

Veterinary Diagnostic Laboratory
College of Veterinary Medicine
1333 Gortner Avenue
St. Paul, MN 55108

1-800-605-8787
612-625-8787
Fax: 612-624-8707
e-mail: vdل@umn.edu
www.vdl.umn.edu

Accession Number: D09-058009

Owner: GRAVES, GENIA
30219 N 164TH AVE
SURPRISE, AZ 85387

Veterinarian:
Sunburst Animal Hospital
5032 W thunderbird Road
Glendale, AZ 85306

Site:
Received: 11/25/2009
Reference:
Species: Canine
Breed: Labrador Retriever
Age: 7/23/08 **Sex:** Intact
Male
Weight:

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

Specimen From: Sure Firen' Charlie

With Identification: N/A

With Registration Number: SR51055801

ID Verified by Veterinarian: No tattoo/microchip

Result: Clear

See following page for interpretation.

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: Your dog is clear of the DNM1 gene mutation highly associated with EIC. This means that your dog has two copies of the normal gene and therefore is highly unlikely to be susceptible to the classic syndrome of EIC. However, this result does not rule out the possibility that your dog could have a collapse condition that is different from the condition most Labrador Retrievers have.

Carrier: Your dog is a carrier of the DNM1 gene mutation highly associated with EIC. This means that your dog has one copy of the normal form of the gene and one copy of the mutated form of the gene associated with EIC susceptibility. Our research indicates that two mutated copies of the gene are almost always required for EIC susceptibility. However, a small percentage of carrier dogs, such as yours, have collapsed under instances of intense exercise and/or excitement/stress. At present, we are unable to state if this collapse is the result of the EIC mutation, or from another unidentified cause. Also, please be aware that a carrier will pass a copy of the EIC gene on to half of its offspring.

Affected: Your dog has two copies of the DNM1 gene mutation highly associated with EIC and is therefore highly susceptible to episodes of EIC. Your dog will pass a copy of this mutation on to all of its 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 EIC can often perform mild to moderate exercise without collapsing.

Further Information

Recent 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. This situation is different from other types of genetic tests that describe only the identification of a DNA marker that could be very far away from the EIC gene, and not be as highly predictive of the true gene and mutation as desired.

Scientists are always cautious in reporting conclusions regarding data to other scientists and to the public, and in so doing usually try not to state anything has a 100% certainty of being correct. However, the chances that the DNM1 mutation is not associated with EIC are less than 1 in a trillion as reported in our Nature Genetics article.

We define EIC as a condition in which collapse usually occurs after 5 - 10 minutes of intense exercise and/or intense excitement/stress. The first signs of an impending episode are typically weakness or wobbliness, especially in the rear legs. Most of the time, a dog with EIC will recover within 15 - 30 minutes of rest. **There are however, affected dogs who 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 in-coordination or wobbliness.**

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 condition is most likely to be autosomal recessive, in which a dog needs to have two mutated copies of the gene (E/E) to be affected. However, it remains possible that a small percentage of dogs with only one copy of the mutated DNM1 gene (E/N carriers) might also collapse under specific circumstances. N/N dogs do not have EIC, however, there are many other causes of collapse that can occur with exercise.

Since available data points to EIC being inherited in a recessive fashion, it requires that both parents be either carriers (E/N) or affected (E/E) to produce a puppy with EIC. The chance of any given puppy with 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

Dam's Genotype	Sire's Genotype		
	N/N	E/N	E/E
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 EIC.

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 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. A few dogs have, however, responded to medical treatment to the degree that they can re-enter training and competition at a high level. However, no treatment has been 100% effective in all dogs.

For additional information please refer to the following website:

www.vdl.umn.edu/vdl/ourservices/canineneuromuscular

***** Disclosure of financial interests: This test was developed through financial support from the AKC Canine Health Foundation. A portion of the proceeds from the test will be returned 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 patent owners of this genetic test and a portion of the proceeds will go toward patent royalties.

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

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Fax Ph (602)9381860

Fax:	Mail:	Written: 12/01/2009	Addendum:
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