

## RECOMMENDED DNA TESTS FOR BREEDERS

The following is a list of current DNA test applicable to the Coton De Tulear:

DNA Test	Advised for ALL DOGS in UK	Recommended	Advised for ALL Imported Dogs
CMR2	Y		Y
MH	Y		Y
DM	Y		Y
HUU	Y		Y
PH1	Y		Y
VWD1	Y		Y
CDDY	Y		Y
CDPA		Y	Y

For all dogs imported to the UK from abroad, i.e. Europe, USA etc we would advise that breeders ensure they received a copy of the DNA test certificates at point of sale.

Although DNA testing is not a requirement by The Kennel Club at the time of publishing. We advise all members partaking in breeding to DNA health test their dogs prior to breeding. The advice given here may change to a requirement in the future.

We give below an explanation of each of the above tests.

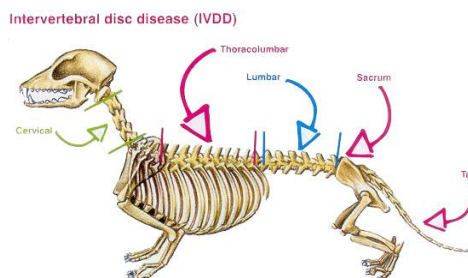
### **Canine Multifocal Retinopathy (CMR)**

Canine Multi-focal Retinopathy (CMR) is a recently identified recessively inherited eye disease observed in a number of dog breeds which is characterised by the presence of numerous distinct (i.e. multi-focal), roughly circular patches of elevated retina with accumulation of material that produces grey-tan-pink coloured lesions. These lesions, looking somewhat like blisters, vary in location and size, although typically they are present in both eyes of the affected dog. Discrete areas of tapetal hyper-reflectivity might also be seen.

The disease generally develops in young dogs before 4 months and might progress slowly, might appear to heal, or might even appear and then go away again. Some dogs affected with CMR do not show clinical symptoms of disease until later in life. Some lesions disappear with no remaining sign, while some lesions leave a wrinkled area. Some leave the lasting lesion of a blister formation. Most dogs exhibit no noticeable problem with vision despite their abnormal appearing retinas and in almost all cases, CMR does not progress significantly over time. The disease seems to have a consistent pattern among the breeds identified so far, although lesions in the Coton de Tulear are often more serious and seem to remain longer than in some of the other CMR-affected breeds. In rare severe cases, the clinical diagnosis could be confused with progressive retinal atrophy (PRA).



## Chondrodystrophy (CDDY with IVDD Risk) and Chondrodysplasia (CDPA)



The test checks for two mutations: CDDY with IVDD Risk, and CDPA.

Chondrodystrophy CDDY (FGF4-18) which causes short legs and the risk of developing Intervertebral Disc Disease (IVDD).

Chondrodysplasia CDPA (FGF4-12), which causes the short-legged phenotype in a number of breeds.

Chondrodystrophy (CDDY with IVDD Risk) is a trait that is common to many dog breeds and it is characterised by shorter legs due to shorter long bones. CDDY can also be associated with Intervertebral Disc Disease (IVDD) due to premature degeneration of the intervertebral disc. The intervertebral disc lies between the vertebrae and it is made of a cartilage which separate vertebrae from each other, absorb shocks and allow slight movement of the vertebrae. In affected dogs, premature calcification of part of the disc at early age (from birth to 1 year of age) results in degeneration of all discs in young dogs. These abnormal discs are susceptible to herniation into the spinal canal where the inflammation, and haemorrhage can cause severe pain and neurological dysfunction.

CDDY is inherited as a dominant trait for intervertebral disc disease and a semi-dominant for height. Which means that dogs with 2 copies of the mutation are smaller than dogs with only 1 copy. As for IVDD, the inheritance follows a dominant mode, meaning that 1 copy of CDDY mutation is sufficient to predispose dogs to IVDD.

The CDDY mutation has been found in breeds such as: Basset Hound, Beagle, Bichon Frise, Cardigan Welsh Corgi, Cavalier King Charles Spaniel, Chesapeake Bay Retriever, Chihuahua, American Cocker Spaniel, Coton de Tulear, Dachshund, Dandie Dinmont Terrier, English Springer Spaniel, French Bulldog, Havanese, Jack Russell Terrier, Nova Scotia Duck Tolling Retriever, Pekingese, Pembroke Welsh Corgi, Poodle (Miniature and Toy), Portuguese Water Dog, Scottish Terrier, Shih Tzu.

