2020 ANNUAL REPORT

Contents

Our Mission = Education, Outreach & Research

The National Canine Cancer Foundation strives to eliminate cancer as a major health problem in dogs through education, outreach and research. We save lives through prevention, more accurate, cost effective diagnostic methods as well as better treatments which will diminish the amount of dogs who are suffering from cancer.

Mission

Reflecting our Mission

The National Canine Cancer Foundation strives to eliminate cancer as a major health problem in dogs through education, outreach and research. We save lives through prevention, more accurate, cost effective diagnostic methods as well as better treatments which will diminish the amount of dogs who are suffering from cancer.

Education

One out of every three dogs will get cancer. To help educate and raise awareness for every dog owner we have created one of the most comprehensive canine cancer libraries including the ten early warning signs of cancer in your pet.

Outreach

Every event that the National Canine Cancer Foundation puts on, every page of our website and every product and email we send out is done to raise awareness of canine cancer. The National Canine Cancer Foundations goal is to save dogs lives, educate and reach all dog owners, find new treatment and a cure for canine cancer.

Research

The National Canine Cancer Foundation helps fund universities who are performing cutting edge research toward prevention, finding cures, better treatments, more accurate cost effective diagnostic methods in dealing with cancer and diminishing dogs suffering from cancer.

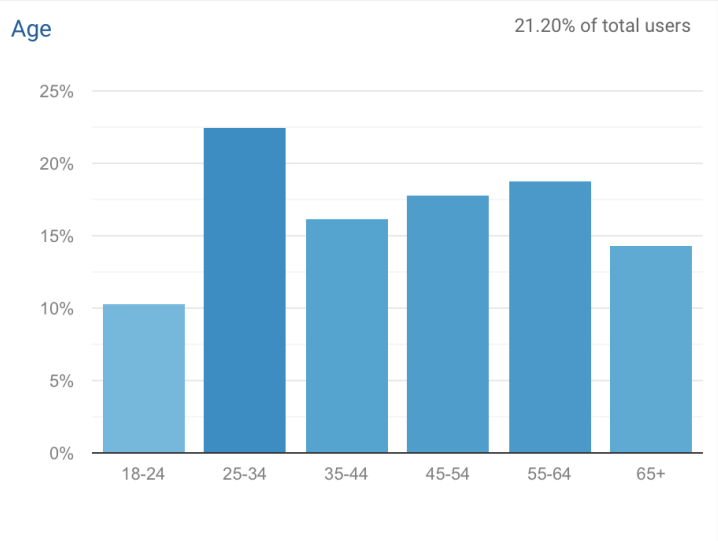
Impact

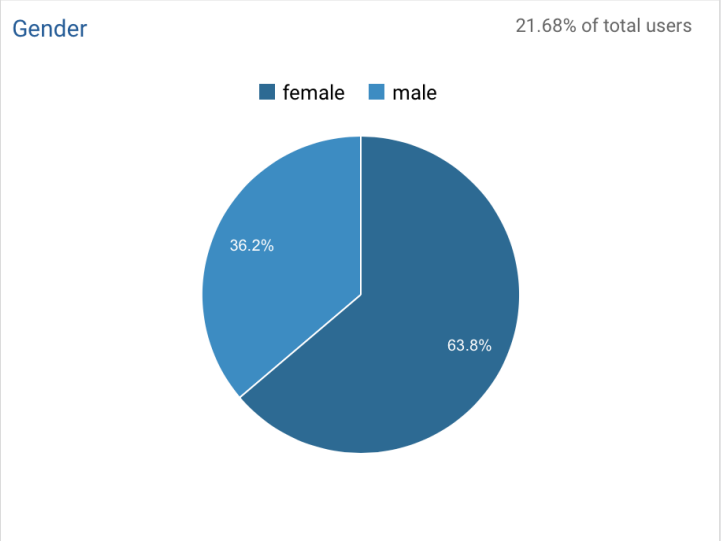
Total Email Database: 80,618

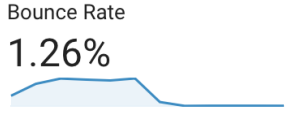
Total Facebook Follower: 51,187

2020 Website Google Analytics

7 Day Active Users	14 Day Active Users	28 Day Active Users
2,042	3,824	7,742
% of Total: 100.00% (2,042)	% of Total: 100.00% (3,824)	% of Total: 100.00% (7,742)







	70,073 % of Total: 100.00% (70,073)
1. Organic Search	**46,150** (65.33%)
2. Direct	**13,362** (18.92%)
3. Social	**6,138** (8.69%)
4. Referral	**3,061** (4.33%)
5. Paid Search	**1,926** (2.73%)
6. (Other)	**5** (0.01%)

Impact

Grants we have funded or are still funding

With 6.5 million new cases of cancer in dogs each year, it is imperative that we continue to fund canine cancer research so we can win this battle. So we can save all of our dog's lives.

