

## *Genetics and Canine Seizures: Building Links to Greater Knowledge, Treatments*

Some five percent of all dogs experience seizures, and medication remains an effective cornerstone of treatment for two-thirds of this group that are identified with primary idiopathic epilepsy. The other third however is resistant to medical therapy and these epileptic dogs never attain satisfactory seizure control despite treatment with two or more drugs at maximally tolerated doses.

It is also well known that some Australian Shepherds, Collies and other herding breeds are highly sensitive to certain drugs. In fact, normal doses of some drugs can be fatal for certain dogs in herding breed groups. At Washington State University, researchers in the Veterinary Clinical Pharmacology Laboratory discovered the cause of this multi-drug sensitivity. Sensitive dogs have a mutation in the MDR1 gene, a gene that produces a protein responsible for keeping these drugs away from the brain. Without this protein, certain drugs accumulate in the brain and cause toxicity. Some of these drugs include Ivermectin, loperamide, and several others.

Investigations underway at North Carolina State University-College of Veterinary Medicine are examining how genetics may play a role in why some dogs respond poorly to seizure medications as well as others listed above. Dr. Karen Munana, associate professor of neurology is collaborating with a Dr. Katrina Mealey at Washington State University in the first investigation, which evaluates the effect of a specific known genetic deletion in epileptic dogs of the herding breeds, such as Rough and Smooth-coated Collies, Shetland Sheepdogs, and Australian Shepherds-both standard and miniatures. This deletion makes these dogs more susceptible to side effects of certain drugs, and the study aims to determine whether it also affects the response to seizure medication. The study is funded by an internal grant provided by the North Carolina State University-College of Veterinary Medicine's State Research Support.

“We hope that the MDR study will reveal the missing-links to why some dogs respond poorly to medication,” notes Munana. “Our goal is to gain additional knowledge in this area of study, to be able to better manage the listed breeds of refractory epileptic dogs, thus offering more options for owners and their companions.” Munana also added that by being able to offer more options, there is a greater likelihood that the quality of life for both the pet and owner will be enhanced long-term.

It is estimated that approximately three of every four collies in the United States have the mutant MDR1 gene. The frequency is about the same in France and Australia, so it is unlikely that most Collies worldwide have this mutation. The MDR1 mutation has also been found significantly in Australian Shepherds (both standard and miniature) Shetland Sheepdogs (Shelties), and a variety of mixed-breed dogs.

“Embarking on this study is an exciting project as we move forward in our understanding, diagnosis and treatment of seizures, including the genetic basis of disease,” notes Munana, adding that a separate fund, The Seizure Studies Fund, is now

being developed that will support additional future projects in this important area of veterinary medicine.

“With a simple blood sample and buccal swab, we now have more “tools” to unravel this missing link,” responds Munana. And more options for making a difference in the lives of many pets and their owners.

Recruitment of cases is now underway. If you are a pet owner with any one of the breeds listed above, or any dog with seizures, NCSU-CVM, please contact study coordinator [Julie\\_Osborne@ncsu.edu](mailto:Julie_Osborne@ncsu.edu) or 919-513-6812, to schedule an appointment.

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