeding purebred dogs, dogs of known heritage, there is an opportunity to screen for diseases to reduce the risk for genetic health issues as much as possible. With genetic testing you can avoid the diseases for which tests are available. Although it will not exclude all possible inherited and acquired diseases, this is the best available option to increase the odds of producing healthy puppies.

DNA Tests that are currently available

It is often daunting for breeders to keep up with rapid advances in diagnostic opportunities. The number of disease-associated mutations, tests offered, and laboratories involved continue to grow and change, rapidly making it hard to know what is available. There is a web application that has been developed to collect and display information on available DNA tests. This tool should provide breeders with a single comprehensive, up-to-date and readily searchable webpage for information on hereditary disease testing and is at the following link: http://research.vet.upenn.edu/WSAVA-LabSearch

Below is the result I did for a search on Ichthyosis in Golden Retrievers. Searches can be done by disease/test, breed or laboratory. Information regarding the selection is used to narrow down the results. Information about the specific disease in this breed is displayed. Information about the laboratories doing the specific test in this breed is displayed.

Canine and Feline Hereditary Disease (DNA) Testing Laboratories

This page is used to search for Genetic Testing Laboratories and their corresponding tests for hereditary diseases in **dogs** and **cats**.
Practically all DNA tests for hereditary diseases are breed specific.

How would you like to search?

◉ **By Disease/Test**	○ **By Breed**	○ **By Lab**
I would like to find genetic disease testing laboratories that test for a particular disease.	I would like to find genetic disease testing laboratories for a particular breed.	I would like to find genetic disease tests for a particular genetic disease testing laboratory.

Select a Disease: Ichthyosis -A (Golden Retriever)
Select a Species: Canine
Select a Breed: Golden Retriever
For mixed breeds select closest similar breed.
Select a Mutation: PNPLA1 3-bp deletion followed by ε

Disease Gene Mutation Information

Disease: Ichthyosis -A (Golden Retriever) **(View Disease Details)**
Mutation: 3-bp deletion followed by an 8-bp insertion, exon 8
Gene: PNPLA1
Disease Code: ICT-A
OMIA: 001588-9615
Chromosome: 12
Research Link: http://www.nature.com/ng/journal/v44/n2/full/ng.10...
Research Citation: Nat Genet. 2012 Jan 15;44(2):140-7
Synonyms/Related Terms: ARCI, Autosomal Recessive Congenital Ichthyosis

Laboratories	
Anicom Specialty Medical Insitute Inc. City Hards Chojamachi Blding., 5F, 2-6-3 Yokohama JAPAN	https://www.anicom-med.co.jp/ anicom_med_info@ani-com.com
Animal DNA Diagnostics William James House, Cowley Rd Cambridge CB4 0WX UNITED KINGDOM	https://www.animaldnadiagnostics.co.uk info@animaldnadiagnostics.co.uk
Animal Genetics Inc. 1336 Timberlane Rd Tallahassee, FL 32312 UNITED STATES	http://www.animalgenetics.us/ contact@animalgenetics.us
Antagene CS60001 La Tour de Salvagny 69890 FRANCE	http://www.antagene.com/ contact@antagene.com
EVG - Molecular Diagnostics Taborska ulica 8 Maribor 2000 SLOVENIA	https://eurovetgene.com/en/ info@eurovetgene.com
Genindexe 6, rue de sports La Rochelle 17000 FRANCE	https://www.genindexe.com/en/ https://www.genindexe.com contact@genindexe.com
Laboklin Steubenstraße 4 Post box 1810 Bad Kissingen D-97688 GERMANY	https://shop.labogen.com/ info@laboklin.de
Laboratorio Genefast Via Castelfranco 17/d Bazzano (BO) 40053 ITALY	http://www.genefast.com/ info@genefast.com
Laboratory of Veterinary Genetics 3220 Sicotte Street Saint-Hyacinthe J2S 2M2 CANADA	http://labgenvet.ca/en/ david.w.silversides@umontreal.ca
Orivet Genetic Pet Care Mezzanine Level Hartford, CT 06103 UNITED STATES	https://www.orivet.com http://www.orivet.com.au info@orivet.com
Paw Print Genetics 220 East Rowan Ave, Ste 220 Spokane, WA 99207 UNITED STATES	https://www.pawprintgenetics.com AskUs@pawprintgenetics.com
Progenus 2 rue des Praules Gembloux 5030 BELGIUM	http://www.progenus.be info@progenus.be
Van Haeringen Agro Business Park 100, PO ox 408 6700 AK Wageningen NETHERLANDS	http://www.vhlgenetics.com info@vhlgenetics.com

Database maintained by: Dr. Urs Giger
Time of last database update: Monday, August 17, 2020

