

Orentreich  
Foundation for the  
Advancement of  
Science, Inc.

# Vital Longevity™

Logo: Life's blood flows through the hourglass; the stopcock represents the alteration of aging and disease as biomedical research progresses.

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## Healthy Pets, Happy People

Because pets contribute so much to human health and longevity, OFAS decided in 2003 to apply its considerable serum banking experience and to extend its resources to include a repository of serum collected from healthy and sick cats and dogs: the Pet Animal Serum Treasury (PAST). These specimens will be used to look for risk factors or early disease biomarkers in pets; early diagnosis can mean a cure. Our motto—PETS HELPING PETS—conveys our position that the pets' welfare comes first; we will conduct no studies that harm pets to benefit human health. If information is learned that furthers human health, so much the better. The Animal Cancer Foundation (ACF) and its founder Dr. Gerald Post, DVM, collaborate with OFAS and generously contribute specimens from cancer patients. The Dalmatian Club of America participates by encouraging members attending national meetings to donate serum (Figure 1). A local free-range cat shelter provides specimens and keeps longitudinal health records on its residents. Other collaborators and collections are always welcome. PAST is part of a new wave in companion animal research.

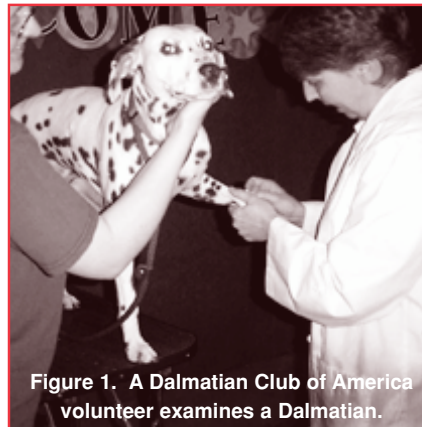


Figure 1. A Dalmatian Club of America volunteer examines a Dalmatian.

## Translational Research

Anyone recently taking a pet for health care had to have been impressed by the options available from preventive medicine and state-of-the-art diagnostic tools to specialist referrals. This explosion in veterinary care opens the door ever wider to the possibilities of combining **comparative pathology**, which identifies commonalities in disease states between species, with **translational research**—that is, enabling science to move from the lab to clinical practice. For example, **comparative oncology** focuses on the striking anatomical, genetic, and biological similarities between certain canine, feline, and human cancers. Such knowledge allows results obtained in clinical trials in dogs and cats, designed to extend life or cure or prevent disease by identifying carcinogens, to become the foundation for human studies. Pets are naturally exposed to many of the same toxins as humans but suffer the consequences more rapidly; by acting as sentinels, they can help to identify dangerous compounds. This is far different from the egregious uses of dogs, usually beagles, in research, e.g., to determine the toxicity of new drugs.

## Cancer in Pets

Cancer, arguably the best target of translational research, occurs spontaneously in pets at twice the rate in humans, with some dog breeds showing genetic predisposition to particular types (Table 1). Breeds are actually partially inbred genetic isolates with disease predispositions derived from a small number of recent ancestors. Like humans, dogs and cats develop tumors later in life, but since the time frame is compressed, identification of relevant exposures or completion of lifelong follow-up after clinical trials becomes feasible. Pets are also unlikely to have been previously treated and thus to have developed drug-resistant tumors before entering clinical trials, a problem common to human studies. The quality of life of animals enrolled in clinical trials is of great concern, allowing less toxic and novel treatment strategies to be tried—strategies that would not be approved for human trials without convincing data from animal studies.

## Best Cancer Models

Not all canine malignancies serve as good models for the corresponding human conditions. Those with comparable behavior and sites for metastases number around twelve and include prostate, bladder, and bone cancer. The canine prostate shares many anatomical and functional similarities to the human gland and undergoes the same multi-step route to carcinogenesis at the same relative age. Also, as in humans, the cancer frequently spreads to bone; however, prostate cancer occurs less commonly in dogs than in men, hindering clinical trials.

A form of bladder cancer, transitional cell carcinoma, occurs in people and in dogs. Suspected etiological agents include hydrocarbons, cigarette smoke, and urinary tryptophan metabolites, similar in humans and dogs. Female dogs urinate less frequently than males and are at 1.5 times greater risk for bladder cancer. A nonsteroidal anti-inflammatory drug, piroxicam, in Phase I and II canine clinical trials proved as active as the best chemotherapeutic agent (cisplatin) tested against canine bladder cancer. Stand-alone therapy with piroxicam for a human clinical trial would not be approved because of the standard dictates of aggressive therapy.

