



Canine Cancer and Clinical Trials

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Since the inception of the National Cancer Act of 1971, science and medicine have waged an intense battle aimed at conquering human cancers. Although considerable progress has been achieved in terms of our understanding of how individual cancers develop and ultimately progress to metastasis, the disease itself remains a significant health, financial, and emotional concern in the United States some 40 years later. Indeed, the American Cancer Society estimates that approximately 1,530,000 Americans will be newly diagnosed with cancer this year, while another 570,000 individuals will succumb to this deadly disease. Collectively, cancer accounts for nearly 25% of all deaths annually in the United States, and in fact, cancer is now the leading cause of death in Americans younger than 85 years of age.

Cancer itself is essentially a disease of aging, which likely reflects the old age adage stating that “if you live long enough, you’ll eventually die of cancer.” In fact, the current lifetime probability of American men developing cancer is 44%, while that of American women is 37%. Medical advances of the 20th century, particularly the development of antibiotics and vaccines, have greatly extended the overall well-being and lifespans of the average American. Thus, as baby boomers begin entering their 7th and 8th decades of life, one might expect cancer incidence and death rates to increase dramatically

amongst aging Americans. Fortunately, nothing could be further from the truth. In fact, new discoveries and improvements in cancer prevention, early detection, and targeted chemotherapies have significantly decreased cancer death rates over the last decade by nearly 21% in men and 13% in women, and these positive trends are expected to continue even in the face of a rapidly aging population in the United States.

So how do the aforementioned statistics relate to our four-legged friends? Passionate dog lovers are undoubtedly familiar with another old age adage stating that “humans and their dogs tend to look alike over time.” Perhaps this is to be expected and is a natural extension of humans and dogs coexisting and coevolving with one another over the last 15,000-40,000 years, and perhaps this explains the striking parallels between human and canine populations in the United States. For instance, more than 73 million dogs live in the United States and are housed within 40% of American households, of which 54% consider their four-legged friends to be bona fide members of the family. In fact, Americans spend more than \$40 billion each year on canine health care, an expenditure that ranks second only to the costs associated with human health care. In addition, dogs age roughly 5-8 times faster than humans, and recent data indicate that 45% of all American dogs are 6 years of age or older, which translates to a human age equivalent

ranging between 60-95 years of age. Moreover, the average life expectancy of dogs is increasing in response to a variety of factors, including advancements in veterinary medicine, improvements in vaccination and nutritional programs, and even the enforcement of leash laws that have curbed deaths due to automobiles. Thus, the canine population in the United States in many respects mirrors that of its human counterpart, and as such, our “baby boomer” canines are also exhibiting elevated incidence of diseases associated with aging, particularly cancer. In fact, cancer is now a leading killer of dogs, accounting for approximately 20% of all canine deaths and nearly 50% of deaths of dogs older than 10 years of age.

In light of the above parallels between human and canine cancers, it seems befitting to pose the straightforward question as to how knowledge of human cancers can be applied to better treat cancers in dogs and vice versa. A major step in addressing these questions derived from the findings garnered by sequencing and mapping the complete human genome in April 2004, followed by similar sequencing and mapping of the canine genome in December 2005. In doing so, it became immediately apparent that human and dog DNA sequences are significantly more similar as compared to the DNA sequences of mice, which have served as the predominant models for human disease over the last several decades. Importantly, nearly 400 inherited diseases are shared between dogs and humans, including cardiovascular, neurological, and neoplastic disorders, and initial mapping analyses have determined that the underlying gene mutations, amplifications, or deletions leading to cancer development in dogs are reminiscent of those found

in their human DNA counterparts. The fact that identical genetic pathways malfunction during tumor formation in dogs and humans has several important ramifications. First, human and dog tumors are histologically similar in their visual appearance and architecture, indicating that these neoplastic lesions develop and progress along similar tracks (albeit more rapidly in dogs). Second, identifying and mapping canine-specific cancer mutations can be used as markers to map analogous mutations in humans and vice versa. Finally, human and dog tumors that arise in identical organs tend to respond similarly to conventional chemotherapies and treatment regimens. Thus, a chemotherapeutic regimen effective against a particular class of tumor in humans is likely to exhibit similar effectiveness in targeting an analogous tumor in dogs. Along these lines, whereas FDA regulations governing human clinical trials are strict and unyielding, those associated with the administration of novel chemotherapeutics to our canine companions is surprisingly unregulated and typically left to the discretion of individual owners. The implications of this situation are two-fold. First, dog owners tend to be highly motivated in providing their four-legged companions with the highest quality of care possible, and as such, canines with cancer are much more likely to receive novel treatment regimens or drug combinations that would otherwise be unavailable to humans harboring similar neoplasms. And second, developing novel treatment regimens that are effective in treating canine cancers can be instrumental in rapidly translating these therapeutic strategies to improve the clinical course of human malignancies. In fact, the participation of dogs in clinical trials has played an essential

role the development of human cancer treatments, including bone marrow transplants for lymphoid tumors, limb salvaging techniques for osteosarcomas, and novel chemotherapeutics to treat B cell malignancies.

So if your four-legged friend is unfortunate enough to be diagnosed with cancer, remember to be proactive and ask your veterinarian about new and innovative treatment options, and consider enrolling your pup in a clinical trial. Likewise, consider providing blood and tumor samples to ongoing Canine Cancer Consortia, whose mission is to improve the overall health and well-being of canines and humans afflicted with cancer. In doing so, you will be playing an active role in one day saving the lives of your four-legged and two-legged family members and friends.

Information related to ongoing Canine Cancer Consortium initiatives and studies can be obtained at the following addresses:

Canine Hereditary Cancer Consortium (CHCC)
Van Andel Institute
Phone: 616-234-5569
Email: CHCC@vai.org
Website: <http://www.vai.org/Research/Labs/CancerAndDevelopmentalCellBiology/chcc.aspx>

Canine Comparative Oncology & Genomics Consortium (CCOGC)
451 Hungerford Drive, Suite 750
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Email: administration@ccogc.net
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