

# **From Bark to Bedside - Dogs Point to Cancer Culprits**

By Nick Duesbery, Ph.D.

It is exciting when a chance encounter leads to unexpected insight. In this case, a brief chat with my dogs' veterinarian set the stage for what is becoming one of the most thrilling scientific experiences of my career.

That veterinarian, Dr. Roe Froman, happened to be the President of the Clumber Spaniel Health Foundation. Roe mentioned that Clumber Spaniels frequently succumbed to a deadly type of cancer called hemangiosarcoma (HSA).

Coincidentally, I had spent the last decade studying the molecular biology of human sarcomas and was particularly interested in vascular tumors like fibrosarcoma, Kaposi's sarcoma, and angiosarcoma, the human equivalent of HSA.

Our discussion and follow-up conversations set in motion a cascade of events that has led to the formation of the Canine Hereditary Cancer Consortium (CHCC), a unique nationwide coalition of veterinarians, scientists, and physicians united by a common goal: using naturally occurring tumors in dogs to help develop new clinical treatments for rare cancers in humans.

Sarcomas are a type of cancer that develops from muscle, bones, fat and connective tissues. As a scientist, I had worked for years with artificial cell cultures in the laboratory to understand how sarcomas develop in people. Because human sarcomas are rare — less than 1 percent of all adult malignancies — it is difficult to study them directly among patients.

However, many of the sarcomas I find most interesting are far more frequent in dogs. For example, the estimated incidence of angiosarcoma in humans is around 2 in 1 million annually. In contrast, these tumors are relatively common in dogs, particularly in older (8-13 years old), large breeds, such as German Shepherds, Golden Retrievers, and Clumber Spaniels, with an overall incidence more than 100 times greater than in humans.

It was clear from an early stage that dogs offered additional advantages for scientific discovery. Because certain breeds of dogs are prone to this disease there must be an underlying genetic component that is more common in these breeds than in others. This has thrilled the scientific community because it should be easier to find genetic mutations that cause disease. Identifying those mutations are what could eventually lead to better treatments, not only for dogs, but also for humans.

To get our hemangiosarcoma project going, Roe and I organized a small group of scientists at the Van Andel Research Institute. With the generous support of the Canine Health Foundation, we began in 2008 a pilot study of HSA in Clumber Spaniels. Right away, we identified regions of DNA that were associated with this disease. This gave us exciting insights into the biology of HSA that has led to additional research.

The scale and scope of our project took a dramatic turn in April after President Barack Obama announced American Recovery and Reinvestment Act funding for the National Institutes of Health. These funds presented an incredible one-time opportunity to transform our approach to developing new clinical therapies.

In collaboration with Dr. Jeffrey Trent, President and Research Director of the Translational Genomics Research Institute (TGen) and the Van Andel Research Institute, and with Dr. Paul Meltzer, Chief of the Genetics Branch of the National Cancer Institute, we quickly laid the plans for an exciting research effort of unprecedented scale and scope. Our core proposal was fairly straightforward: take advantage of canine genetics and the high incidence of disease in certain breeds to gain insight into the underlying causes of cancer. Then, use this insight to guide clinical trials in humans.

But we added an important and novel twist. Our proposal called for the introduction of a revolutionary new approach, called personalized medicine, to the treatment of dogs and people. Personalized medicine refers to the practice of using an individual's genetic information to guide clinical treatment. It holds the promise that therapies tailored to an individual's genes will increase drug selectivity and response, resulting in better clinical outcomes.

One major obstacle to the advancement of personalized medicine in humans has been the difficulty in identifying cancer causing genetic mutations in the sea of genetic differences that exists between people. However, because of selective breeding in dogs, this genetic background is more uniform and changes in the genetic code may be more easily identified.

Recognizing that no one veterinarian, scientist, or physician possesses the breadth of experience to tackle such a complex project we broadened our consortium to include leading veterinarians, scientists, and physicians from across the nation. The CHCC now includes more than 25 members from 15 academic, clinical and private institutions.

The National Institutes of Health notified us in October that our grant proposal was selected for funding. Now the hard work must begin. In the first two years of the project we will focus our efforts on unraveling the genetic causes of five cancers, angiosarcoma, osteosarcoma, oral melanoma, malignant histiocytosis and non-Hodgkin's lymphoma.

Our goals are ambitious but this is a one-time opportunity to make an incredible difference in the diagnosis and treatment of cancer — not only in dogs, but also in humans. If we are to succeed, we will need help from all quarters. Therefore, I would like to appeal to AKC affiliated dog owners and breed clubs for help.

Should misfortune strike and your dog is diagnosed with cancer, please consider asking your veterinarian to collect blood and tumor samples for our research. If your dog is healthy but is a member of a breed with elevated cancer risk, why not ask your vet to collect an extra tube of blood for us the next time you take your dog for a check up? Together, with your dog's help we can make a difference in the lives of our loved ones.

Additional information about our research, as well as downloadable instructions and consent forms, may be found at our website [www.vai.org/helpingdogs](http://www.vai.org/helpingdogs).

*Dr. Nick Duesbery is Deputy Director of Research Operations for the non-profit Van Andel Research Institute in Grand Rapids, Mich. With CHF permission, the article above was reprinted in Poodle Papers from the Winter 2010 issue of the AKC Canine Health Foundation's newsletter Discoveries.*