



INTERPRETIVE GUIDE

Thank you for your purchase of the International Genetics genotyping product. This is your interpretive guide to understanding the DNA genetic results listed on the certificate. InGen gives you genetic information about your pet. The following is your guide to understanding these results:

DISEASE SCREENING

InGen can screen for the following inherent, genetic diseases. Although these may be listed as breed specific, it is possible that these diseases can be detected in other breeds.

- **PROGRESSIVE ROD-CONE DEGENERATION (PRCD)**

The genetic disorder, prcd-PRA, causes cells in the retina at the back of the eye to degenerate and die, even though the cells seem to develop normally early in life. The “rod” cells operate in low light levels and are the first to lose normal function. This results in night blindness. Then the “cone” cells gradually lose their normal function in full light situations. Most affected dogs will eventually be blind. Typically, the clinical disease is recognized first in early adolescence or early adulthood. Since age at onset of disease varies among breeds, you should read specific information for your dog. Diagnosis of retinal disease can be difficult. Conditions that seem to be prcd-PRA might instead be another disease and might not be inherited.

Prcd-PRA is inherited as a recessive trait. This means a disease gene must be inherited from each parent in order to cause disease in an offspring. Parents were either “carrier” or affected. A carrier has one disease gene and one normal gene, and is termed “heterozygous” for the disease. A normal dog has no disease gene and is termed negative – both copies of the gene are the same. And a dog with two disease genes is termed positive – both copies of the gene are abnormal.

Unfortunately, at this time there is no treatment or cure for PRA. If your dog is affected, you may find it helpful to read about other owners’ experiences living with blind dogs. (Suggested links: www.eyevet.org and www.blinddogs.com).

Commonly affected breeds are the American Cocker Spaniel, American Eskimo Dog, Australian Cattle Dog, Australian Shepherd, Australian Shepherd, Miniature, Australian Stumpy Tail Cattle Dog, Chesapeake Bay Retriever, Chinese Crested, Cockapoo, Dwarf Poodle, English Cocker Spaniel, Entlebucher Mountain Dog, Finnish Lapphund, Golden Retriever, Golden Doodle, Karelian Bear Dog, Kuvasz, Labradoodle, Australian Labradoodle, Labrador Retriever, Lapponian Herder, Miniature & Toy Poodle, Norwegian Elkhound, Nova Scotia Duck Tolling Retriever, Portuguese Water Dog, Spanish Water Dog, Swedish Lapphund, Yorkshire Terrier.

- **MULTI DRUG RESISTANCE IN CANCER (MDR1)**

Some breeds of dogs are more sensitive to certain drugs compared to other breeds. For example, Collies, Australian Shepherds and other breeds are often more sensitive to the antiparasitic drug, Ivermectin. It is well known that Collies and related breeds can have adverse reactions to drugs such as Ivermectin, Loperamide (Imodium®), and others. It was previously unknown why some individual dogs were sensitive and others were not. The problem is due to a mutation in the multi-drug resistance gene (MDR1). This gene encodes a protein, P-glycoprotein, which is responsible for pumping many drugs and other toxins out of the brain. Dogs with the mutant gene can not pump some drugs out of the brain as a normal dog would, which may result in abnormal neurological signs. The result may be an illness requiring an extended hospital stay--or even death. Approximately 3 of every 4 Collies in the United States have the mutant MDR1 gene. The frequency is about the same in France and Australia, so it is likely that most Collies worldwide have the mutation. The only way to know if an individual dog has the mutant MDR1 gene is to have the dog tested. As more dogs are tested, more breeds will probably be added to the list of affected breeds.

Breeds found to be effected as of late 2007 include Collies, Shetland Sheepdogs (Shelties), Australian Shepherds, Old English Sheepdogs, German Shepherds, Long-haired Whippets, Silken Windhounds, and a variety of mixed breed dogs.

- **CANINE DEGENERATIVE MYELOPATHY (DM)**

Degenerative myelopathy in dogs is a condition that develops as a result of nerve function loss in the spinal cord. The nerves are protected by a sheath called myelin. Myelin is also responsible for decreasing the amount of time it takes a

nervous impulse to travel along the length of a nerve. In degenerative myelopathy, the myelin surrounding the nerves start to breakdown and nerves begin to degenerate in the spinal cord. Both of these processes cause changes to nervous signals as they travel up and down nerves. The cause of degenerative myelopathy is unknown. However, because of breed predispositions, it is thought that there might be a genetic component. This disease results in slowly progressive neurologic disease that is not painful and non-reversible. Dogs affected with degenerative myelopathy ultimately lose muscle mass from the disuse of their back legs and have difficulty getting up to go outside to urinate and defecate.