Grant No. EP15MN-000 | Development of an Autologous Tumor Lysate Vaccine for Immunotherapy of HSA

Principle Investigator:
G. Elizabeth Pluhar, D.V.M., Ph.D.
Surgeon at the Veterinary Medical Center
Veterinary Clinical Sciences
University of Minnesota

Amount of Grant:
$55,550 -100% Funded

Title:
Development of an Autologous Tumor Lysate Vaccine for Immunotherapy of HSA

Abstract:
Hemangiosarcomas (HSAs) are highly malignant tumours of endothelial origin. They may originate from any vascular site, but the most frequent locations in dogs are the spleen, the right atrium and the skin (Locke and Barber, 2006). The auricular appendage, liver, lungs and kidneys are further recognized primary sites (Brown et al., 1985; Pulley and Stannard,1990; Goldschmidt and Hendrick, 2002). HSAs are common in dogs (Hosgood, 1987; Johnson et al.,1989) and are rarely reported in other species including cats, cattle, sheep and horses (Goldschmidt and Hendrick, 2002). An increased incidence of HSA in man has been shown with exposure to insecticides and irradiation (Paik and Komorowski, 1976; Restucci et al., 2004) as well as vinyl chlorides (Block, 1974). However, primary malignant vascular tumours are rare in people and the prevalence is much lower than in dogs (Oksanen, 1978). Benjamin et al. (1975) suggested that inhalation of radionuclides could trigger canine HSAs, but Oksanen (1978) found no such correlation between the development of these tumours and environmental factors.

Canine splenic HSAs occur mainly in older animals. A predisposition is described for dogs of the German shepherd (Oksanen, 1978; Brown et al., 1985; Johnson et al., 1989, Goritz et al., 2013) and golden and Labrador retriever breeds (Spangler and Culbertson, 1992; Clifford et al., 2000; Schultheiss, 2004; Christensen et al., 2009; Goritz et al., 2013). The boxer, Bernese mountain dog, German pointer and flat-coated retriever are also breeds with a high relative risk (Moe et al., 2008). Microscopically, HSAs consist of irregular vascular channels (‘capillary’ growth pattern) or expanded caverns (‘cavernous’ growth pattern), which are lined by variably differentiated neoplastic endothelial cells (Pulley and Stannard, 1990; Goldschmidt and Hendrick, 2002; Maxie and Robinson, 2007). Socalled ‘honeycomb’ or ‘spongiform’ growth patterns can be found in human HSAs and appear to be equivalent to the cavernous pattern in animals, but with smaller spaces or clefts (Falk et al., 1993). Growth characterized by solid sheets (‘solid’ growth pattern) is seen rarely in animals. These solid HSAs represent a diagnostic challenge as they can mimic other sarcomas (Bettini et al., 2001; Yonemaru et al., 2006; Gamlem and Nordstoga, 2008).

Impact

Grants we have funded or are still funding

Grant No. MC15IN-001 | Biodynamic imagings as a promising strategy for personalized therapy of canine diffuse large B-cell lymphoma
Principle Investigator:
Michael O. Childress, DVM, MS
Assistant Professor of Comparative Oncology
Co-Section Head, Oncology
Purdue Comparative Oncology Programe (PCOP)
Purdue University College of Veterinary Medicine

Amount of Grant:
$145,539 -100% funded

Title:
Biodynamic imaging as a promising strategy for personalized therapy of canine diffuse large B-cell lymphoma.