The second mutation Chondrodysplasia (CDPA) explains the short-legged phenotype known as chondrodysplasia (CDPA) in breeds such as Basset Hound, Pembroke Welsh Corgi, Dachshunds, West Highland White Terriers and Scottish Terriers. CDPA inheritance is considered to follow an autosomal dominant mode.

In some breeds both mutations are present and so breeders will be able to plan breeding to reduce occurrence of CDDY, while retaining the short-legged phenotype CDPA.



### **Degenerative Myelopathy (DM)**

Canine degenerative myelopathy (also known as chronic degenerative radiculomyelopathy) is a progressive disease of the spinal cord in older dogs. The disease has an insidious onset typically between 7 and 14 years of age. It begins with a loss of coordination (ataxia) in the hind limbs. As of 15th July 2008, the mutated gene responsible for DM has been found present in 43 breeds including German Shepherds, Boxers, Chesapeake Bay Retrievers, Rhodesian Ridgebacks, and both breeds of Welsh Corgis. The disease is chronic and progressive, and resulting in paralysis.

Degenerative myelopathy initially affects the back legs and causes muscle weakness and loss, and lack of coordination. These cause a staggering effect that may appear to be arthritis. The dog may drag one or both rear paws when it walks. This dragging can cause the nails of one foot to be worn down. The condition may lead to extensive paralysis of the back legs. As the disease progresses, the animal may display symptoms such as incontinence and has considerable difficulties with both balance and walking. If allowed to progress, the animal will show front limb involvement and extensive muscle atrophy. Eventually cranial nerve or respiratory muscle involvement necessitates euthanasia. Progression of the disease is generally slow but highly variable. The animal could be crippled within a few months or may survive up to three years.

### **Hyperuricosuria (HUU)**

Hyperuricosuria is characterized by elevated levels of uric acid in the urine. This disease predisposes dogs to form stones in their bladders or sometimes kidneys. The trait can occur in any breed but is most commonly found in the Dalmatian, Bulldog and Black Russian Terrier.

### **Malignant Hyperthermia (MH)**

Malignant hyperthermia (MH) is an inherited disorder of skeletal muscle characterized by hypercarbia, rhabdomyolysis, generalized skeletal muscle contracture, cardiac dysrhythmia, and renal failure, that develops on exposure to succinylcholine or volatile anaesthetic agents. Specific interventions, including use of the calcium release channel antagonist dantrolene, are efficacious in reversing signs of the canine syndrome.

### **Primary Hyperoxaluria type 1 (PH1)**

Primary Hyperoxaluria (PH) is an inherited disease affecting the Coton de Tulear breed and characterised by build-up of excess calcium oxalate in a number of tissues, in particular in the kidney where calcium oxalate stones form leading to progressive kidney failure. The crystals also accumulate in other tissues including bones, joints, cartilages, retina and muscles. Symptoms include intense abdominal pain radiating to the groin, blood can be seen in the urine, and the passage of kidney stones.



### **Von Willebrand disease Type 1 (VWD 1)**

von Willebrand disease (vWD) is probably the most common inherited bleeding disorder in dogs. It is caused by lack of von Willebrand factor which is a protein that plays a key role in the blood clotting process resulting in prolonged bleeding. The disorder occurs in varying degrees of severity ranging from trivial bleeding to excessive life-threatening haemorrhages. Symptoms include spontaneous bleeding from the nose, gum and other mucous membranes. Excessive bleeding occurs after an injury, trauma or a surgery. Often dogs don't show clinical signs until something starts the bleeding, such as nail trimming, teething, spaying, sterilizing, tail docking, cropping or other causes. Bleeding also occurs internally in the stomach, intestines, urinary tracts, the genitals and / or into the joints.

### **Trait of Inheritance**

The conditions of CMR, MH, PH1, HUU, DM and vWD1 are all classed as autosomal recessive and can be transmitted to offspring. The following table below is provided to assist you in ascertaining whether to breed or not.

<b><i>Clear</i></b>	<b><i>Carrier</i></b>	<b><i>Affected</i></b>	<b><i>Offspring</i></b>
<i>Dam and Sire</i>			<i>100% Clear</i>
<i>Dam or Sire</i>	<i>Dam or Sire</i>		<i>50% carrier 50% Clear</i>
<i>Dam or Sire</i>		<i>Dam or Sire</i>	<i>100% carrier</i>
	<i>Dam and Sire</i>		<i>25% affected 25% clear 50% carrier</i>
	<i>Dam or Sire</i>	<i>Dam or Sire</i>	<i>50% carrier 50% affected</i>
		<i>Sire and Dam</i>	<i>100% affected</i>

Source: Laboklin (14/8/2019)

### **Chondrodystrophy**

The condition of Chondrodystrophy (CDDY) is classed an autosomal dominant trait for intervertebral disc disease and a semi-dominant for height. Dogs with 2 copies of the mutation will be smaller than those with 1 and can be transmitted to offspring. Below is a table which is hoped will help clarify whether it is wise to breed or not. It has been sourced from US Davis but has been simplified to make it easier to understand.