Degenerative myelopathy is mostly seen in the German Shepherd Dog but can also be seen in the Welsh Corgi, Chesapeake Bay Retriever, Irish Setter, Dalmatian, Weimaraner, Great Pyrenees, Samoyed, Boxer, Briard and others. The disease can present itself as early as 5 years of age in some cases and has been seen in young German Shepherd puppies. The average age of onset is between 9 and 11 years. It is more common in males than females.

- **EXERCISE INDUCED COLLAPSE (EIC)**

Labrador retrievers are the most common dog breed in the world, with over 200,000 new kennel club registrations per year. The syndrome of exercise-induced collapse (EIC) in this breed is manifested by muscle weakness, lack of coordination and life-threatening collapse after intense exercise. Using a genome-wide microsatellite marker scan for linkage in pedigrees, we mapped the EIC locus to canine chromosome 9. We then used SNP association and haplotype analysis to fine map the locus, and identified a mutation in the dynamin 1 gene (DNM1) that causes an R256L substitution in a highly conserved region of the protein. This first documented mammalian DNM1 mutation is present at a high frequency in the breed and is a compelling candidate causal mutation for EIC, as the dynamin 1 protein has an essential role in neurotransmission and synaptic vesicle endocytosis.

- **VON WILLEBRAND DISEASE (vWD)**

Von Willebrand Disease (vWD) is a common genetic bleeding disorder that can occur in dogs. In fact, it is not a single disease, but a family of related diseases of variable severity. All the different types in humans and in dogs are caused by a problem with the Von Willebrand Factor (vWF). This is a protein in blood which is necessary for proper blood coagulation, or clotting. When there is not enough of the protein in the blood, bleeding can be uncontrolled and sometimes life threatening. Symptoms can include undue bleeding of the umbilical cord at birth, extended bleeding at the time of tail docking, blood in the urine, or swelling in various body parts. Not all animals show clinical symptoms

The disease is inherited in an autosomal recessive mode.

Different types of vWD are found in different breeds of dogs.

- **PHOSPHOFRUCTOKINASE DEFICIENCY (PFK)**

The enzyme PFK is important in energy metabolism in red blood cells and in skeletal muscle during intense exercise. Canine Phosphofructokinase Deficiency is an inherited disorder that causes premature breakdown (hemolysis) of red blood cells, and a reduced tolerance for exercise. Affected dogs have chronic mild anemia with intermittent bouts of acute hemolysis, often associated with intense exercise, overheating or prolonged barking. Affected dogs have a persistent mild anemia (low level of red blood cells) for which they are generally able to compensate. Intermittently, they will have acute episodes of red blood cell breakdown when they become lethargic and weak. This is usually associated with intense exercise or excessive barking or panting. Their mucous membranes (e.g. gums) are pale or jaundiced and they usually run a high fever. You may notice the urine is brown due to the excretion of blood breakdown products. At these times, your dog will require veterinary attention.

Commonly affected breeds are Cocker Spaniel, English Springer Spaniel.

- **NEONATAL ENCEPHALOPATHY (NEWS)**

Neonatal encephalopathy with seizures (NEWS) is a previously undescribed autosomal recessive disease of standard poodle puppies. Affected puppies are small and weak at birth. Many die in their first week of life. Those surviving past 1 week develop ataxia, a whole-body tremor, and, by 4 to 6 weeks of age, severe generalized clonic-tonic seizures. None have survived to 7 weeks of age. Cerebella from affected puppies were reduced in size and often contained dysplastic foci consisting of clusters of intermixed granule and Purkinje neurons.

Visit www.ingen.bs for a Glossary of common genetic terms

The inheritance of Genetic Disease

To be affected (Positive), a dog must have received the mutated version of the gene from both parents.

Negative – Clear

A dog that has two copies of the normal version of the gene. Clear dogs will pass on the normal version of the gene to all of their offspring.

Carrier – Clear/Affected

A dog that has one copy of the normal gene and one copy of the mutated gene. **Carrier dogs do not normally show signs of the disease.** On average, carrier dogs will pass on the mutated copy of the gene to half of their offspring. By mating a carrier dog to a clear dog, you will, on average, produce litters that are 50 percent clear and 50 percent carriers, with **no affecteds**.

Positive – Affected/Affected

A dog that has two copies of the mutated gene. An affected dog will pass on the mutated gene to all of its offspring. By mating an affected dog to a clear dog, you will produce a litter that is made up of 100 percent carrier offspring – **no clears**, but also **no affecteds**.



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