NC State College of Veterinary Medicine

Veterinary Cardiac Genetics Laboratory

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Genetic Results Interpretations

See the following pages for interpretations of your results.

Rhodesian Ridgeback Inherited Arrhythmia (RR IVA) Genetic Testing

Rhodesian Ridgeback Inherited Arrhythmia (RR IVA) is an inherited disease that results in an abnormality of the cardiac electrical system leading to the development of abnormal heart beats (ventricular premature beats (VPCs). In some cases these abnormal heart beats can result in sudden death. It appears that the most severe disease may be present between 6 and 30 months of age and many dogs appear to outgrow the problem.

Our current interpretations of the possible test results are:

Negative Result:	The absence of the mutation in this dog, does not mean that it will never develop heart disease. It means that it does not have the known mutations that can cause the disease in the dog at this time.
Positive Result:	Dogs that are positive for the test will not necessarily develop significant heart disease (arrhythmias) and die from the disease. Our current results suggest that about 60% of the dogs that are positive will develop a cardiac arrhythmia and may need treatment. Many dogs appear to outgrow the disease between 2 and 3 years of age. We recommend that dogs that are positive have a Holter monitor performed periodically between 6 months to 3 years of age.
Breeding recommendations:	Importantly, breeding decisions should be made carefully. At this time we do not yet know what percentage of Rhodesian Ridgebacks will be positive for the mutation. However, removal of a significant number of dogs from the breeding population could be very bad for the breed. Remember that dogs that carry this mutation also carry other important good genes that we do not want to lose from the breed.

If you would like to learn more about Holter monitoring or request a Holter monitor rental through the NC State Holter Monitor Service, please visit: https://cvm.ncsu.edu/nc-state-vet-hospital/holter-monitor/

Boxer Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) Testing

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a fairly common form of heart disease in the boxer dog. It is inherited and our laboratory has identified two mutations associated with the disease in some boxers. However, it should be noted that in human beings with the same disease, there are many different genetic mutations which can cause this disease. Please keep in mind that we are continually learning about this disease and recommendations will be altered as we obtain more information.

Our current interpretations of the possible test results are:

Negative Result for both ARVC1 and ARVC2:	The absence of both mutations in a Boxer indicates that the risk of developing ARVC is low. It is still possible for a dog to develop heart disease. However, a negative result for both ARVC1 and ARVC2 indicates that a dog does not have either mutation known to cause ARVC.
Positive result for NCSU ARVC1 only :	Dogs that are positive for only ARVC1 have an increased likelihood of developing ARVC, but are not necessarily guaranteed to experience symptoms of serious disease. Dogs that are Positive Heterozygous, meaning they only have 1 copy of this mutation, should be evaluated for signs of disease. If an arrhythmia is detected, possible treatment options should be discussed with your veterinarian. Dogs that are Positive Homozygous, meaning they have 2 copies of the mutation, appear to have more significant disease and should be carefully monitored for symptoms of disease.
Breeding recommendations:	Dogs that are positive for ARVC1 should NEVER be bred to a dog that is positive for NCSU ARVC2 since this will lead to dogs that are at highest risk of developing ARVC. Dogs that are positive homozygous for ARVC1 should ideally not be bred.
Positive Result for NCSU ARVC2 only :	Dogs that are positive for only ARVC2 have an increased likelihood of developing ARVC, but are not necessarily guaranteed to experience symptoms of serious disease. Dogs that are Positive Heterozygous, meaning they only have 1 copy of this mutation, should be evaluated for signs of disease. If an arrhythmia is detected, possible treatment options should be discussed with your veterinarian. Dogs that are Positive Homozygous, meaning they have 2 copies of the mutation, appear to have more significant disease and should be carefully monitored for symptoms of disease.
Breeding recommendations:	Dogs that are positive for ARVC2 should NEVER be bred to a dog that is positive for NCSU ARVC1 since this will lead to dogs that are at highest risk of developing ARVC. Dogs that are positive homozygous for ARVC2 should ideally not be bred.
Positive result for both NCSU ARVC1 and NCSU ARVC2 :	**Dogs that are positive for BOTH ARVC1 & ARVC2 are at a very HIGH risk of developing ARVC** and should be carefully monitored by your veterinarian for signs of disease. Annual evaluation by a cardiologist with an echocardiogram and Holter monitor after 3 years of age is recommended.
Breeding recommendations:	Dogs that are positive for both ARVC1 & ARVC2 are at the HIGHEST risk of developing ARVC and should ideally not be bred since they can pass both traits on. They should NEVER be bred to a dog that is positive for either test.