Abstract:
The responsiveness of canine diffuse large B-cell lymphoma (DLBCL) to standard chemotherapy is highly variable; some dogs are afforded long term survival by chemotherapy, while other dogs' cancers respond poorly. A critical need exists for a method to predict a priori which dogs' cancers will respond best to existing therapies. Biodynamic imaging (BDI) is a highly novel personalized medicine technology which predicts responsiveness of individual patients' cancers to drug treatment by measuring alterations in cellular motility in living tissue biopsy samples exposed to chemotherapy drugs ex vivo. Our central hypotheses are that: 1.) In dogs with untreated DLBCL, BDI data will predict objective response (OR) to chemotherapy and progression free survival time (PFST) following chemotherapy; and 2.) In dogs with relapsed DLBCL, OR rate and PFST will be significantly better in dogs treated with a chemotherapy drug selected for optimal efficacy by BDI when compared to those for dogs treated with an empirically selected chemotherapy drug. Our specific aims are: 1.) To validate BDI as a tool for predicting treatment outcome following standard combination chemotherapy in individual dogs with DLBCL; and 2.) To validate BDI as a tool for selecting optimal chemotherapy drugs for individual dogs' cancers from an array of established therapies. To meet these aims, we will enroll 20 dogs with untreated DLBCL and treat them with standard combination chemotherapy (CHOP). Tumor biopsies taken from each dog at enrollment will be treated with CHOP ex vivo and analyzed using BDI. At the time of cancer relapse, all dogs will undergo a second biopsy, which will also be analyzed with BDI. Ten dogs will then be randomly assigned to empiric rescue chemotherapy with lomustine, and 10 dogs will be randomly assigned to therapy with the single drug with best predicted activity by BDI. Using multivariate logistic regression, BDI data will be statistically correlated with OR rate and PFST following CHOP and rescue chemotherapy. Ultimately, we expect BDI to radically transform the therapy of canine DLBCL by enabling the prediction of response to drug therapy and by informing the selection of optimal therapeutic protocols for individual dogs.

Impact

Grants we have funded or are still funding

Grant No. AB15MN-002 | Preclinical Evaluation and Clinical Translation of Novel Bispecific Targeted Toxins for the Treatment of Sarcomas
Principle Investigator:
Antonella Borgatti, DVM
Assistant Clinical Professor of Oncology
Veterinary Clinical Sciences
University of Minnesota

Amount of Grant:
$151,951 – 100% funded

Title:
Preclinical Evaluation and Clinical Translation of Novel Bispecific Targeted Toxins for the Treatment of Sarcomas

Abstract:
Canine hemangiosarcoma (HSA) is a lethal disease typically arising from the spleen and for which there are no effective treatments. The expected survival for dogs with HSA treated with standard of care therapy is less than 6 months and only 10-15% survive a year or longer. There has been increasing interest in developing novel agents that can specifically target growth factor pathways with reduced toxicity. We developed a bispecific ligand targeted toxin called EGFuPA designed to simultaneously target the epidermal growth factor receptor (EGFR), which is upregulated in a variety of cancers (1), and the urokinase receptor (uPAR), which is expressed on sarcomas, endothelial cells, and tumor vasculature (2). EGF and uPA are conjugated to a truncated Pseudomonas exotoxin (PE) A, with potent anticancer activity via inhibition of protein synthesis (3-5). EGFuPA has shown exquisite activity to kill chemoresistant canine HSA cells, as well as HSA tumor initiating cells at clinically achievable concentrations (6). Additionally, EGFuPA can target tumor cells and the associated vasculature in vivo with high specificity (7). Our goal is to identify an optimal, safe and effective dose of EGFuPA to treat canine hemangiosarcoma in a clinical trial using a continuous reassessment model. We designed and initiated SRCBST, a Phase I/II Bayesian dose-finding trial enrolling dogs with non-metastatic splenic HSA to test the hypothesis that EGFuPA is a safe and effective adjunct to standard care to treat chemoresistant, highly metastatic hemangiosarcoma in dogs. Our specific aim is to determine the activity, toxicity, and optimal dose of EGFuPA in dogs with hemangiosarcoma when given as an adjunct to standard of care surgery (splenectomy) and doxorubicin chemotherapy. We have enrolled 16 dogs thus far and our current funding is sufficient to enroll up to 20 dogs. While the estimates of dose limiting toxicities (<10%) and six-month survival (90%) for the current optimal dose (50 ug/kg) are promising, we have determined that a sample size of 30 dogs will enable us to increase the precision with which we can estimate the occurrence of dose-limiting toxicity, establish an expectation for efficacy, and identify biomarkers for likely responders.

