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Beagles help hunt for genes associated with canine, human bladder cancer

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Beagles aren't just one of America's most popular dog breeds. According to new research from North Carolina State University, they're also key to new findings about the chromosomal changes associated with urothelial

carcinoma, or bladder cancer. These findings could lead to better diagnostic tests for both canine and human patients.

Urothelial carcinoma is the most common form of bladder cancer in both canines and humans, and certain breeds of dogs – beagles, shelties, and several varieties of terrier – are more prone to the disease than others. Over 40,000 new cases of bladder cancer are estimated to occur in the canine population each year (there are approximately 74,000 new cases per year in humans). Since symptoms often mimic those of routine bladder infections and benign lesions, the disease is difficult to catch early.

Adding to the difficulty of diagnosing the disease is the fact that there is some evidence that performing biopsies on suspicious masses in dogs can lead to spread of the disease and make the cancer harder to treat. "Bladder cancer is relatively treatable and median survival with standard of care therapy is generally around seven months, though about 20 percent of dogs can live for over a year," says Matthew Breen, professor of genomics at NC State and senior author of a paper describing the research. "A confirmed diagnosis generally needs a biopsy specimen, but obtaining these may cause the cancer to disperse across the bladder. What we need is an accurate means of diagnosis with a specimen that is both noninvasive and easy to collect, such as a sample of free-catch urine."

Breen and a team of researchers from NC State decided to look at the genomes of the canine tumors to identify a signature that would identify these cancers. Susan Shapiro, a DVM/Ph.D student in comparative biomedical sciences and the paper's lead author, evaluated a series of canine specimens, isolated DNA samples from dogs with bladder cancer, and looked for genetic similarities.

"We found that in all cases of urothelial carcinoma we evaluated there

was an aberrant number of copies of three particular canine chromosomes: 13, 19, and 36," Shapiro says. "Dogs with bladder cancer would either gain extra copies of chromosomes 13 or 36, or lose one or both copies of chromosome 19.

"These were really exciting findings for us, since all patients showed at least one of these chromosome changes and most commonly a combination of the three," Shapiro adds. "I'm really optimistic that these findings can help us create a reliable diagnostic test to help clinicians catch tumors before they become aggressive and serve as a screening test for predisposed breeds."

Breen decided to take the information one step further and determine the value of the canine data for advancing what is known about human bladder cancer. Collaborating with a group at the University of Utah led by pediatric oncologist Joshua Schiffman, the team mapped the canine genome to that of humans. "We are able to take the genetic information from the dog and rearrange it so that it maps exactly to the human genome," Breen says. "We then look at where the canine 'trouble spots' are on the human genome, and it helps us narrow down the search for genes that may play a role in cancer." With input from Schiffman's lab, Breen and his team found a gene located on human chromosome 8 called PABPC1 that looks very promising for both dogs and humans.

"The fact that we know with almost 100 percent certainty what to look for chromosomally in canine bladder cancer means that we are now are well on the way to developing a highly effective and noninvasive assay for early detection of canine bladder tumors" Breen says. "And the identification of PABPC1 as associated with bladder cancer in both dogs and humans may help us with early detection and better treatment options for those patients as well."

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More information: "Canine urothelial carcinoma: genomically aberrant and comparatively relevant." *Chromosome Research* March 2015 DOI: 10.1007/s10577-015-9471-y

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