As always, breeding decisions should be made carefully. Removal of a significant number of dogs from the breeding population could be very bad for the Boxer breed. Remember that dogs that carry this mutation may also carry other important good genes that we do not want to lose from the breed.

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Doberman Pinscher Dilated Cardiomyopathy (DCM) Genetic Testing

Dilated cardiomyopathy mutation (DCM) is a form of heart disease in the Doberman Pinscher dog. It is an inherited disease, and our laboratory has identified two mutations responsible for the development of DCM. Dogs that are positive for both mutations are at the highest risk of developing DCM.

Our current interpretations of the possible test results are:

Negative Result for both DCM1 and DCM2:	The absence of both mutations in a Doberman indicates that the risk of developing DCM is low. It is still possible for a dog to develop heart disease. However, a negative result for both DCM1 and DCM2 indicates that a dog does not have either mutation known to cause DCM.
Positive result for NCSU DCM1 only :	**About 40% of dogs with this mutation will develop DCM.** Dogs that are positive for only DCM1 will not necessarily develop significant heart disease.
Breeding recommendations:	Dogs that are positive for DCM1 should NEVER be bred to a dog that is positive for NCSU DCM2 since this will lead to dogs that are at highest risk of developing DCM. Dogs that are positive homozygous for DCM1 should ideally not be bred at all, as they will certainly pass along the mutation to their offspring.
Positive Result for NCSU DCM2 only :	**About 50% of dogs with this mutation will develop DCM.** Dogs that are positive for only DCM2 will not necessarily develop significant heart disease.
Breeding recommendations:	Dogs that are positive for DCM2 should NEVER be bred to a dog that is positive for NCSU DCM1 (PDK4) since this will lead to dogs that are at highest risk of developing DCM. Dogs that are positive homozygous for DCM2 should ideally not be bred at all, as they will certainly pass along the mutation to their offspring.
Positive result for both NCSU DCM1 and NCSU DCM2 :	**Dogs that are positive for BOTH DCM1 & DCM2 are at a very HIGH risk of developing DCM** and should be carefully monitored by your veterinarian for signs of disease. Annual evaluation by a cardiologist with an echocardiogram and Holter monitor after 3 years of age is recommended.
Breeding recommendations:	Dogs that are positive for both DCM1 & DCM2 are at the HIGHEST risk of developing DCM and should ideally not be bred since they can pass both traits on. They should never be bred to a dog that is positive for either test.

As always, breeding decisions should be made carefully. Removal of a significant number of dogs from the breeding population could be very bad for the Boxer breed. Remember that dogs that carry this mutation may also carry other important good genes that we do not want to lose from the breed.

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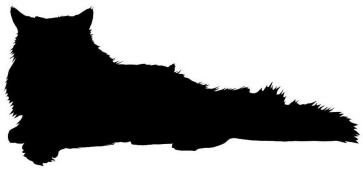
Maine Coon Hypertrophic Cardiomyopathy (HCM) Testing

Hypertrophic cardiomyopathy (HCM) is the most common form of heart disease in the cat. In many breeds it is an inherited disease. Our laboratory has identified a mutation responsible for the gene in Maine Coon cats. However, it should be noted that in human beings with the same disease, there are many different genetic mutations which can cause this disease. It is likely the same cats.