### **Trait of Inheritance for CDDY and CDPA**

<b><i>Test Result</i></b>	<b><i>What they mean</i></b>
<i>N/N</i>	<i>No copies of the CDDY mutation</i>
<i>N/CDDY</i>	<i>1 copy of the CDDY mutation. This mutation causes leg shortening compared to N/N dogs. Dog is at risk for IVDD.</i>
<i>CDDY/CDDY</i>	<i>2 copies of CDDY. This mutation causes leg shortening compared to N/N dogs. Dog at risk for IVDD.</i>



### Outcome of Offspring from mating

<b>Parent 1</b>	<b>Parent 2</b>	<b>Offspring</b>
<i>N/N</i>	<i>N/N</i>	<i>100% clear of CDDY mutation</i>
<i>N/N</i>	<i>N/CDDY</i>	<i>50% clear 50% carrier of the CDDY mutation</i>
<i>N/N</i>	<i>CDDY/CDDY</i>	<i>100% carrier of the CDDY mutation</i>
<i>N/CDDY</i>	<i>N/CDDY</i>	<i>25% affected 25% clear 50% carrier of the CDDY mutation</i>
<i>N/CDDY</i>	<i>CDDY/CDDY</i>	<i>50% carrier 50% affected of the CDDY</i>
<i>CDDY/CDDY</i>	<i>CDDY/CDDY</i>	<i>100% affected. All puppies at risk for IVDD and will carry 2 copies of the CDDY mutation</i>

### Chondrodysplasia

<b>Test Result</b>	<b>What they mean</b>
<i>N/N</i>	<i>No copies of CDPA mutation</i>
<i>N/CDPA</i>	<i>1 copy of CDPA. Mutation causes leg shortening compared to N/N dogs</i>
<i>CDPA/CDPA</i>	<i>2 copies of CDPA. Mutation causes leg shortening compared to N/N dogs.</i>

### Our conclusion

From the research the safest breeding options would be to mate a (N/N) with a (N/N) dog or a (N/N) with a (N/CDDY) dog to reduce the risk of IVDD. Mating a Clear (N/N) with a (CDDY/CDDY) dog will produce 100% of puppies with at least 1 copy of the CDDY mutation & ALL puppies at risk of IVDD.

It should be noted that dogs which carry either one copy or two copies of the mutated gene could be **at risk of developing IVDD**. However, the results are only an indication and does not necessarily mean that they will. Lifestyle, weight, diet and exercise also has a part to play in bone development.

Concerning CDPA, from the research data received so far there appears to be a trend that our breed will have 2 copies of the CDPA mutation, which contributes to the breeds short stature and we believe, at present, this should not pose any health problems within our breed. However, research into CDPA and CDDY mutation is still ongoing and once more information is available our views could change in the future.



### Outcome of offspring from mating with a risk for IVDD

<b>Parent 1</b>	<b>Parent 2</b>	<b>Offspring</b>	<b>Offspring risk for IVDD</b>
<i>N/N</i>	<i>N/N</i>	<i>100% clear of CDDY mutation</i>	<i>0% at risk for IVDD</i>
<i>N/N</i>	<i>N/CDDY</i>	<i>50% clear 50% carrier of the CDDY mutation</i>	<i>50% at risk for IVDD</i>
<i>N/N</i>	<i>CDDY/CDDY</i>	<i>100% carrier of the CDDY mutation</i>	<i>100% at risk for IVDD</i>
<i>N/CDDY</i>	<i>N/CDDY</i>	<i>25% affected 25% clear 50% carrier of the CDDY mutation</i>	<i>75% at risk for IVDD</i>
<i>N/CDDY</i>	<i>CDDY/CDDY</i>	<i>50% carrier 50% affected of the CDDY</i>	<i>100% at risk for IVDD</i>
<i>CDDY/CD DY</i>	<i>CDDY/CDDY</i>	<i>100% affected. All puppies at risk for IVDD and will carry 2 copies of the CDDY mutation.</i>	<i>100% at risk for IVDD</i>

