

GENETICS

The Long and Winding Road

Controlling epilepsy has never been quick or easy, but we are making progress.

by C.A. Sharp, Guest Editor

The epilepsy issue in Australian shepherds has always been a tough nut to crack. Initially, people had difficulty accepting that the problem was real; the lack of any positive diagnostic test, the variable course of the disease, and symptoms (seizures) that can also be caused by many other things obscured the fact that epilepsy was spreading through the breed like a malignancy.

Fortunately, we have rallied. The breed community is now meeting the crisis head on. Recognition began with a few people and grew into a breeders' grass-roots movement that cut across working/show and AKC/ASCA lines. Everyone realized it was a breed-wide problem and we all needed to work together or we'd never get the disease under control. After a while, epilepsy became Topic One whenever breed health issues were discussed.

But knowledge that our breed had a serious problem wasn't enough. Most pedigrees were—and remain—so riddled with epilepsy connections that making a low- or even moderate-risk cross is very difficult. We knew that it would take molecular genetics research to give us a DNA screening test to help us bring epilepsy to heel.

For years now, that has been the sticking point: The lack of successful research. The first study, launched in the mid-1990s by VetGen, a commercial laboratory, was abandoned after a few years. They were unable to get sufficient cooperation from the breed community by way of samples. In the meantime, the University of Missouri had started collecting samples for its own planned study. We learned a hard lesson from the demise of the VetGen effort and rallied to support the Canine Epilepsy Network (CEN) study being planned by the University of Missouri. According to the university, CEN has over 3000 Aussie samples, significantly more than they have for any other breed. Of those, over 130 are from affected dogs, with the rest being from normal relatives.

In 2005, the Missouri team announced at the USASA National Specialty that they were close to having a test:

They would have an answer for us in one year, or on the outside, two years! Unfortunately, research is no different than the rest of life—things can go terribly awry when you least expect it. The University of Missouri has not succeeded in finding the genes responsible for epilepsy in Aussies.

Just when things began to look hopeless, two new studies came along. In mid-2007 the European Union decided to provide full funding for a major research project focusing on canine epilepsy. This project involves multiple researchers and a number of different European institutions. One of these scientists, Dr. Hannes Lohi of the University of Helsinki in Finland, is looking at the disease in Aussies. [See "Current Aussie Epilepsy Studies."] He has already gathered samples from nearly a third of the Finnish breed population and CEN has forwarded approximately five dozen samples from its collection to him. European Aussie owners and breeders should do everything in their power to support Dr. Lohi's work.

Things are picking up in the U.S. as well. In September 2007, Pam Douglas, president of Toby's Foundation, an organization dedicated to assisting pet owners with epilepsy-afflicted dogs and supporting epilepsy research, attended the Tufts University Canine Genetics Conference. The conference program focused on epilepsy. There she met Dr. Ned Patterson of the University of Minnesota, a member of CEN who has studied the disease in a number of other breeds. Pam told him about our epilepsy issue. She emphasized the breed community's dedication to pursuing active research. Dr. Patterson indicated interest in looking at Aussies.

Current Aussie Epilepsy Studies

Dr. Ned Patterson, University of Minnesota

Dr. Patterson hopes to determine what regions of chromosomes are associated with epilepsy in Aussies and ESS. These regions may or may not be the same in the two breeds. This will be the first step in identifying the gene or genes that cause the disease. Once the genes are pinpointed, it will be possible to develop a marker test. If the study is successful, studies in other breeds could determine whether they share some of the same mutations that cause the disease in Aussies or ESS and might ultimately lead to DNA tests for those breeds, as well. The results might ultimately be helpful to research focusing on human epilepsy.

Sample submission and consent forms can be downloaded from the ASHGI website: <http://www.ashgi.org/research.htm>

EU Study, Dr. Hannes Lohi (Finland)

If you have friends or know people with Aussies in Europe, make sure they know about this study and urge them to cooperate by providing samples if they have dogs affected with epilepsy.

http://www.koirangeenit.fi/index.php?Itemid=44&id=32&option=com_content&task=view

He had an existing study focusing on English springer spaniels to which he could add another breed, but advised her that he needed a minimum number of samples plus financial support.

Pam assured him that neither samples nor funds were going to be a problem, thanks to the dedication of people in our breed who had already built up a sizable sample collection at CEN. Pam also let him know that the various clubs and fundraising organizations in the breed had already been working hard to get money together to support a viable research project.

Since then, Toby's Foundation, along with the Australian Shepherd Health & Genetics Institute and the United States Australian Shepherd Club and its foundation, USASF, have put together the \$50,000 dollars needed to fund a \$100,000 additional grant that would expand Dr. Patterson's work to include Aussies. The grant is being provided through the AKC Canine Health Foundation (CHF also put up \$50,000 toward the expansion of the ESS study.) The grant amendment received full approval in late 2007.

This level of cooperation is unusual among dog-focused entities. A. Duane Butherus, PhD, chair of the Canine Health Foundation Grants Committee, called our inter-organizational alliance a "distinctive partnership." He went on to state: "The alliance proves the old adage that there is 'strength in numbers,' and makes the case for future partnerships between like-minded clubs."

But it isn't time for us to rest on our laurels. Dr. Patterson could use additional samples from affected dogs and their unaffected relatives two generations any direction. He would also like samples from a few unaffected dogs six years or older who are not related to the affected dogs in the study. These will serve as controls.

These new samples should be sent directly to him. [See *Current Aussie Epilepsy Studies* for details.]

Since Dr. Patterson is a member of CEN, he has access to the samples stored there, but if anyone who has already contributed would like to send him a second sample, our dogs have a virtually limitless supply of DNA. It never hurts to have a little more on hand for important research like this.

The journey toward an epilepsy screening test has been bumpy, sometimes due to circumstances beyond our control. More than a few people have lamented the loss of a dog before it could be sampled, or one whose sample was sent to the VetGen study and effectively lost to us when that study shut down. There is a way you can hedge your bets, not just for epilepsy but for countless health issues, now and into the future: The Canine Health Information Center (CHIC) DNA Repository. [See *Gene Insurance*.]

The road has been long. It still has a few twists and turns we must complete, but at last we seem to be over the crest. Let's all hope that the rest of the trip is an easy downhill ride.

Gene Insurance: The CHIC DNA Repository

CHIC's DNA Repository collects and stores DNA samples from purebred dogs, along with pedigree and phenotypic data. While there are numerous research institutions that have amassed significant numbers of samples and most are willing to share samples with other researchers, without a centralized database to track samples and associated data, researchers may be unaware of available samples that could help their projects. CHIC's centralized repository provides "one-stop shopping" for researchers and facilitates research by expediting sample collection—often one of the most time-consuming aspects of a dog genetics project. It provides researchers with optimized sample sets, whether they are seeking family groups, groupings of affected dogs and unrelated phenotypic normals, or control groups. It also fosters a team effort between breeders and researchers, improving the likelihood of research that will benefit our dogs.

For the dog owner, CHIC's DNA Repository helps prevent "sample fatigue" and allows breeders to take advantage of future DNA-based disease tests. Not long ago, the repository allowed the owner of a deceased Kuvasz to utilize a new PRA test. The dog had been a popular sire and knowing his genetic status for this disease was important. If people have samples on file with CHIC, even from dogs with no known epilepsy connection, when we get an epilepsy test breeders could screen dogs that have already passed and know their genetic status. This could be terribly important to making informed breeding decisions.

Information about sample submission and fees can be found on the CHIC website: <http://www.caninehealthinfo.org/dnabank.html>

ASHGI Website
www.ashgi.org

Toby's Foundation Website
www.tobysfoundation.org