Our current interpretations of the possible test results are:

Negative:	Negative cats have two copies of the normal, unmutated gene. Very importantly, the absence of the mutation in this cat does not mean that it will never develop the disease. It means that it does not have the only known mutation that can cause the disease in the cat at this time. In the future, additional mutations may be identified that may be tested for as well.
Positive Heterozygous:	Cats who are Positive Heterozygous for the HCM mutation have 1 copy of the mutated gene and 1 copy of a normal gene. Cats that are positive for the test will not necessarily develop significant heart disease and die from the disease. Some cats will develop a very mild form of the disease and will live quite comfortably. We recommend annual evaluation by an echocardiogram and discussion with a veterinarian for treatment options if hypertrophy develops.
Positive Homozygous:	Cats who are Positive Homozygous for the HCM mutation have 2 copies of the mutated gene and may have a greater likelihood of showing severe signs of hypertrophic cardiomyopathy.

Importantly, breeding decisions should be made carefully. At this time we have observed about 33% maine coon cats that we have tested carry at least one copy of the gene. Removal of all of these cats from the breeding population could be very bad for the maine coon breed. Remember that hcm affected cats also carry other important good genes that we do not want to lose from the breed. We recommend not breeding the homozygous cats and, if needed, breeding heterozygotes to unaffected cats to decrease the risk of producing affected cats. As we move forward we should try to select more and more negative kittens from these lines to use for breeding. Keep in mind that we are continually learning about this disease and recommendations will be altered as we obtain more information.



Ragdoll Hypertrophic Cardiomyopathy (HCM) Testing

Hypertrophic cardiomyopathy (HCM) is the most common form of heart disease in the cat. In many breeds it is an inherited disease. Our laboratory has identified a mutation responsible for the gene in Ragdoll cats. However, it should be noted that in human beings with the same disease, there are many different genetic mutations which can cause this disease. It is likely the same cats.

Our current interpretations of the possible test results are:

Negative:	Negative cats have two copies of the normal, unmutated gene. Very importantly, the absence of the mutation in this cat does not mean that it will never develop the disease. It means that it does not have the only known mutation that can cause the disease in the cat at this time. In the future, additional mutations may be identified that may be tested for as well.
Positive Heterozygous:	Cats who are Positive Heterozygous for the HCM mutation have 1 copy of the mutated gene and 1 copy of a normal gene. Cats that are positive for the test will not necessarily develop significant heart disease and die from the disease. Some cats will develop a very mild form of the disease and will live quite comfortably. We recommend annual evaluation by an echocardiogram and discussion with a veterinarian for treatment options if hypertrophy develops.
Positive Homozygous:	Cats who are Positive Homozygous for the HCM mutation have 2 copies of the mutated gene and may have a greater likelihood of showing severe signs of hypertrophic cardiomyopathy.

Importantly, breeding decisions should be made carefully. Removal of all cats with the mutation from the breeding population could be very bad for the breed. Remember that hcm affected cats also carry other important good genes that we do not want to lose from the breed. We recommend not breeding the homozygous cats and, if needed, breeding heterozygotes to unaffected cats to decrease the risk of producing affected cats. As we move forward we should try to select more and more negative kittens from these lines to use for breeding. Keep in mind that we are continually learning about this disease and recommendations will be altered as we obtain more information.

Sphynx Hypertrophic Cardiomyopathy (HCM) Testing

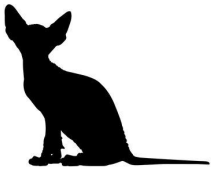
Hypertrophic cardiomyopathy (HCM) is the most common form of heart disease in the cat. In many breeds it is an inherited disease. Our laboratory has identified a mutation responsible for the gene in some cats. However, it should be noted that in human beings with the same disease, there are many different genetic mutations which can cause this disease. It is likely the same cat.

Our current interpretations of the possible test results are:

Negative:	Negative cats have two copies of the normal, unmutated gene. Very importantly, the absence of the mutation in this cat does not mean that it will never develop the disease. It means that it does not have the only known mutation that can cause the disease in the cat at this time. In the future, additional mutations may be identified that may be tested for as well.
Positive Heterozygous:	Cats who are Positive Heterozygous for the HCM mutation have 1 copy of the mutated gene and 1 copy of a normal gene. Cats that are positive for the test will not necessarily develop significant heart disease and die from the disease. Some cats will develop a very mild form of the disease and will live quite comfortably. We recommend annual evaluation by an echocardiogram and discussion with a veterinarian for treatment options if hypertrophy develops.
Positive Homozygous:	Cats who are Positive Homozygous for the HCM mutation have 2 copies of the mutated gene and may have a greater likelihood of showing severe signs of hypertrophic cardiomyopathy.