Impact

Grants we have funded or are still funding

Grant No.LT15WI-003 | Discovering genetic and environmental risk factors for bladder cancer in dogs

Principle Investigator:
Lauren Trepanier, DVM, PhD, DACVIM, DACVCP
Professor of Internal Medicine
Department of Medical Sciences, School of Veterinary Medicine
University of Wisconsin-Madison

Amount of Grant:
$79,703 –100% funded

Title:
Discovering genetic and environmental risk factors for bladder cancer in dogs

Abstract:
Bladder cancer (transitional cell carcinoma, TCC) accounts for up to 2% of all canine cancers, and often leads to euthanasia. However, the causes and individual risk factors for this disease are not understood. Human bladder cancer is associated with environmental chemicals such cigarette smoke, industrial pollution, herbicides and pesticides, and arsenic in well water. In dogs, bladder cancer has been associated with older flea and tick dips and some lawn herbicides. However, the predilection for certain breeds such as Scottish terriers, along with these environmental associations, suggest a gene-environment interaction for this cancer in dogs.

Bladder cancer risk in humans is influenced by genetic variation in GSTT1 and GSTM1, which are glutathione- S-transferase (GST) enzymes that detoxify environmental carcinogens. In dogs, only the GSTT1 enzyme has been evaluated to any extent, with 12% of dogs showing very low GSTT1 expression; canine GSTM1 has not yet been characterized. We hypothesize that genetic variants in canine GSTT1 and GSMT1 interact with specific environmental chemicals to increase bladder cancer risk in dogs. The specific aims of this proposal are to determine whether GSTT1 and GSTM1 variants are over-represented in dogs with bladder TCC, compared to age- and breed-matched controls, and to determine whether exposures to aromatic amines, polycyclic aromatic hydrocarbons, herbicides/pesticides, or well water are risk factors for bladder cancer in dogs, particularly when GSTT1 and GSTM1 genotypes are considered.

We will address these aims by resequencing canine GSTT1 and GSTM1 from buccal swab genomic DNA obtained from affected and control dogs. In addition, we will assess environmental exposures over the previous year for both groups using a targeted client questionnaire. Our team includes a veterinary epidemiologist who is a leader in bladder cancer risk studies, a veterinary oncologist who is a leader in clinical trials in canine TCC, a scientist with expertise in predictive models of gene variants, and a statistical geneticist with expertise in evaluating complex gene interactions.

The long-term objective of this study is to identify specific genetic and environmental risk factors for bladder cancer in dogs, so that dog owners can be offered rational screening and cancer prevention and strategies.

Impact

Grants we have funded or are still funding

Grant No. JHK15MN-004 | Discovery and pathogenic significance of chromosome translocations in canine hemangiosarcoma
Principal Investigator:
Jong Hyuk Kim
Research Associate
Veterinary Clinical Sciences
University of Minnesota

Amount of Grant:
$149,860
This grant is still being funded by donations to the NATIONAL CANINE CANCER FOUNDATION and the CHASE AWAY K9 CANCER (A DONOR ADVISED FUND WITHIN THE NCCF).

Title:
Discovery and pathogenic significance of chromosome translocations in canine hemangiosarcoma

Abstract:
Canine hemangiosarcoma (HSA) is a common, devastating, incurable disease of dogs. Recent efforts have started to unravel the molecular ontogeny and pathological features of HSA: specifically, we recently reported the existence of molecular subtypes of HSA that are characterized by angiogenic, inflammatory, and adipogenic signatures, and that these signatures are defined at least in part by the tumor microenvironment. However, specific driver events for canine HSA remain to be identified. Therefore, we have focused our efforts on identification of chromosomal translocations and their putative fusion genes using our unique next generation RNA sequencing (RNA-seq) datasets. The central hypothesis is that unique chromosomal translocations are major determinants of the observed heterogeneity, progression, and resistance to therapy in canine HSA. Firstly, we will confirm newly discovered, recurrent chromosomal translocations and their resulting fusion genes in canine HSA, and identify their association with distinct molecular subtypes of this disease. RNA-seq data (84 HSAs and 13 hematomas including tissues and cell lines) will be used to determine chromosome translocations and transcriptome expression by bioinformatics tools. The resulting fusion genes will be validated using qRT-PCR and FISH. Secondly, we will verify the presence of recurrent fusion genes in archival HSA samples using FISH and immunohistochemistry and determine their utility as diagnostic and prognostic tools. Finally, we will discover effective therapies for canine HSA by targeting fusion genes as driver events in tumor progression. HSA and non-malignant endothelial cells will be genetically engineered to induce or silence the fusion genes using isopropyl-beta-thiogalactopyranoside or transcription activator-like effector nucleases. We will screen drugs to select most effective chemicals via cheminformatics analysis followed by structure-based high throughput virtual screens, and then chemosensitivity assays will be tested in fusion-gene engineered cells. From these approaches, we expect that non-random, recurrent fusion events will be identified that give rise to productive transcripts and to generate fusion proteins as well as they will correlate with molecular subtypes and clinicopathological features. In addition, the fusion genes are anticipated to affect chemosenstivity of canine HSA cells. This project will allow us to develop new diagnostic and prognostic tools as well as novel target-specific chemotherapeutics.

