

University of Minnesota

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Accession Number: D12-032420

Owner: PFISTER, KIM
RAINMAKER LABS, LLC
W720 COUNTY HWY A
STONE LAKE, WI 54876

Veterinarian:

Site:
Received: 08/01/2012
Reference:
Species: Canine
Breed: Labrador Retriever
Age: 7/21/10 **Sex:** Intact
Female
Weight:

Diagnostic Report: Genetic Test for Canine Exercise Induced Collapse (EIC)

Specimen From: Rainmaker's Rough Ride

With Identification: N/A

With Registration Number: SR63355403

ID Verified by Veterinarian: Not indicated

Result: Clear

See interpretation below.

Orthopedic Foundation for Animals (OFA) International DNA Based Genetic Database: To register your result with the OFA, make a copy of this result page, sign below, and mail WITH FEE to:

Orthopedic Foundation for Animals
2300 E Nifong Blvd
Columbia, MO 65201-3806
or FAX to: 573-875-5073

I hereby certify that the sample submitted was of the animal described on this application. I authorize the OFA to verify any attached laboratory reports with the issuing lab. I further authorize the laboratory issuing the attached documentation to verify the reported test results with the OFA upon their direct request. I authorize the OFA to release all information on the test results thus placing the results in the public domain and I hereby release OFA from any and all liability associated with the release of test information.

Signature of owner or authorized representative: _____

Fees

- Submission fee/individual.....\$15.00
- A litter of 3 or more submitted together.....\$30.00 total
- **Kennel rate:** Individuals submitted as a group, owned/co-owned by the same person
- 5 or more individuals.....\$7.50 each

Payments can be made by check, money order (U.S. funds drawn on a U.S. bank), cash, Visa, or MasterCard, payable to the Orthopedic Foundation for Animals.

Visa/MasterCard Number

Name on Card

Exp Date

CVV (security code)

Affected dogs at any age are no charge

Interpretation

Clear: A clear dog has two copies of the normal *dynamin 1* (DNM1) gene and therefore is extremely unlikely to be susceptible to the classic syndrome of d-EIC (DNM1- associated exercise-induced collapse). However, this result does not rule out the possibility that a dog could have a collapse condition that is different from the condition most Labrador Retrievers have.

Carrier: A carrier dog has one copy of the normal form of the DNM1 gene and one copy of the mutated form of the gene associated with d-EIC susceptibility. A carrier will ON AVERAGE pass the d-EIC gene on to half of their offspring. Our research indicates that two mutated copies of the gene are required for d-EIC susceptibility. Although, a small percentage of carrier dogs have collapsed under instances of intense exercise and/or excitement/stress, the percentage of carrier dogs with a reported collapse is no different from that seen in clear dogs. It appears that the vast majority of these collapses can be attributed to other medical conditions, or their signs are not consistent with the classic signs of d-EIC (see Further Information). In other words, at this time we have no evidence for association of carrier status and d-EIC.

Affected: An affected dog has two copies of the DNM1 gene mutation and is therefore highly susceptible to episodes of d-EIC. Your dog will pass a copy of this mutation on to all of their offspring. Some dogs have died during an EIC episode so we recommend that you have your dog stop exercising at the first signs of any weakness or wobbliness and that you have them avoid collapse "triggers" such as hunt test and field trial training, or upland game hunting. Dogs with susceptibility to d-EIC can often perform mild to moderate exercise without collapsing.

Further Information: Research at the University of Minnesota has identified a genetic mutation that is highly associated with EIC susceptibility. This discovery was published in the October 2008 issue of Nature Genetics, one of the most highly regarded journals of genetic research. The article can be found under the following citation:

Patterson EE, Minor KM, Tchernatynskaia AV, Taylor SM, Shelton GD, and Mickelson JR. (2008). A canine dynamin 1 (*DNM1*) mutation is highly associated with the syndrome of exercise-induced collapse. Nature Genetics 40, 1235-1239.

We are testing for a single DNA base pair change in a specific gene, the DNM1 gene; therefore this can be referred to as a gene mutation test. We now refer to the collapse condition that results from this mutation as DNM1- associated exercise-induced collapse, or d-EIC, to distinguish this specific genetic cause of collapse during exercise from the many other potential causes of collapse during exercise. d-EIC affected dogs can tolerate mild to moderate exercise, but 5 to 20 minutes of strenuous exercise with extreme excitement induces weakness and then collapse. Severely affected dogs may collapse whenever they are exercised to this extent - other dogs only exhibit collapse sporadically.