Importantly, breeding decisions should be made carefully. At this time, we do not know what percent of the overall Sphynx cat population carry at least one copy of the gene. Removal of a large number of cats from the breeding population could have a negative impact on the breed. Remember that HCM affected cats also carry other important good genes that we do not want to lose from the breed.

In general, we recommend not breeding homozygous cats and, if needed, breeding heterozygotes to unaffected, negative cats to decrease the risk of producing affected cats. As we move forward, we should try to select more and more negative kittens from these lines to use for breeding. Keep in mind that we are continually learning about this disease and recommendations will be altered as we obtain more information.



Old English Sheepdog and Gordon Setter
Cerebellar Ataxia (CA) Testing

Cerebellar degeneration (also called Cerebellar Ataxia) is a hereditary disease that is recognized in several different breeds of dog. This neurodegenerative condition is associated with gradual death of neurons in the cerebellum. It causes a progressive loss of coordination resulting in the hallmark ataxic gait characterized by dramatic overstepping, particularly obvious in the forelimbs. As signs progress, dogs develop an intention tremor of their head and an obvious sway to their trunk as they walk. Onset of signs ranges from 6 months to 4 years of age and disease progression varies between dogs, but tends to be slow, occurring over several years and ultimately results in an inability to walk without falling and difficulty in eating and drinking.

Our team identified the mutation that is associated with this disease in a gene called Rab24 in both Old English Sheepdogs and Gordon Setters. This gene encodes a protein that plays a role in autophagy, a process by which cells dispose of their waste. It is a recessive condition, and so dogs that have only 1 copy of the gene do not develop clinical signs. Thus far, to the best of our knowledge, 100% of dogs with 2 copies of the gene have developed clinical signs.

Our current interpretations of the possible test results are:

Negative: (Clear)	Negative dogs have two copies of the normal, unmutated gene.
Positive Heterozygous: (Carrier)	Dogs who are Positive Heterozygous for the CA mutation have one copy of the mutated gene. Since this is a recessive disease dogs with 1 mutation do not develop the clinical signs but are considered a **carrier** of the trait. If your dog has signs of cerebellar disease, it is likely due to another cause. If the dog has many other positive traits it may be reasonable to consider breeding a heterozygous dog to a Negative dog, screening the puppies and trying to select a Negative puppy to keep as a replacement breeding animal in the next litter or so. Over time this will gradually reduce the prevalence of the disease in the breed. We would never recommend breeding a positive heterozygous dog to a positive heterozygous dog since this could produce homozygous dogs which will develop this disease.
Positive Homozygous: (Affected)	Dogs who are Positive Homozygous for the CA mutation have two copies of the mutated gene and are at extremely high risk of developing signs of the disease. Your dog has a 100% chance of passing the mutation on to all of its puppies. We would not recommend using these dogs for breeding purposes if possible.

Importantly, breeding decisions should be made carefully. Removal of a significant number of dogs from the breeding population could be very bad for the old english sheepdog or gordon setter breed. Remember that dogs that carry this mutation also carry other important good genes that we do not want to lose from the breed.

JAK2 Polycythemia Vera Mutation

A mutation has been identified at V617F in the JAK2 gene in dogs with primary polycythemia vera. At this time the mutation has not been associated with a specific breed, but as in humans the mutation was associated with the development of polycythemia vera, an increase in red blood cells. We are able to test for this variant in dogs.

Our current interpretations of the possible test results are:

Negative:	Animals who test negative for the JAK2 mutation have the normal (wildtype) sequence at the variant location.
Positive Heterozygous:	Animals who test positive heterozygous for the JAK2 mutation have a single copy of the DNA variant.
Positive Homozygous:	Animals who test positive homozygous for the JAK2 mutation have 2 copies of the DNA variant.