Impact

Grants we have funded or are still funding

Grant No. GL15OH-005 | Targeting Heat Shock Proteins in Canine Lung Cancer: Translating Hypotheses into Clinical Promise
Principle Investigator:
Gwendolen Lorch D.V.M., PhD.
Assistant Professor, Veterinary Clinical Sciences
College of Veterinary Medicine
The Ohio State University

Amount of Grant:
$108,447 – 100% funded

Title:
Targeting Heat Shock Proteins in Canine Lung Cancer: Translating Preclinical Hypotheses into Clinical Promise

Abstract:
Response rates to therapies for canine lung cancer (LC) are poor. The metastatic incidence is ~71% at diagnosis, resulting in a dismal survival time of only 90 days in dogs with stage T3 tumors. While low-grade solitary primary tumors are potentially cured by complete surgical resection, unresectable or metastatic tumors require additional therapy.
Hypotheses: We hypothesize 1) defining canine somatic genomic profiles will identify frequent driver mutations that can be targeted by existing drugs, 2) heat shock protein (Hsp90) inhibitors will provide superior in vitro biologic activity relative the other monotherapies, and 3) Hsp90 therapy will suppress tumor growth in xenograft models.
Aim 1: Define canine LC somatic mutations – DNA copy number alterations (CNAs) and sequence variation – through whole exome sequencing in one breed with high LC prevalence and canine LC cell lines. High interest tumors with many CNAs will be analyzed by ultra-high resolution array comparative genomic hybridization.
Aim 2: Determine (a) the relative activity of Hsp90 when used as a monotherapy on cell viability (defined as the half maximal inhibitory concentrations) compared to treatment with platinum chemotherapies, torceranib, crizotinib, or radiation (b) the biologic activity of Hsp90 inhibitor combined with a Hsp70 inhibitor, (c) the depletion of client protein activation and effector signaling intermediates after Hsp90 treatment using Western blots and, (d) tumor growth inhibition and client protein depletion of Hsp90-treated xenograft models derived from two canine LC cell lines.
Anticipated Outcomes: Identification of LC driver genes and signaling pathways would constitute a major advancement for the development of new targeted therapies and complement our Hsp90 inhibitor studies.
Impact: The discovery of LC pathways of major effect would be immediately pursued with new therapies using current available drugs. This would be the first dog cancer study to apply such a high-yield mutation discovery approach. While canine GWASs can be said to have similar properties, those are limited to germline (and it is unknown what percent of risk genes are therapeutically relevant). Moreover , this would be the first study of a canine cancer that is common in humans and will bring resources to bear on translation.

Impact

Grants we have funded or are still funding

Principle Investigator:
Andrei Thomas-Tikhonenko, Ph.D.
Chair, Cancer Biology Graduate Program
Chief, Division of Cancer Pathobiology
Department of Pathobiology
University of Pennsylvania

Amount of Grant:
$150,000 – 100% funded.

Title:
Therapeutic inhibition of angiogenesis in canine tumors.

