

## **LAD –I Variant or LAD-III in German Shepherd Dogs**

A combined leukocyte/platelet disorder has been identified in a German Shepherd Dog associated with a mutation in the gene encoding Kindlin-3. Kindlin-3 is a signal transduction protein vitally important for mediating integrin activation in platelets and leukocytes. Starting at 6 months of age the affected dog had persistently elevated white cell counts, persistent infections including deep pyoderma and pododermatitis, gingivitis, and cellulitis, often accompanied by fever as well as abnormal bleeding. The affected dog was euthanized after developing profuse hemorrhage after a laceration on the lip at 6 years of age. A male sibling of the affected dog bled to death at 3 years of age.

Platelets are small, circulating cytoplasmic fragments that are the first line of defense in stopping the flow of blood from injured blood vessels. An important aspect of platelet function is their ability to stick to each other (aggregate) and plug holes in damaged vessels until blood clotting and tissue repair can occur. The platelets in affected German Shepherd Dogs are unable to respond properly to any platelet activating agent because of a dysfunctional or missing Kindlin-3 protein. Kindlin-3 is necessary for transmitting signals to the platelet surface that allow the platelet to bind fibrinogen and aggregate. Kindlin-3 is also important in transmitting signals to the surface of leukocytes needed for them to leave the blood circulation and enter tissue for fighting infections. Therefore, these dogs are at increased risk for spontaneous hemorrhage and are at high risk for excessive hemorrhage as a result of injury or surgery. They are also at high risk for infections and have persistently elevated leukocyte counts even when treated with antibiotics.

By using DNA testing, affected and carrier animals can be identified by submitting a blood sample through the mail. Carrier detection is vital in controlling spread of inherited defects and DNA testing is the only reliable method of detecting these animals.

The sample required for testing for LAD-1 Variant/LAD-III in German Shepherd Dogs is a 2 ml EDTA tube (purple top) containing at least 1 ml of whole blood. Care should be taken to not cross contaminate samples during collection, particularly if more than one dog is collected at the same time. Samples should be labeled clearly so that there is no confusion regarding sample identification. Samples should be kept cold (ice packs) and shipped overnight to the address below. Take care to make sure tubes are protected well to prevent breakage during shipping. Please do not ship on Friday or the day before a holiday. The fee for testing is \$100 per sample. **Make checks payable to: Auburn University, Department of Pathobiology.**

Please provide the following information on each dog being tested:

**Name and Registration Number** \_\_\_\_\_

**Male or Female** (Circle one)

**Age at time of sampling or Date of Birth** \_\_\_\_\_

**Registration Number of Sire** \_\_\_\_\_

**Registration Number of Dam** \_\_\_\_\_

**I am hereby requesting this sample be tested for the mutation causing an inherited LAD-I Variant/LAD-III syndrome in German Shepherd Dogs. I understand that my individual test results will only be released to me. I certify that I am the owner of this dog. I understand and agree that the results of this test may be confidentially combined with those of other owners and used in aggregate result form for research purposes including publication. I understand in aggregate result form my individual results will not be identifiable specifically to my dog. I release Dr. Boudreaux and any associates working with her and Auburn University from all liability regarding this sample.**

\_\_\_\_\_  
**Owner's Signature**

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Owner's Name (print clearly or type)**

\_\_\_\_\_  
**Telephone number/Email Address**

**Address Results should be sent to:**  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Send samples to: Mary K. Boudreaux, DVM, PhD  
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166 Greene Hall  
College of Veterinary Medicine  
Auburn University, Alabama 36849-5519  
(334) 844-2692