Morris Animal Foundation is a nonprofit organization that improves the health and well-being of companion animals and wildlife by funding humane health studies and disseminating information about these studies.

Where Science Meets Hope

Morris Animal FOUNDATION

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vetNEWS

Companion Animal GENETICS TODAY

By Jean Vore

Thanks to genomics research, we expect veterinarians in the near future will be better able to provide real-time data on specific disease risks for their patients, i.e., personalized veterinary care. While we haven't yet reached this level of genomic veterinary medicine, advancements in the field are now evident, and Morris Animal Foundation funding has helped lead the way.

Early Genetic Studies and Screening Tests

Since the early 1960s, Morris Animal Foundation has funded genetic studies that addressed elbow dysplasia and heart disease in dogs. Due in part to our funding, specific genetic screening tests are available for identifying disease carriers in several species. These include, but are not limited to, tests for canine progressive retinal atrophy, dilated cardiomyopathy in Doberman Pinschers, combined immunodeficiency in Arabian horses, equine type I polysaccharide storage myopathy, and hypokalemic polymyopathy in Burmese cats. Recent screening tests for subvalvular aortic stenosis in Newfoundlands and for a behavior and seizure disorder in Belgian Malinois are also now available commercially.

Genetic screening tests like these are helping veterinarians, breeders and owners make informed diagnostic and breeding decisions to reduce the incidence of these inherited diseases.

Building Better Animal Genomes

Analysis of complex diseases is more difficult. With diseases such as cancer and diabetes mellitus, more than one genetic mutation or genomic region is likely involved. Building better species-specific genomic databases, or maps, helps researchers study complex diseases by exploring interactions between genetically related components that may contribute to disease. While this strategy may not yield a simple test, it will help researchers develop better diagnostics and advance patient-tailored treatments for complex diseases.

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Message from Diane Brown, DVM, PhD, DACVP

Chief Scientific Officer
Morris Animal Foundation

Dear Fellow Veterinarians,

Morris Animal Foundation helps lay the groundwork for cutting-edge genomics research that will advance the health of multiple species. This includes researching the use of new genomic technologies to study viral diseases and cancer.

The list of research studies is long and includes study of the diseases that we as veterinarians have struggled with in our patients for years, from ruptured cruciate ligaments and portosystemic shunts in dogs, to exertional rhabdomyolysis in horses, to hypertrophic cardiomyopathy, inflammatory disease and gastrointestinal lymphoma in cats.

We invite you to read on for a glimpse into this broad and important field in animal health. You will see that the seeds planted through our funding in basic genomics research grow into exciting new diagnostics and therapeutics for clinical practitioners on the frontlines of advancing animal health.

Spring is just around the corner, and we take this opportunity to thank you for all you do for the animals we all love.

Sincerely,

Diane

Research Team Maps Specific Genomic Regions Predisposing to RISK OF CANINE LYMPHOMA AND HEMANGIOSARCOMA

By Allen Byrne

Breed susceptibility to cancer has long been reported, but the relationship between inherited traits and susceptibility to cancers has been largely unknown. With funding from the Morris Animal Foundation and the Golden Retriever Foundation, Kerstin Lindblad-Toh, PhD, at the Broad Institute and Uppsala University, Jaime Modiano, DVM, PhD, at the University of Minnesota, and Matthew Breen, PhD, at North Carolina State University, have discovered and characterized genetic and biological cancer mutations in Golden Retrievers.

Their three-year, $1 million project examined genetic traits associated with risk and progression of hemangiosarcoma and lymphoma in Golden Retrievers. They uncovered two specific gene regions that predispose these dogs to lymphoma and hemangiosarcoma and that potentially explain 20 to 50 percent of the total risk for these two cancers in the breed.

"We were intrigued to find two gene regions, which each affected both cancers. Although we were examining B-cell lymphoma, it was also striking that both regions affect T-cell activation. We look forward to examining the overall contribution of these risk factors to these cancers in Golden Retrievers and other breeds," Dr. Lindblad-Toh says.