Abstract:
During the last decade, human medicine has witnessed the emergence of the new generation of cancer drugs, which were rationally designed to block pathways crucial to tumor growth. One eloquent example is the inhibitors of angiogenesis (the ingrowth of new blood vessels into the tumor). All tumors need a blood supply to provide rapidly dividing cancerous cells with oxygen and nutrients. The task of generating new vessels is two-fold: it requires an increased production of pro-angiogenic molecules and a decreased production of anti-angiogenic molecules. The chief proangiogenic molecule is a protein called VEGF (for Vascular Endothelium Growth Factor.) The chief anti-angiogenic molecule is a protein called TSP (for ThromboSPondin.) That most tumors go to extraordinary lengths to overproduce VEGF and silence TSP attests to the significance of these molecules.
In our proposal, we will focus on three complementary Aims.
1. To generate canine "VEGF trap" proteins capable of binding and sequestering this pro-angiogenic factor. This will be achieved by artificially truncating naturally occurring cell membrane-bound form of VEGF sensors (known as VEGF receptors). The truncated forms typically do not possess pro-angiogenic activities. Instead they channel VEGF into dead-end protein-protein interactions.
2. To test anti-angiogenic activities of polypeptides based on the canine thrombospondin-1 protein. Experimental tumors will be treated with either polypeptides themselves or DNA fragments encoding such peptides.
3. To identify molecules capable of re-activate endogenous (tumor-produced) thrombospondin.
Two classes of molecules are under investigation:
a) compounds that directly increase the half-life of thrombospondin-1 messenger RNA; b) compounds that increase the half-life of the protein called p53, which is the major activator of thrombospondin.
By the end of the 3d year of NCCF-funded research, we expect to have begun clinical trials involving at least some of these newly developed therapeutics. By the very nature of anti-angiogenic compounds, they can be applied towards a wide range of common canine neoplasms ranging from Hemangiosarcoma to breast cancers to B-lymphomas, which collectively account for the majority of cancer-related deaths in dogs.

Impact

Grants we have funded or are still funding

Grant No. DM06CO-002 | Innovative Molecular Targets for Prevention and Treatment of Canine Hemangiosarcoma
Principle Investigator:
Jaime F. Modiano, V.M.D., Ph.D.
Perlman Professor of Oncology/Comparative Medicine
College of Veterinary Medicine and Masonic Cancer Center
University of Minnesota

The National Canine Cancer Foundation has restructered this grant with Dr. Modiano. Instead of one large grant, we are funding the entire study in a series of smaller grants so that we can move the research ahead in a more expedient manner. Listed below are the grants funded and the most recent in the series of grants to be funded.

First in the Series of Grants
Amount of Grant:
$25,000 – 100% funded

Title:
Innovative Molecular Targets for Prevention and Treatment of Canine Hemangiosarcoma

Abstract:
Recent work indicates that some cancers arise from cells that acquire properties of self-renewal that resemble those seen in stem cells. These cells, called “cancer stem cells” or “tumor-initiating cells” have been isolated from a variety of blood-derived tumors (leukemias and multiple myeloma) and solid tumors (colon cancer, breast cancer, brain tumors, and others). However, it is not known if the origin of hemangiosarcoma in dogs (or angiosarcoma in people) conforms to this cancer stem cell theory. We have shown that there is a subpopulation of cells in canine hemangiosarcoma tumors that express cell surface proteins that are consistent with those seen in a cell type called “hemangioblast” that is predicted to exist in the bone marrow as an early progenitor cells that can give rise to both endothelial (blood vessel lining) cells and blood elements (red cells, white cells, and platelets). Although the existence of hemangioblasts remains a matter of some controversy, there is evidence to support their existence in some species. Here, we propose to test the hypothesis that the “progenitor” cells in hemangiosarcoma resemble hemangioblasts both functionally and by assessing their molecular profiles. We predict that hemangiosarcoma cells will show both multipotency and the ability to regenerate cell lines in culture.

Impact

Grants we have funded or are still funding

Second in the Series of Grants
Amount of Grant:
$28,000 – 100% funded

Title:
Tumor-Environment Interactions in Canine Hemangiosarcoma – Principal Investigators: Leslie Sharkey, DVM, PhD, DACVP and Jaime F. Modiano, VMD, PhD

Abstract:
Canine hemangiosarcoma (a tumor of blood vessel lining cells) represents one of the deadliest cancers that affect dogs. While there is predilection for certain organs such as the spleen, skin and heart, these tumors can arise in any organ, they are highly metastatic, and they are poorly responsive to conventional therapies. The common prevalence and poor response of this tumor have led many groups to test new experimental therapies, including metronomic chemotherapy, various anti-angiogenic strategies, the histone deacetylase inhibitor (DNA modifier) SAHA (vorinostat), immunotherapeutic approaches, protein tyrosine kinase inhibitors, and others. While these approaches have reported anecdotal success, none have shown conclusively that they can produce equal or better responses than the current standard of care (surgery plus cytotoxic chemotherapy).

