



Cocker Spaniel Update

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Cocker Spaniel DNA Bank Begins with Epilepsy Research

When a puppy buyer called Wilma Parker to report that her Cocker Spaniel had tested positive for hypothyroidism, Parker was surprised. As she began calling owners of littermates to make them aware, she learned that two Cockers from the litter were having seizures.

Parker was baffled. She and her husband, Sam, of West Chester, Ohio, had been breeding Triannon Cocker Spaniels since 1978. Though they had bred many litters, this was the first time they had experienced epilepsy in their dogs.

"When I asked these pet owners why they had not contacted me, they replied that their veterinarians had told them epilepsy was common in Cockers and that seizures could be expected," Parker recalls.

Parker called her friend, Martha Bell, who owned a finished male Cocker from the litter. CH Triannon Wonderful Wizard ("Ozzie") had gone on to sire several litters and had puppies on the ground. Sadly, it turned out that Ozzie, too, developed epilepsy, although the disease did not begin until he was 3 years old.

The sire of the litter was owned by another breeder; he was a handsome show dog and popular stud dog that had produced many offspring. Parker, who owned the dam, felt responsible for the epilepsy and began calling Cocker enthusiasts who owned dogs related to her bitch and who had bred to Ozzie to inform them of the possibility of epilepsy.

"I was on the phone nightly for weeks calling people and letting them know about the epilepsy," Parker says.

When she learned that researchers thought that epilepsy is possibly due to a recessive gene, Parker searched her bitch's pedigree to see if she had any dogs related to the stud dog. She found a few Cockers several generations back.

After realizing the prevalence of epilepsy in the breed, Parker contacted Bobbie Kolehouse, grant and scholarship director for the American Spaniel

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Club Foundation (ASC-F), about the possibility of collecting DNA samples from affected dogs and their relatives and banking them at a facility doing epilepsy research.

Parker and Kolehouse learned that researchers at the University of Missouri College of Veterinary Medicine had been studying canine epilepsy for several years in English Springer Spaniels and Standard Schnauzers and that the researchers had an extensive bank of DNA taken from blood samples. The University of Missouri investigators agreed to add Cocker Spaniels to the epilepsy research.

"The positive aspect of collecting and storing DNA is that then we don't have to collect samples of DNA every time we want to look at a disease or

trait," explains Liz Hansen, the DNA bank project coordinator at the University of Missouri. "In some breeds, breeders send us DNA from every puppy they whelp. Some of these breeders have been doing this for six or seven years, establishing extensive family group data."

The American Spaniel Club already had a comprehensive online health survey with data about epilepsy and other diseases common to Cockers. DNA samples were needed to augment the survey information. Parker began calling owners and breeders from her pedigree asking them to donate blood samples.

"We wanted to collect as many samples from one family as we could get," Parker says. "Other people started helping me recruit participants for the study. Not a single person refused to send DNA. We collected blood samples from about 125 dogs in one family, one of the largest family groups we collected. We set up the Cocker DNA bank in 2002, and the first collection at the ASC National Specialty was in 2004 in Indianapolis."

"We are collecting blood samples from affected and unaffected Cockers from around the world," says Kolehouse. "The data collection is an ongoing process. A statistician and epidemiologist are working with us. The statistician has control of the database, but information about individual dogs is not shared. Even the epidemiologist doesn't know who the dogs are. No names or registration numbers are attached to the data."

Understanding Epilepsy Genetics

Epilepsy affects from 2 percent to 4 percent of Cocker Spaniels, a statistic that is similar to most other breeds, although individual bloodlines may have a higher incident rate. A complex, difficult disease to understand, epilepsy is most likely caused by a biochemical defect in the brain cells or in the brain cell environment.

Idiopathic epilepsy is a diagnosis that comes from excluding other causes

Submitting Blood Samples for Cocker DNA Bank

Cocker Spaniel breeders and enthusiasts who are interested in submitting blood samples for the breed's DNA bank at the University of Missouri College of Veterinary medicine are encouraged to visit the American Spaniel Club Web site at www.asc-cockerspaniel.org for information.

You also may contact Liz Hansen, the DNA bank coordinator at the University of Missouri, by sending an e-mail to HansenL@missouri.edu or calling (573) 884-3712. For information about epilepsy, visit www.canine-epilepsy.net.

Epilepsy Research

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of seizures, such as a brain tumor, brain infection, metabolic disease (such as hypoglycemia or low blood sugar due to various causes or certain types of liver disease), or an abnormally formed brain. In about 66 percent of idiopathic epilepsy cases, dogs have their seizure onset from 1 to 3 years of age. An affected dog has normal physical, neurological and laboratory examinations during intervals between seizures. Confirming the cause of epilepsy is critical to successful treatment.

In 1999, the epilepsy researchers at the University of Missouri and those at the University of Minnesota formed the Canine Epilepsy Research Consortium. The unofficial group includes veterinary and human clinicians, neurologists and geneticists dedicated to better understanding the disease and ultimately reduce disease incidence in dogs.