Emerging information indicates that lymphoma and hemangiosarcoma are very diverse cancers with varied behavior. The results from this study confirmed that theory, although the persistent association between genomic risk markers and the type and magnitude of immune response detected in the tumors "tells us that heritable traits not only contribute to the risk for these two malignancies, but they also might determine how the tumors progress and possibly how they respond to therapy," says Dr. Modiano.

The investigators also learned that abnormalities in the chromosomes in B-cell lymphoma cases are subtle, although there are DNA copy number aberrations (CNAs) in lymphomas of Golden Retrievers. Dr. Breen states that "the presence of these abnormalities might influence the immune response to these tumors."

In contrast, hemangiosarcomas are highly diverse at the chromosomal level, and there were extensive variations in the pattern of abnormalities evident in tumors sampled from different individuals. The results suggest that specific CNAs found in hemangiosarcomas are preferentially associated with certain breeds.

"These findings indicate that several genomically distinct subtypes of the disease may exist," says Dr. Breen.

"The immediate next step is to validate the presence of these risk factors and their association with hemangiosarcoma and lymphoma in independent populations of Golden Retrievers," adds Dr. Modiano. "This is necessary to enable development of tests that could inform breeding decisions." ■

For more information:
Go to http://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1004922

Original image credits:
Page 1: "DNA," Kyle W. Brown
Page 2 (above): "Golden Red," Thomas Stevens

ask THE EXPERT

By Kelly Diehl, DVM, MS, DACVIM

As the Golden Retriever Lifetime Study (GRLS) completes enrollment of its 3000th dog and closes in on its third year, many study participants have asked "When will we see the results of all this data collection? Where does the data go? Who is going to analyze the data?" Morris Animal Foundation recently spoke with Dr. Rod Page, principal investigator for the GRLS, former member of the Morris Animal Foundation Small Animal Scientific Advisory Board, recipient of numerous Morris Animal Foundation grants as well as administrator of one of the largest training grants given by the Morris Animal Foundation. We asked him to answer some questions about the data collection process and analysis.

Morris: Let's begin with how you became involved in the Golden Retriever Lifetime Study?

Dr. Page: I had received some grants from Morris Animal Foundation, and in 2007 I was asked to join the Small Animal Scientific Advisory Board, which is a group of volunteer scientists who review grants submitted to Morris Animal Foundation, in order to ensure the highest quality studies are approved. In 2005, the Flint Animal Cancer Center received a large training grant to help address the need for more veterinary cancer researchers. This generous grant was renewed in 2010, and is one of the largest of its kind. I was part of the initial discussions surrounding the need for a large, longitudinal study that would follow a defined group of dogs for their entire life. We assembled a team of experts to craft a protocol for such a study; the result being the Golden Retriever Lifetime Study.

Morris: What is your experience with cancer in Golden Retrievers? Have you seen any changes in cancer rates, age of onset or other parameters in your practice?

Dr. Page: I don't know if I see many changes. Golden Retrievers have been recognized as a breed that has a high incidence of cancer—we've known this for a long time. It was this increased incidence that was part of our decision to select this breed for study.

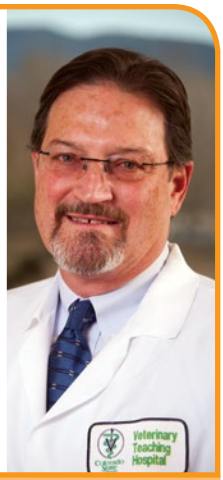
Morris: What happens to the questionnaire data and samples once they are collected?

Dr. Page: Some test results are run immediately through the generous support of Antech laboratories, and those results are returned to the study veterinarians. Then any remaining sample is stored for future analysis. A few samples are earmarked for immediate storage, such as the blood sample for DNA analysis. The questionnaire data is actually analyzed on a running basis every six months; in other words, it isn't being put aside for analysis later. There is also a possibility we will analyze some of the data more frequently as the study progresses. As we analyze this data, we plan on disseminating the results as trends emerge. To help us with this, we are hiring a veterinary epidemiologist onto the GRLS team. Our goal is to get the findings out as quickly as possible once we feel comfortable that the statistics support a solid trend.