Our group has devoted considerable resources to understand the etiology of hemangiosarcoma at the cellular and the molecular level, hoping to generate new knowledge that might lead to more successful management of this cancer. Our preliminary results suggest that a specialized cell type that participates in blood vessel formation (hemangioblast) may give rise to the tumors. These cells have the potential to alter their surroundings to maximize their potential for growth and survival. Furthermore, they have certain features that could be responsible for the resistance of these tumors to conventional chemotherapy drugs. These findings have encouraged us to be circumspect about the dogma surrounding hemangiosarcoma. In fact, these tumors are complex tissues, and it is not clear which components within this tissue arise from the malignant population and which components are derived from normal cells recruited into (or responding against) the malignant cells. In fact, it is well established that many tumor lesions are comprised of a mix of malignant and non-malignant origin cells, and that the behavior of the non-malignant origin cells can be pivotal in influencing the biological behavior of neoplastic cells and thus patient prognosis. This raises several important questions regarding the aggressive biological behavior of canine hemangiosarcoma. To begin to answer how the local tissue microenvironment contributes to the biological behavior of canine hemangiosarcoma, we propose to define which components of canine hemangiosarcoma lesions arise from a malignant cell population and which components are derived from normal cells using in vivo models. Increasing evidence suggests that many cancers rely on the activity of normal surrounding tissue to achieve their malignant phenotype, and modification of their environment may influence the biological behavior of the tumor. Once we have a better understanding of the interactions between the malignant hemangiosarcoma cells and the normal supporting microenvironment cells (inflammatory, angiogenic, stromal, and nerves), will we be able to determine how to develop strategies to target microenvironmental factors to improve the therapeutic options for this disease.

Impact

Grants we have funded or are still funding

Third in the Series of Grants
Amount of Grant:
$55,550 – 100% funded

Title:
Tumor-Environment Interactions in Canine Hemangiosarcoma – Principal Investigators: Jaime F. Modiano, VMD, PhD

Abstract:
This application is designed to continue past work supported by NCCF to define the molecular pathogenesis of canine hemangiosarcoma and develop rational and effective strategies for prevention, diagnosis, and treatment.
Our group has devoted considerable resources to understand the etiology of hemangiosarcoma at the cellular and the molecular level, helping to generate new knowledge that might lead to more successful management of this cancer. The underlying theme of work supported by NCCF in our laboratories has focused on answering three fundamental questions:

1. Does the local tissue microenvironment contribute to the biological behavior of canine hemangiosarcoma?
2. Does the local microenvironment of hemangiosarcoma differ among tumors arising at different sites or in different organs (for example, spleen, heart, liver, skin)?
3. Can we target the microenvironment to deprive the tumors of specific factors that are essential for tumor growth and survival, or to eliminate the capacity of the tumor to spread to distant sites?

Data from Milestone Project 2 showed that hemangiosarcoma cells have broad potential for growth at various sites in xenogeneic hosts (immunocompromised mice) with no apparent preferences based on their site of origin. This project also supported work that suggests canine hemangiosarcoma conforms to the hierarchical (“cancer stem cells”) model of cancer.

Our data suggest that local tissue microenvironment does influence growth and progression of canine hemangiosarcoma, although the precise mechanisms that account for this remain to be determined. On the other hand, there appear to be no major differences between hemangiosarcoma cells that arise from distinct anatomical sites with regard to growth potential and tumor formation, although it remains possible that the observed absence of site specificity was due to selection of tumors with high metastatic potential. The potential to target the microenvironment for therapy is the focus for this Milestone 3 project. The hypothesis is that preferential bias towards use of different chemokine receptors alters the growth, differentiation and/or lineage commitment of hemangiosarcoma. The results from this project will guide development of subsequent milestones, with the ultimate goal to fundamentally understand the disease in order to develop effective means for timely diagnosis and therapy.