Using DNA tests in a breeding program

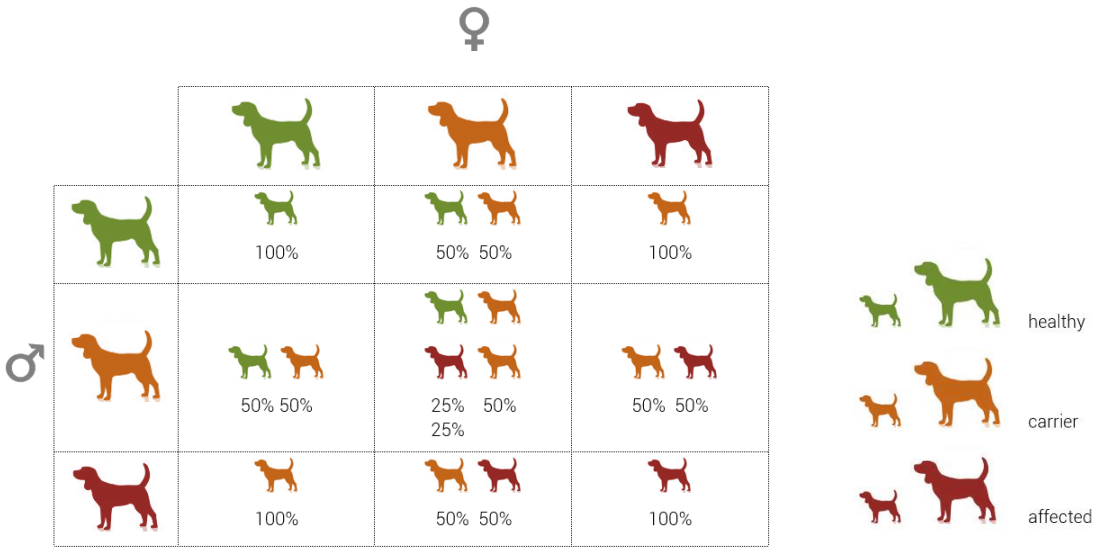
So what information does a DNA test certificate provide us and how can we use this in our breeding programs? A DNA test certificate will identify whether a dog is normal, affected or a carrier for the disease tested. A mating which has the potential to produce affected puppies should never knowingly be done (carrier to carrier, affected to carrier). However, there is a lot of confusion about what the result carrier means and whether these dogs should be used. Breeders often seem shocked or in a way disappointed when their dog tests as a carrier for a specific mutation. So, what does "carrier" in the test certificate exactly mean and should carriers be included in a breeding program?

Inheritance

Most of the current DNA tests available are for genetic disorders that are inherited in an autosomal recessive pattern. Each dog has two specific genes, each inherited from one parent. Genes for a specific disorder can be normal (do not cause the disorder) or can be mutated. If the disease is recessive two copies of the mutated gene are needed for the disease to be present. If only one mutated copy is present, and the other copy of the gene is normal the dog is clinically healthy. Many of the inherited eye disorders are examples of this type of disease, such as Progressive Retinal Atrophy, GR_PRA1. Before DNA tests were developed for this disease, breeding decisions were based solely on yearly physical examinations of a dog's eyes by an Ophthalmologist. However, such examinations do not guarantee that a dog doesn't have GR_PRA1. Physical symptoms of this disease do not develop until later in life, after the dog has already being used in a breeding program. This means that the affected dog will have already mated and passed on the genes that cause the disorder by the time the dog is clinically diagnosed as being affected. Additionally, a physical examination can't identify carriers. This leads to the disease popping up in future generations when the breeder unknowingly breeds two carriers together.

Keeping the gene pool stable – breeding carriers

The only way to be sure of a dog's actual disease status is DNA testing. Responsible breeders are aware of the importance of such tests and get their dogs tested to maintain or improve the quality of their dogs. Often when the results show that their dog is a carrier for certain autosomal recessive disorder, owners appear confused or disappointed. Considering centuries of inbreeding among pure bred dogs, the appearance of carriers is not unusual. Additionally, some breeders appear discouraged from using their carrier dogs in the breeding program. Although the dog carries one copy of the causative mutation, the other copy of the gene is healthy. With autosomal recessive disorders carrier dogs will be completely healthy dogs. When breeding a carrier with a clear dog, there is 50% chance that puppies will be clear and 50% chance that puppies will be carriers, but ALL THE PUPPIES WILL BE HEALTHY. If we, exclude carriers completely from the breeding program we will drastically reduce the gene pool for this breed of dog's genetic material. This in turn, can lead to an increase in inbreeding and the appearance of some new, until now unknown or extremely rare inherited diseases. Dramatically affecting the welfare of a breed. Carrier dogs are an important part of breeding programmes and should not be immediately discarded as an option. When used responsibly (i.e., only breeding to a clear dog), they can ensure good genetic diversity remains maintained.



New era, new approach

Over the last decades dogs have been excluded from breeding programs based on their phenotype which are characteristics that we can see. This has failed to eliminate genetic disorders because we can't identify carriers of autosomal recessive disorders and the disease pops up in future generations even when using clinically normal parents. Today with the development of DNA tests we can use the dogs actual genotype for a genetic disease. This gives us a tool to identify, affected, carrier and normal individuals even in young puppies. The ability to recognise carriers of genetic disorders allows us to confidently use them in our breeding programs and only produce healthy puppies if mated with a clear dog. At the same time, it enables avoiding mating two carriers or affected dogs that aren't showing any clinical signs at the time of mating. Keeping carriers in cleverly planned breeding programs will maintain the stability of the gene pool, without increasing the risk of new, unknown genetic disorders emerging. Genetic tests for dogs offer an easy and simple way for the identification of genetic traits in dogs and improve the quality of future litters, without the harmful effects of gene pool shrinkage. Being a breeder isn't an easy task because as well as genetic disease, a breeder should also consider genetic diversity, temperament, conformation and general health of the dogs when considering a breeding pair.