The first thing noted is usually a rocking or forced gait. The rear limbs then become weak and unable to support weight. Many affected dogs will continue to run while dragging their back legs. Some of the dogs appear to be in-coordinated, especially in the rear limbs, with a wide-based, long, loose stride rather than the short, stiff strides typically associated with muscle weakness. In some dogs the rear limb collapse progresses to forelimb weakness and occasionally to a total inability to move. Muscles are relatively flaccid during collapse, although when restrained in lateral recumbency some dogs exhibit increased extensor tone in the forelimbs. Manipulation and palpation of the muscles, joints, and spine during or after an episode does not seem to cause discomfort. Affected dogs always completely lose their patellar reflexes during collapse and for a short period of time during recovery - even while they are able to walk relatively normally.

Some dogs appear to have a loss of balance and may fall over, particularly as they recover from complete collapse. Most collapsed dogs are totally conscious and alert, still trying to run and retrieve during an episode but as many as 25% of affected dogs have had at least one episode where the owner reports that they appear stunned or disoriented during the episode.

It is common for the symptoms to worsen for 3 to 5 minutes even after exercise has been terminated. **NOTE: A few affected dogs have died during exercise or while resting immediately after an episode of exercise-induced collapse, so an affected dog's exercise should ALWAYS be stopped at the first hint of incoordination or wobbliness.**

Inheritance

We have designated the letter E to indicate the mutant (EIC) form of the DNM1 gene and N to indicate the normal form of the gene. A dog's particular combination of N or E forms of the gene is known as its genotype. The genotype of a normal dog is designated as N/N and is clear of the mutation. The genotype of a d-EIC carrier is designated as E/N, and the genotype of a d-EIC affected dog is designated as E/E.

d-EIC is inherited in an autosomal recessive fashion; therefore both parents must be either carriers (E/N) or affected (E/E) to produce a puppy with d-EIC. The chance of any given puppy with d-EIC (i.e., with the E/E genotype) being born from a litter produced by parents of all possible genotypes is indicated in the following table.

Chance of an EIC affected (E/E) puppy being born from parents of known genotypes

	Sire's Genotype		
	N/N	E/N	E/E

Dam's Genotype			
N/N	0%	0%	0%
E/N	0%	25%	50%
E/E	0%	50%	100%

For example, breeding an E/N sire to an N/N dam can only produce puppies that are E/N or N/N. On the other hand, breeding an E/N sire to an E/E dam gives a 50% chance that a puppy will have EIC, since puppies can be either E/N or E/E. All puppies from the mating of two E/E parents will be E/E, and thus susceptible to d-EIC.

Current data shows that 35-40% of Labrador retrievers are d-EIC carriers; therefore, we do not recommend selecting dogs for breeding based solely on their being N/N for the DNM1 gene. Such a drastic strategy, although more quickly eliminating the possibility of producing E/E and EIC affected dogs, also has the undesired result of potentially losing many of the outstanding exercise and performance traits expected of many superior lines of Labrador Retrievers. A breeding program that utilizes E/N or even E/E dogs can be logically implemented by mating to N/N dogs and retaining E/N or N/N puppies for future breeding that also retain most or all of the other highly desired characteristics. There is no chance of producing an E/E puppy if it is known that at least one of the parents is N/N. In general, we recommend matings that produce fewer carrier (E/N) dogs in each successive generation.

Outlook and Treatment

Dogs with the E/E genotype and exhibiting signs of d-EIC are rarely able to continue training or competition. The best treatment in most dogs consists of avoiding intensive exercise in conjunction with extreme excitement/stress and ending exercise at the first sign of weakness/wobbliness.

Anecdotal reports indicate that medical treatment with the anti-convulsant Phenobarbital has been effective at preventing or decreasing episodes in some dogs when restricting participation in trigger activities was not an option. In particular, some field trial dogs have been able to re-enter training and competition at a high level during treatment. The actual mechanism underlying the effectiveness of Phenobarbital in dogs with d-EIC is uncertain. It is possible that this drug "takes the edge off" and decreases the dog's level of excitement, thus making it less likely that it will have an episode. This drug should only be administered with strict veterinary supervision and monitoring. No treatment has been 100% effective in all dogs.

If a d-EIC affected dog does collapse, (1) make sure that it has unobstructed breathing so it can hyperventilate to blow off heat, (2) offer water and ice orally, and (3) cool the dog by immersing it in cool water or wetting it down. Enforce rest until the dog is fully recovered.

For additional information please refer to the following website:

<http://www.vdl.umn.edu/ourservices/canineneuromuscular/home.html>

***** Disclosure of financial interests: This test was developed through financial support from the AKC Canine Health Foundation. **To date, proceeds from EIC testing at the University of Minnesota have returned more than \$100,000 to the AKC Canine Health Foundation to further its mission to improve the health of all dogs.** Drs. Mickelson, Patterson, and Taylor; and Minor, RN are the owners of US Patent 8,178,297 and a portion of the proceeds will go toward patent royalties.

James E. Collins, DVM, PhD, Diplomate, ACVP

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Fax:	Final:	Written: 08/06/2012	Addendum:
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