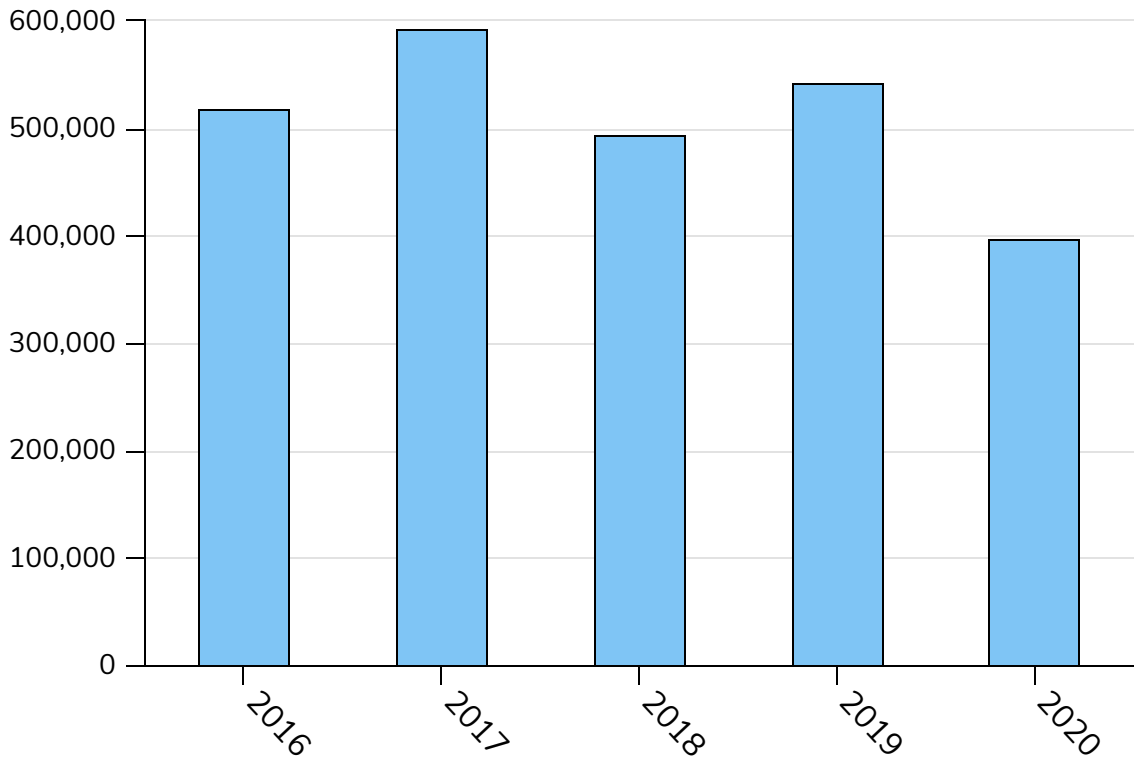
Finance

Donations

Donations to National Canine Cancer Foundations were significantly down in the year 2020 due to Covid-19. Normally, a significant amount of our donations come from live events such as our Bark N' Bowl's in various cities and our Cincy Pup Crawl. All these events were cancelled in 2020. In fact, the NCCF has not been able to hold any live events in 2021 and it is unclear when it will be safe to hold them in the future.

We are continually trying to find new ways to raise money through online opportunities including unique virtual events. Another stream of revenue will come from new and different designs of merchandise.

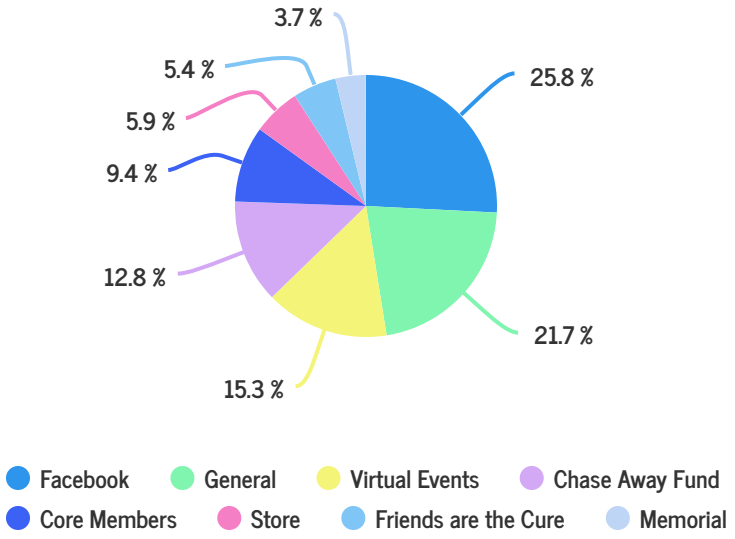
Below is a five years chart of total donations per year. 2020 has been $100,000 to $200,000 less that the past years.



Finance

Breakdown of Donations

This breakdown shows the sources through which donations are received.



Breakdown of Expenses

Expenses are shown in three categories:

1. Program - the cost of grants, outreach and education.
2. Fundraising - raising funds to facilitate our program.
3. Administrative - the cost of operating the non-profit.