

## Canine genetic disease testing

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### What is a genetic disease or disorders?

There are a number of untreatable diseases or disorders that occur in dogs that are passed on from parent to puppy and are called genetic diseases. All animals have two copies of each gene, one copy inherited from each parent. The building blocks of genes are nucleotide base pairs. There are only four base pairs (A, T, G and C) which are arranged in different orders. For the gene to be expressed correctly the base pairs need to be in the correct sequence. Sometimes the sequence becomes altered and this change is called a mutation. The mutation could be the substitution of one base (e.g. an A) for another (e.g. a G), or a deletion or insertion of one or more bases.

The mutation causes the gene to be expressed incorrectly and this leads to the development of the genetic disease. For example von Willebrand's disease Type I is caused by a mutation in the gene that controls the manufacturing of a blood clotting protein. The gene is not processed correctly and an insufficient quantity of this protein is manufactured to ensure sufficient blood clotting.

### What is genetic health screening?

Genetic Health screening is the test that is conducted to find out if an animal carries the mutant copy of the gene.

### Which diseases can be tested for?

Over 500 canine diseases are classified as "genetic" or "inherited" but only a handful can be diagnosed with a genetic test. The tests currently offered are for autosomal recessive diseases. These diseases are caused by a mutation in only one gene. The recessive gene is the mutant gene and two copies of this gene need to be present before the animal presents the symptoms of the disease. Disorders like hip dysplasia, allergies or cancer can not (yet) be diagnosed with a simple genetic test. It is caused by a number of genes that sometimes even interact to cause the disorder.

The diseases Inqaba biotec animal genetics currently offer include:

1. **von Willebrand's disease Type I:** Bleeding disorder affecting Dobermanns
2. **prcd-PRA:** Eye disorder that could lead to blindness that affects over 27 breeds including Labrador retrievers, Golden retrievers, English Cocker spaniels, Australian shepherds, Toy- and Miniature Poodles, Australian Cattle dogs, Yorkshire terriers and Chinese Crested dogs.
3. **cord 1-PRA:** Eye disorder that could lead to blindness that affects Miniature Long- and Smooth-haired Dachshunds and English Springer spaniels
4. **rcd1-PRA:** Eye disorder that could lead to blindness from 8 weeks of age affecting Irish Setters
5. **Collie eye anomaly:** Eye disorder that could lead to blindness affecting Australian Shepherds, Border collies, Rough- and Smooth Collies and Shetland Sheepdogs
6. **Multiple Drug Resistance (MDR1):** Disorder that leads to a sensitivity or resistance towards certain drugs that could lead to death affecting Border collies, Australian Shepherd, English Shepherd, German Shepherd Dog, Old English Sheepdog, Rough- and Smooth Collies and Shetland Sheepdogs
7. **Familial Nephropathy (FN):** Renal disorder that could lead to renal failure affecting English Cocker spaniels
8. **Ceroid Lipofuscinosis:** a neurodegenerative disease affecting Border collies.
9. **Fucosidosis:** a fatal metabolic and neurological disorder that affects English Springer Spaniels.
10. **Phosphofructokinase (PFK):** a metabolic disorder affecting English Springer Spaniels.
11. **Cystinuria:** a renal disorder affecting Newfoundlands
12. **L2HGA:** a neurological disorder affecting Staffordshire bull terriers
13. **Heritable cataracts:** an eye disorder affecting Staffordshire bull terriers and Boston terriers. An autosomal dominant mutation in the same gene affects Australian Shepherds.
14. **CLAD:** Immunity disorder affecting Irish Setters
15. **Exercise induced collapse (EIC):** Muscular disorder affecting Labrador retrievers