Norwich Terrier Cystic Renal Dysplasia and Hepatic Fibrosis Genetic Testing

Cystic Renal Dysplasia and Hepatic Fibrosis is a disease that can be fatal in Norwich Terrier puppies. A causative mutation was identified in a family of Norwich Terriers in the Anttila lab in Finland. The mutation is thought to be inherited as a recessive trait and careful breeding practices can be used to remove the prevalence of this disease.

Our current interpretations of the possible test results are:

Negative:	This dog does not have the INPP5E variant that has been associated with the development of this disease.
Positive Heterozygous:	This dog has one copy of the INPP5E variant. It is thought to be a silent carrier of the disease. The dog would not be expected to develop the disease.
Breeding recommendations:	This is a recessive disease and the breeding of two silent carriers could produce affected puppies that die soon after birth and is not recommended. Breeding of this dog could be acceptable if the dog has many positive characteristics but only if it bred to a dog that is negative for the variant. This breeding should not produce affected puppies. However, it could produce additional silent carriers so the puppies should be screened before selecting them for breeding purposes.
Positive Homozygous:	This dog has two copies of the INPP5E variant and is likely to have significant health issues, including very early death, due to the variant.
Breeding recommendations:	A dog with this result is not recommended for breeding.

As always, breeding decisions should be made carefully. Removal of a significant number of dogs from the breeding population could be very bad for the Norwich Terrier breed. Remember that dogs that carry this mutation may also carry other important good genes that we do not want to lose from the breed.

Newfoundland Subvalvular Aortic Stenosis (SAS) Genetic Testing

Subvalvular aortic stenosis is a hereditary disease that is recognized in several different breeds of dog. We have identified a mutation that is highly associated with the disease in Newfoundland dogs and occasionally other breeds of dogs. The disease is incompletely penetrant- meaning that not all dogs with this mutation will develop SAS. The disease is known to have variable expression, meaning that all dogs with the same mutation will not have the same severity of disease. Although these points are important, the mutation is highly associated with disease and the penetrance is around 80%.

The disease is autosomal dominant and as such dogs have to inherit only a single copy of the mutated gene to show signs of the disease. If they have two copies the likelihood of them developing signs is extremely high, but please keep in mind that we are continually learning about this disease, and our understanding of the risk associated with the mutation may change as we obtain more data.

Our current interpretations of the possible test results are:

Negative:	Negative / Normal (0 copies of the mutated genes). These dogs are genetically clear of the mutation we have identified as a cause of subvalvular aortic stenosis.
Positive Heterozygous:	Heterozygous (1 copy of the mutated gene). Dogs that are heterozygous often show signs of subvalvular aortic stenosis by echocardiogram. Breeding these animals should be done under genetic guidance to clear animals only to gradually reduce the prevalence of this mutation.
Positive Homozygous:	Positive homozygous (2 copies of the mutated gene). Dogs that are positive homozygous are likely to have evidence of subvalvular aortic stenosis by echocardiographic examination. These dogs will pass on the mutation and we recommend that they not be bred.

Importantly, breeding decisions should be made carefully. Removal of a significant number of dogs from the breeding population could be very bad for the newfoundland breed. Remember that dogs that carry this mutation also carry other important good genes that we do not want to lose from the breed.

Boykin Spaniel Hereditary Ataxia Genetic Testing

This neurodegenerative condition has emerged recently in Boykin Spaniels, and appears to be a rare condition. The first signs shown by dogs with this neurodegenerative condition are weakness and loss of coordination in the hind limbs. These signs progress slowly to involve the front legs and tremors of the head develop. Owners note a clear problem with gait within the first 6 months of life, but in retrospect, they comment that as early as 8 weeks, hind limb strength was not normal.

Our team identified the mutation that is associated with this disease in a gene called SLC12A6. It is a recessive condition, and so dogs that have only 1 copy of the gene do not develop clinical signs. Thus far, to the best of our knowledge, 100% of dogs with 2 copies of the gene have developed clinical signs, but this is a relatively new disease and the number of dogs tested is low.