Perhaps the best canine model of human cancer is osteosarcoma, primarily affecting large and giant breeds.

This bone cancer in dogs shares many similarities to the disease in children, including location, aggressiveness, and common site for metastasis, the lung. Amputation and chemotherapy are used in both children and in dogs, but strategies to spare limbs can be more readily carried out in dogs. Novel immunomodulatory agents have been tested in dogs and shown to prolong survival, paving the way to human trials. The National Cancer Institute (NCI) Comparative Oncology Program recently began a clinical trial in dogs with osteosarcoma that involves a new way to shrink tumor blood vessels using the cytotoxic tumor necrosis factor.

Other cancers of interest because of similarities to human tumors include epithelial ovarian, mammary, feline leukemias and lymphomas, kidney (which preferentially affects male dogs and men, possibly because of sex hormones), and certain brain tumors.

## Sentinels

No one intentionally wants their pet to play the role of the canary in the coal mine, but because pets travel less, are more sensitive to toxins (due to their smaller size), and explore their environments by licking, toxic events in them can raise red flags. For example, the recent, tragic pet food contamination serves as a warning against dependence on unregulated foreign sources for food and drugs.

Purdue University School of Veterinary Medicine and Banfield Pet Hospitals, a chain of 314 hospitals across the United States that see 60,000 pets each week, are developing a national pet surveillance system. Timely analysis of health data from these hospitals makes possible rapid detection of infectious and chemical threats to both animals and humans. Dogs and cats are sensitive to most major bioterrorism agents—anthrax, botulism, plague, and tularemia—and any occurrence of these rare diseases in animals can alert officials to imminent danger. The system will also track **zoonoses**—diseases

transmissible between humans and animals, e.g., West Nile Virus—as well as perform **pharmacovigilance**—the monitoring of vaccine- and drug-related adverse events—and look for hot spots of cancer incidence. Unfortunately, this surveillance system awaits a Federal mandate and funding and thus was not ready to respond to the recent food poisoning challenge.

## Animal Tumor Registries and Banks

While many now recognize the potential of this vastly underutilized resource, much must be done to reap the full benefits. Scientists began sequencing both the canine and

feline genomes a number of years ago to facilitate **comparative genomics**; these efforts are now bearing fruit. The domestic dog, because of inbreeding, is an excellent animal for searching for risky genotypes and the cat genome is remarkably similar in its organization to the human.

A large part of the translational endeavor will be the creation of tumor registries, perhaps requiring the reporting of pet cancers to a central agency as we do for human cancer. The first comprehensive pet tumor registry was begun in

California in the late 1960s, but the project, with few exceptions, was not emulated and the idea languished. More recently, Cornell College of Veterinary Medicine and the Animal Cancer Foundation started a pilot program in two New York counties to monitor cancers in cats and dogs. Preliminary reports indicate that breast cancer in dogs is declining, probably due to the rise in spaying, but that lymphoma has risen alarmingly, possibly because of increased use of the herbicide 2,4-D.

Similar to OFAS's PAST, the NCI, in collaboration with the Canine Comparative Oncology and Genomics Consortium, plans to store a 3,000-patient biospecimen collection of tumors, blood, cells, and urine that will be contributed by a community of investigators and made available to qualified researchers.

**Table 1. Dog breeds most likely to get cancer.**

Breed	Most susceptible to
Burmese Mountain Dog	Histiocytic sarcoma (soft tissues)
Boxer	Lymphoma (lymph nodes) Brain cancer
English Bulldog	Astrocytoma (brain)
Cocker Spaniel	Lymphoma (lymph nodes)
Golden and Labrador Retrievers	Lymphoma (lymph nodes) Hemangiosarcoma (blood vessels/spleen)
English Springer Spaniel, Miniature Poodle	Mammary gland (breast)
Pug and Shar-pei	Mast cell (skin)
Greyhound, Rottweiler, Any large or giant breed	Osteosarcoma (bone)
Collie	Nasal cancer
Scottish Terrier and Flat-coated Retriever	Transitional cell carcinoma (bladder) Melanoma (skin/mouth)
Chow Chow	Stomach cancer
Shetland Sheepdog, Scottish Terrier, Collie, Beagle	Bladder cancer

## Information for Donors

The Orentreich Foundation for the Advancement of Science, Inc., was founded in 1961. OFAS is a non-profit institution dedicated to biomedical research to prevent, halt, or reverse those disorders that decrease the quality or length of life. It is duly registered with the US Internal Revenue Service as an Operating Private Foundation under Section 4942(j)(3).

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