The interesting part about the data is that it provides a lifetime story for one individual. This banked data can be looked at in a number of different ways. Once a dog's "life story" is known, researchers can go back and analyze the patient over time. Researchers can also look at any specific point in that dog's life—for example, you can look at a sample of dogs at the same stage of life; what changes are present? Another potential use of the data is to confirm an observation. Suppose someone finds a gene they think might be associated with a disease. They can look at a sample of dogs from the study to look for the gene—did these dogs get sick or exhibit signs of the disease of interest?

Morris: How will the saved samples be used by researchers?

Dr. Page: Researchers will be able to submit grants requesting access to the data through the grant submission process already in place. Their proposals will go through the same approval process as any other grant application. The questionnaire data will be handled a bit differently: we have some partners that will have access to the questionnaire data early in the collection process then the data will be available to other researchers and interested scientists. ■



Rod Page, DVM, Director of the Flint Animal Cancer Center (FACC) at Colorado State University College of Veterinary Medicine and Biomedical Sciences.

Dr. Page received his DVM from Colorado State University College of Veterinary Medicine, before entering the clinical oncology residency program at the Animal Medical Center in New York City. Prior to coming to FACC, Dr. Page taught at Cornell University where he was the founding director of the Sprecher Institute for Comparative Cancer Research.

Continued from page 1

As part of the larger human genome project, the first draft sequences of several animal-specific genomes were assembled, including the mouse in 2002 and the dog in 2004. To expand upon these species-specific resources, Morris Animal Foundation funded studies to improve the cat genome assembly in 2006, and to develop the first drafts of the horse genome in 2006 and the alpaca genome in 2008. Today, the Foundation continues to fund ongoing work to improve the horse, alpaca, dog and cat genomes.

Creating an Even Research Playing Field for Cats

The cat genome assembly continues to lag behind the dog genome, and according to William Murphy, PhD, professor at Texas A&M University and principal investigator on the cat genome project, there is a large fraction, nearly 10 to 15 percent, of the feline genome sequence that is unassembled or unresolved on chromosomes.

"A more detailed assembly will help researchers in their genome-wide association studies to identify genes or groups of genes involved in complex feline diseases," he says.

Another important genomic tool for feline researchers has been the feline single nucleotide polymorphism (SNP) array, which enables investigators to look for genetic predispositions to feline diseases. Researchers can submit study proposals and purchase feline SNP arrays through Morris Animal Foundation's online grant application site at **www.MorrisAnimalFoundation.org/researchers/small-animal/purchase-feline-snp-chip.html**.

The promise of good health for all animals continues to be a priority for the Foundation, and the work in genomics is helping to carry this mission forward. ■

did YOU KNOW?

Construct of the First Cytogenetic Map for Marine Mammals

Many types of cancers in mammals share common genetic mutations. With the help of funding from the Morris Animal Foundation, Matthew Breen, PhD, professor of genomics at North Carolina State University and Frances Gulland, Vet MB, MRCVS, PhD and senior scientist at the Marine Mammal Center in Sausalito, California, have identified genes associated with reproductive and urinary cancers in California sea lions.

"The chromosome abnormalities we identified were detected in numerous genitourinary carcinomas of the sea lions," Dr. Breen says. "Using comparative analyses, we were able to show the same aberrations were present in corresponding tumors from both humans and dogs. These data suggested a strong association between the shared genetic abnormalities and genitourinary cancers in all three species."

Born from this research were the first cytogenetic map of any marine mammal and the creation of the Sea Lion Cancer Consortium (http://www.smru.st-andrews.ac.uk/slicc/), an international group of researchers looking at scientific, environmental and welfare issues associated with the high incidence of cancer in this species. The research team is now investigating whether the identified genes play a role in genitourinary cancers; the information may provide insight into the development of future treatments. ■

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