Our current interpretations of the possible test results are:

Negative:	Negative / Normal (0 copies of the mutated genes). This means that your dog does not have the genetic mutation for Cerebellar Degeneration in Boykin spaniels and cannot pass it on to their puppies.
Positive Heterozygous:	Heterozygous (1 copy of the mutated gene). This means that your dog has 1 copy of the genetic mutation and 1 copy of a normal gene. Since this is a recessive disease dogs with 1 mutation do not develop the clinical signs but is considered a carrier of the trait. If your dog has signs of cerebellar disease, it is likely due to another cause. If the dog has many other positive traits it may be reasonable to consider breeding a **Heterozygous** dog to a Negative dog, screening the puppies and trying to select a Negative puppy to keep as a replacement breeding animal in the next litter or so. Over time this will gradually reduce the prevalence of the disease in the breed. We do not recommend breeding a positive heterozygous dog to a positive heterozygous dog since this could produce homozygous dogs which will develop this Disease.
Positive Homozygous:	Positive homozygous means that your dog has 2 copies of the genetic mutation and can be diagnosed with this disease if it is showing signs. These dogs will pass on the mutation and we recommend that they not be bred. A **homozygous** dog has a 100% chance of passing the mutation on to all of its puppies. We would not recommend using these dogs for breeding purposes if possible.

As always, breeding decisions should be made carefully. Removal of a significant number of dogs from the breeding population could be very bad for the Boykin Spaniel breed. Remember that dogs that carry this mutation may also carry other important good genes that we do not want to lose from the breed.

American Staffordshire Terrier Neuronal Ceroid Lipofuscinosis Genetic Testing

This condition is also known as Cerebellar Cortical Degeneration and has been documented in American Staffordshire Terriers as well as mixed breed dogs. It is caused by a mutation in the Arylsulfatase gene (ARSG).

Progressive loss of neurons within the cerebellum, and subsequently in other regions of the brain result initially in subtle signs of loss of balance, particularly when shaking the head, or making a fast turn. These signs progress to an uncoordinated gait, with high stepping, swaying of the trunk and frequent falls. Onset is usually between 3 and 6 years of age but can be earlier or much later and rate of progression is over months to years and varies between dogs.

This is a recessive condition, and so dogs that have only 1 copy of the gene do not develop clinical signs. Of 142 dogs that were homozygous for the mutation, 4 did not show signs at time of testing, thus 2% of dogs that tested positive did not, to our knowledge, develop signs of disease.

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Our current interpretations of the possible test results are:

Negative:	Negative / Normal (0 copies of the mutated genes). This means that your dog does not have the genetic mutation for Cerebellar Degeneration in American Staffordshire Terriers and cannot pass it on to their puppies.
Positive Heterozygous:	Heterozygous (1 copy of the mutated gene). This means that your dog has 1 copy of the genetic mutation and 1 copy of a normal gene. Since this is a recessive disease dogs with 1 mutation do not develop the clinical signs but is considered a carrier of the trait. If your dog has signs of cerebellar disease, it is likely due to another cause. If the dog has many other positive traits it may be reasonable to consider breeding a **Heterozygous** dog to a Negative dog, screening the puppies and trying to select a Negative puppy to keep as a replacement breeding animal in the next litter or so. Over time this will gradually reduce the prevalence of the disease in the breed. We do not recommend breeding a positive heterozygous dog to a positive heterozygous dog since this could produce homozygous dogs which will develop this Disease.
Positive Homozygous:	Positive homozygous means that your dog has 2 copies of the genetic mutation and can be diagnosed with this disease if it is showing signs. These dogs will pass on the mutation and we recommend that they not be bred. A **homozygous** dog has a 100% chance of passing the mutation on to all of its puppies. We would not recommend using these dogs for breeding purposes if possible.

As always, breeding decisions should be made carefully. Removal of a significant number of dogs from the breeding population could be very bad for the American Staffordshire Terrier breed. Remember that dogs that carry this mutation may also carry other important good genes that we do not want to lose from the breed.