### About Cranial Cruciate Ligament Rupture

### Incidence

Cranial cruciate ligament (CCL) rupture is the most common cause of lameness in dogs. The VMTH surgeons treat over 150 patients every year for this issue. It is common for patients with CCL rupture in one knee to rupture the other knee within a year of the initial rupture.

### Causes

The cause of most CCL ruptures is not associated with a traumatic injury; this is referred to as non-contact cruciate rupture. Current knowledge indicates that CCL rupture has a genetic component. Inflammation within the knee contributes to CCL weakening. Over time, the ligament progressively frays until it has completely ruptured.

## **Clinical Signs**

Lameness of one or both hind limbs is often the first sign of CCL rupture in dogs. This lameness can be mild to severe and may have gradual or acute onset. Patients may lean to one side while sitting (pictured below) or hold up one leg while standing.



### **Treatment Options**

CCL rupture causes joint instability or excessive movement of the knee joint. Other structures within the knee, including the menisci cartilage, may also become damaged as a result of this instability.

#### **Conservative Therapy**

CCL ruptures can be treated conservatively with rest, pain-relieving medications, and diet. While this will make the patient more comfortable, it does not reduce the development of arthritis, further joint damage, or resolve lameness.

#### **Surgical Stabilization**

The goal of surgery is NOT to repair the torn CCL. Surgery stabilizes the knee to eliminate abnormal movement. There are currently three surgical procedures that can be used for stabilization: Extra capsular stabilization, Tibial Plateau Leveling Osteotomy (TPLO), and Tibial Tuberosity Advancement (TTA).

Some disadvantages to surgical stabilization include:

- 1. Surgery does not cure the process that caused the CCL to rupture
- 2. There is still a risk of meniscal tear following surgery, requiring another procedure.
- 3. All surgeries carry some risk for complications.
- 4. Surgery is expensive for owners

### Investigators

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#### Labrador Retriever CCL Genetic Study

## Comparative Orthopaedic Research Laboratory

Making Strides Toward Better Orthopaedic Care

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Genetic basis of non-contact cruciate rupture in dogs

Comparative Orthopaedic Research Laboratory SCHOOL OF VETERINARY MEDICINE

### **Genetic Basis of Cranial Cruciate Ligament Rupture**

### Study Information Background

Non-contact cruciate rupture (rupture not associated with any known trauma) occurs in about 8% of the Labrador retriever population. It is responsible for 20% of canine lameness and burdens U.S. pet owners with at least \$1 billion in healthcare costs each year. It is accepted that a majority of ruptures are degenerative, but the explanatory mechanism is not known. The high heritability of the condition suggests a genetic component. Advancements in gene sequencing technology now allow us to look for the genetic mutations responsible for cruciate rupture and other orthopaedic canine diseases.

#### Trait-mapping in Dogs

Individual breeds have not had time to acquire novel genetic mutations in recent centuries. It is more likely that the mutated genes that cause disease were present in dogs before specific breeds were developed. Therefore, when several breeds are commonly affected with the same disease, it is likely that the same mutated gene is responsible in all of them.

### **Study Design**

This research takes a two phase approach: first identify mutations within a breed (Labrador retriever), then narrow results by studying the same genes in other breeds affected with the disease. In the case of non-contact cruciate rupture, Labrador retrievers together with Golden retrievers, Newfoundlands, German shepherds, and Rottweilers will be compared in the second phase of this study.

#### **Genomic Sequencing**

The Dog Genome Sequencing Project was completed in 2005. Just a few years ago, a genome-wide association (GWA) study such as this one would have been prohibitively expensive. Recent advancements in technology have significantly decreased the costs of genetic sequencing. The first GWA study of an orthopaedic disease in dogs was published in 2010. Today, GWA studies are investigating a variety of canine diseases.

# Why is this research important?

After we've identified genetic mutations for non-contact cruciate rupture, the goal of this study is to develop a genetic test. This test would be available for use by any veterinarian. A blood sample taken in puppyhood would identify dogs at risk for non -contact cruciate rupture. This will provide information for purchasing and breeding decisions and allow medical intervention to slow disease progression.

Moreover, it has long been established that dogs and humans share a similar profile of diseases, and cruciate rupture is no exception. Evidence exists for genetic contribution to ACL (anterior cruciate ligament) rupture in humans. Therefore, it is possible that this research will contribute to human as well as veterinary medical knowledge.

#### Funding

This research is supported by the Morris Animal Foundation and the Marjorie Siebert Aylen Foundation.

### "Can my dog participate in the study?"

### **Pedigree Information**

The dogs enrolled in this study must not be closely related to each other. If your dog is AKC registered, the AKC number is used to check whether he/she is related to the dogs currently in our study. If your dog is not registered, we can use the AKC registration numbers of his/her parents. You can find these numbers on the certificate of pedigree that was given to you when you purchased your dog.

Affected dogs can be of any age and must have had a complete rupture of the cruciate ligament in one or both knee joints. Surgery may or may not have been performed.

Unaffected dogs must be 8 years of age or older and have no history of knee problems.

#### If your dog qualifies for the study we will obtain the following:

- A small blood sample from your dog
- Standing x-rays of both knee joints: NO SE-DATION IS REQUIRED. Your dog is in a comfortable standing position while we obtain the images.
- A short questionnaire, completed by you, pertaining to the lifestyle of your dog