Dilated Cardiomyopathy 1 and 2 in Doberman Pinschers

Quick Summary

Dilated cardiomyopathy is a condition in which the heart has a decreased ability to pump blood. Two mutations associated with dilated cardiomyopathy in Doberman Pinschers have been identified. Testing for these mutations can identify individuals at risk for developing clinical symptoms of disease.

Phenotype: Dilated cardiomyopathy is a heart condition in which the muscles degenerate, causing the walls of the heart to become thin, resulting in reduced contractibility. This can lead to congestive heart failure.

Mode of Inheritance: Autosomal dominant with **incomplete penetrance**

Alleles: N = Normal, **DCM1** = dilated cardiomyopathy 1 variant present, **DCM2** = dilated cardiomyopathy 2 variant present

Breeds appropriate for testing: Doberman Pinscher

Explanation of Results:

- Dogs with **N/N** genotype do not have either of the known DCM variants.
- Dogs with **N/DCM1** or **N/DCM2** genotypes are at risk to develop cardiomyopathy. If two **heterozygotes** with the same mutation are mated, approximately 75% of the puppies are at risk of developing disease. Dogs heterozygous for both variants, **N/DCM1** and **N/DCM2**, are at greater risk to develop clinical symptoms relative to those with only one variant.
- Dogs with **DCM1/DCM1** or **DCM2/DCM2** genotypes are at risk to develop cardiomyopathy. All puppies produced from matings of dogs with either of these **homozygous** genotypes are at risk for developing dilated cardiomyopathy.

Price

$50 **one test** per animal

$30 **as additional test** (same animal)

Order Test

Panels Available

Doberman Pinscher Health Panel $130 per animal

Additional Details

Dilated cardiomyopathy is an inherited, potentially fatal heart disorder. In affected dogs, the left ventricle is often dilated, resulting in a progressive thinning of the wall and irregular heartbeat, thus decreasing overall cardiac function and output. This lack of adequate circulation can lead to fluid accumulation in the lungs as well as other parts of the body. Affected dogs can show progressive deterioration leading to death or can be relatively asymptomatic and then die suddenly.

In humans, over 60 different **genes** have been identified that result in inherited cardiomyopathy. Dr. Kate Meurs and colleagues at North Carolina State identified mutations in two independent genes that have been associated with dilated cardiomyopathy. Specifically, a **deletion** of 16 DNA bases in *pyruvate dehydrogenase kinase 4* (PDK4 g.20,829,667_20,829,682del), known as DCM1, results in a gene product suspected to cause cardiac issues. The DCM1 variant is predicted to alter the mitochondrial PDK4 protein assembly pattern because it eliminates a **splice site**. Since mitochondria are one the major sites of energy generation within a cell, the resulting negative impact of reduced energy generation within cardiac tissue is hypothesized to result in cardiomyopathy.

The second associated variant is a **missense mutation** in *titin* gene (TTN, g.22321955C>T, p. 8898G>R) known as DCM2. The DCM2 variant, which changes an amino acid conserved across mammals, is predicted to alter one of the gene products (protein) immunoglobulin -like (Ig)

For DCM1 the risk of developing cardiac disease is 7 fold for animals with one or two copies of this variant. The relative risk for DCM2 has not been determined. Dogs with both DCM1 and DCM2 have been reported to be at the highest risk for developing disease.

A single affected copy of either gene is necessary to develop symptoms, but not all dogs with DCM1, DCM2, or both mutations will develop disease. Since a single copy of either mutation can increase risk for disease, this trait is considered a **dominant** trait. However, since not all dogs with these mutations go on to develop disease, these mutations are thought to be **incompletely penetrant**. Other factors likely explain the incompletely penetrant nature of this disease, and studies to investigate additional genetic and non-genetic risk factors are ongoing. Recently it was noted that in a European Doberman Pinschers sample set, the DCM1 mutation was not as correlated with disease risk as it is in the original Doberman study cohort.

Further, not all Doberman Pinschers with dilated cardiomyopathy have either of these mutations. Therefore, it is also likely that additional as of yet unidentified variants in these or other genes are involved in disease presentation and progression. Continued research is needed to identify additional genetic and non-genetic risk factors.

However, these DNA tests can help owners and clinicians identify at-risk dogs for careful clinical evaluation. Further, breeders can use the results of this test in assisting with mate selection.

> ***Note:*** *These tests are specific for the autosomal dominant mutations present in the Doberman Pinscher. Other as of yet unidentified variants that cause dilated cardiomyopathy are thought to be present in this breed.*

Turnaround Time

At least 15 business days

Type of Sample

Interdental/GUM brushes - supplied by owner
Cytology Brush - supplied by VGL at no additional charge

Dog

Breed

Doberman Pinscher

Type of Test

Health

Results Reported As

Test Result	Dilated Cardiomyopathy 1 (DCM1)
N/N	Dog does not have the variant associated with Doberman DCM1.
N/DCM1	*Heterozygous. Dog has one copy of the Doberman DCM1 associated variant and is at risk to develop dilated cardiomyopathy.
DCM1/DCM1	*The dog has two copies of the Doberman DCM1 associated variant and is at risk to develop dilated cardiomyopathy.

Test Result	Dilated Cardiomyopathy 2 (DCM2)
N/N	Dog does not have the variant associated with Doberman DCM2.
N/DCM2	*Heterozygous. Dog has one copy of the Doberman DCM2 associated variant and is at risk to develop dilated cardiomyopathy.
DCM2/DCM2	*The dog has two copies of the Doberman DCM2 associated variant and is at risk to develop dilated cardiomyopathy.

References

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License Info

The test for DCM2 is performed under a license agreement with North Carolina State University.

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