The members share samples, data and resources to help advance the research. They also collaborate on papers. The consortium includes research teams at the University of Missouri, University of Minnesota and Florida State University and internationally at the

Hospital for Sick Children in Toronto, Canada, and University of Helsinki in Finland. Altogether more than 100 canine breeds are being studied.

When canine epilepsy research began, the canine genome was not yet sequenced. Now, research is significantly easier to find mutated genes once a chromosomal area likely to contain the gene has been identified. The process involves conducting whole genome scans using SNP (single nucleotide polymorphisms) chips to identify specific gene sequence variants. Although canine chromosomes from different dogs are more than 99 percent identical, they still vary at millions of sites. The majority of differences are SNP letter changes.

"We have mapping data that is being analyzed," says Hansen. "If we can identify some mutations, then we can look at other breeds. If we find a mutation in one flushing spaniel, it may be the same in all flushing breeds. If we learn that the mutation involves one or two chromosomes, we can find it quite easily. If not, we can do fine-mapping that involves looking for more markers."

Though a single autosomal recessive gene is suspected to be the epilepsy

gene mutation, investigators won't know definitely until the SNP chip analysis is completed. If epilepsy turns out to be a polygenic condition, it could be more complicated to identify the mutation. The goal is to develop a direct DNA test that will allow breeders to identify which dogs have the potential to develop the disease and which healthy dogs are carriers.

Parker looks forward to the day when a DNA test is available to identify carriers of epilepsy. "Having a genetic test for this disease will help us to make informed decisions when we choose breeding partners," she says. "In the meantime working together to collect blood samples and educate breeders about the disease is the best way to help decrease disease incidence." ■

Purina appreciates the support of the American Spaniel Club and particularly Bobbie Kolehouse, director of the grants committee and member of the scientific research committee of the ASC Foundation, in helping to identify topics for the *Purina Pro Club Cocker Spaniel Update* newsletter.

Canine Phenome Project Enhances Genetic Testing

Epilepsy is one of a handful of diseases in which Cocker Spaniels are included in research at the University of Missouri. Owners whose dogs have been diagnosed with these diseases have sent blood samples to help researchers learn more about them.

Cocker Spaniels are one of about 175 breeds in which owners have submitted blood samples over the past 15 years. The library of DNA consists of more than 57,000 samples that have been collected primarily for University of Missouri genetic research projects working with breed clubs and individuals.

Additionally, stored in freezers at the University of Missouri is DNA from thousands of blood samples submitted to the Canine Health Information Center (CHIC), a canine health information database sponsored by the Orthopedic Foundation for Animals (OFA) and the AKC Canine Health Foundation.

Key to any genetic research is having adequate DNA from affected dogs and their relatives as well as normal controls to conduct comparative analysis. Phenotypic information about dogs whose DNA is stored for study can also be instrumental. This is the purpose of the Canine Phenome Project.

A collaborative effort between the University of Missouri College of Veterinary Medicine and OFA, the Canine Phenome Project began in 2003 with a goal of establishing a broad-based database of phenotypic information and DNA from individual dogs within participating breeds. As technological advances are made that ease the processing of DNA and study of gene mutations, the database and its wealth of information will be available to help researchers studying specific diseases.

The Canine Phenome Project was initiated by Gary Johnson, D.V.M., PH.D., associate professor of veterinary pathobiology at the University of Missouri College of Veterinary Medicine. A molecular geneticist, Johnson studies canine genetics and gene mutations. His work to identify the gene marker for Fanconi syndrome, a late-onset, fatal kidney disease, in Basenjis led to the origin of the Canine Phenome Project.

"The focus was on creating an online interactive

program," Johnson says. "We wanted people to be able to key in information on their individual dogs on an ongoing basis. As we were doing the Fanconi syndrome research, we realized we had lots of DNA, but we didn't know that much about the dogs. People submit blood samples, but then their dogs' health status may change. We wanted to be sure to get as much phenotypic information as possible."

Among the capabilities of the Canine Phenome Project are:

- Collection of blood or tissue samples for DNA testing;
- An online survey to assess disease prevalence and phenotypic information;
- A system for collecting health records for individual dogs; and
- A means for owners to contribute to research that benefits their breed.

Besides the Basenji, participating breeds are Clumber Spaniel, Collie, Kerry Blue Terrier, Coton de Tulear, and Soft-Coated Wheaten Terrier. Parent clubs enroll their breeds and pay a fee covering costs for two years. Parent clubs may elect to cover costs for individuals to enroll their dogs, or individuals may enroll their dogs for a one-time fee of \$40.

Among the benefits for owners who take part in the Canine Phenome Project is the ability to keep track of their dog's health records by entering them in an online health record diary. Owners can include a dog's photo and can scan and upload laboratory results. The information can be shared with veterinarians via a password to the account.

Fine-tuning of the Canine Phenome Project is an ongoing project. The software currently is being updated. With its rich database, including both DNA and phenotypic information, the Canine Phenome Project offers parent clubs and breeders alike a meaningful tool.

For information about the Canine Phenome Project, contact project coordinator Liz Hanson at HansonL@missouri.edu or by calling (573) 884-3712. To view the Web site for the Canine Phenome Project, go to www.caninephenome.org.