### What does the test indicate?

The tests only cover the region of interest that is associated with a specific disease mutation and does not give you a profile of all the dog's genes. The test indicates if the dog is clear (no mutant copies for that gene present), a carrier (only one mutant copy present) or affected (two mutant copies present). In Figure 1 an example of a chromatogram of the region of the gene associated with the PRA-prcd disease is shown. The mutation is indicated within the two lines and is a base pair substitution of a G to an A. Each peak on the graph indicates a different base to represent the sequence of the gene. A clear dog

will have a G on both copies of the gene and will never display the symptoms of the disease nor will it pass the mutant gene to its offspring. On the graph only one peak is visible as they align on top of each other. A carrier dog will not display the symptoms of the disease but may pass the gene to its offspring. This dog has a G on one copy of the gene and an A on the other copy presenting as two peaks on the graph. An affected dog has an A on both copies of the gene and will pass the mutant gene to its offspring. The probability of an affected dog presenting the symptoms is high, but for most diseases it is not a guarantee that the dog will develop the disease.

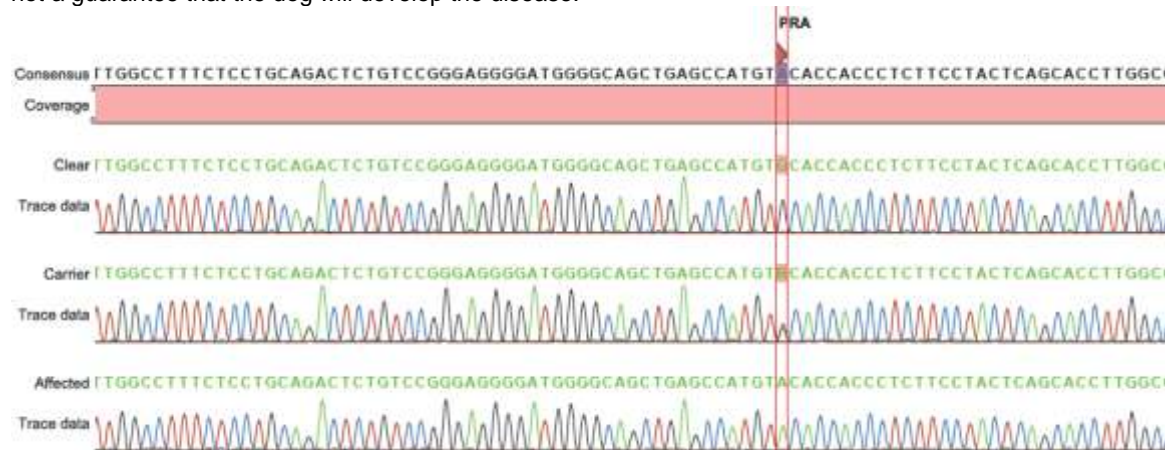


Figure 1: A chromatogram illustrating the three different statuses of PRA-prcd found in dogs

#### Why do I have to test my dog?

For most genetic diseases there is no cure. Dogs affected by von Willebrand's disease Type I could bleed to death and PRA affected dogs could go blind at a young age. Nobody wants to have dog suffering from a disorder and much less wants to sell a puppy that has this disorder. The only way to manage this disease is by selective breeding.

Parent 1 genotype	Parent 2 genotype		
	Normal	Carrier	Affected
Normal (No mutant copies)	All normal	50% Normal 50% Carrier	All carriers
Carrier (One mutant copy)	50% Normal 50% Carrier	25% Affected 25% Normal 50% Carrier	50% Carrier 50% Affected
Affected (Two mutant copies)	All Carrier	50% Carrier 50% Affected	All Affected

Table 1: Possible breeding outcomes when mating dogs with different statuses

Ideally all mating should be between two clear dogs. Unfortunately dogs with excellent features for other traits might be a carrier. There are many opinions as to if carriers should be used for breeding. However most scientists agree that they should be kept in a breeding line if they are only mated to clear dogs and the puppies tested and the carrier puppies removed from the breeding lines and only clear puppies kept. The genetic health screening tests are a breeding tool that a breeder can use to select the correct breeding pair and should not be viewed as a "death sentence".

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