ABCF MESSENGER

Official Newsletter of the American Boxer Charitable Foundation

November 2019

PRESIDENT'S REPORT

The American Boxer Charitable Foundation continues to have a very important record of canine health research grant support in collaboration with the AKC Canine Health Foundation (CHF). ABCF grant support now totals $1,767,325.

With the help of ABCF donors, CHF has been able to double annual canine health research programs funding since 2015, with over $3 million in research and educational grants program funding awarded already in 2019. ABCF has shared in this success, and as a result, CHF can now put more dollars to work directly for Boxer research diseases. CHF once again earned the highest industry standard four-star Charity Navigator and GuideStar Platinum rating in 2019. These measures assure the members of the ABCF that CHF is a trusted partner for canine health research through their research and educational programs.

Exciting news this summer and fall has been progress in hemangiosarcoma research, which is, as you know, a particularly challenging area of canine cancer. A new multi-institutional/multi-investigator clinical trial has been launched to investigate the promising research that showed propranolol given in conjunction with hemangiosarcoma standard of care therapy may potentiate treatment and slow cancer progression. Also interesting are preliminary findings from Dr. Breitschwerdt's research to investigate a possible association between Bartonellosis and hemangiosarcoma where his team has identified Bartonella in about 75% of hemangiosarcoma tumors in dogs tested to date; this work is ongoing. Progress continues with Dr. Modiano's group on Boxer/Golden/Portuguese Water Dog study to find a means for early diagnosis and prevention of hemangiosarcoma – work is ongoing to meet the lofty goals of this research, demonstrating the power of collaboration between breed organizations.

The ABC's investment in new and ongoing research for canine degenerative myelopathy continues and to date has led directly to genetic, pathologic and biomarker discoveries for this devastating disease, with research still underway. ABCF has led the way in the study of this canine disease.

ABCF support for research across program areas and all aspects of health and disease in dogs, including cancer, neurologic disease, kidney disease,

inflammatory bowel disease, and autoimmune disease, reproductive disease, regenerative medicine and stem cell research, corneal disease, atopy, tick-borne disease, and emerging infectious diseases such as bartonellosis and brucellosis. As we know, scientific research is a series of building blocks that over time result in incremental change for better health for dogs.

The research study to fully characterize kidney disease in Boxer continues, and the need for samples continues to slow the progress of this study.

Additional ongoing studies specific to Boxers are addressing hemangiosarcoma, genetic and environmental risk factors for lymphoma, cardiomyopathy, both inherited and acquired through potential association with infectious disease and diet, and now-published study on steroid-responsive meningitis-arteritis (SRMA) in young Boxer dogs.

The American Boxer Charitable Foundation is most appreciative for your donations, and continued support in the quest for the betterment of Boxer health.

Respectfully

Bill Truesdale

2019 ABCF Fundraiser

The 2019 Auction was a success with many participants who came to celebrate Boxer Health. Your presence was a testimony of commitment and dedication in the pursuit of healthier living Boxers.

A special thanks to the folks who brought us so many beautiful and memorable auction items. We truly appreciate your kindness and assure you that all proceeds derived from the auction is designated to Boxer Health research.

ABCF is currently invested in multiple studies of Boxer disease, and Thanks to your generosity, we are funding studies that may also benefit humans.

Thank you volunteers for your amazing contribution. We could not have done it without you. I look forward to 2020 Auction and many more participants.

Respectfully,

Tina Truesdale

Auction chair

FROM THE TREASURER

Wow, what a year and what an experience! This first year as the Foundation's Treasurer has been one of learning, excitement and finding a true sense of the value of what our Foundation does.

With the help of my two predecessors, Sharon Fosseen and Joyce Baker-Brown, we have been able to consolidate our various assets into two manageable entities. We moved from Wells Fargo Bank to Bank of America where we combined checking, savings, annuities and small investment accounts. Under our Finance Committee (chaired by Sharon Steckler, along with fellow member Bob Erickson and me), we were able to convert our large Lithium investment portfolio into an Endowment and investment account with Charles Schwab.

Interacting with the wonderful people that make up this Foundation through membership and memorial donations, I realized how far and wide the love of our Breed reaches. For those who have been patient with me as I transitioned into the person responsible for memorial notifications, I am forever grateful.

Now to answer the question, "How viable are we as a Foundation?" We are not only solvent, but we are financially healthy. We have over $350,000.00 in our operating checking and savings accounts. We have a Certificate of Deposit for $60,000.00 and our Endowment investments exceed $900,000.00.

With that being said, we are also focused on maintaining and expanding our positions for the future of our Foundation and its mission of supporting research into the medical and health needs of our Boxers. As we reach the end of the year and we look forward to the inevitable income taxes, please think of ABCF in your end-of-the-year donations. Remember ABCF is totally operated and supported by volunteers. No one is paid for their services. So, every dollar of your donation goes directly to our primary purpose of supporting research into the health and well being of our beloved Boxer breed.

Thank you to all of you for enabling me to have this wonderful experience. And remember, our Boxers love you.

Gary Ryan

ABCF is please to have several new members serving on the ABCF Board. Each newsletter we will introduce one of the new members. This month we introduce Gary T Ryan, Ph.D.

A life member of the American Boxer Club and current Treasurer of the American Boxer Charitable Foundation, I've owned and loved Boxers for over 60 years. And as we all know, once a Boxer enters your life you are never the same. And that's a good thing.

On the personal front, I received my M.A. from the University of Rhode Island in 1972 and my Ph.D. from the University of Texas at Austin in 1978. My academic preparation was in the areas of communications and systems analysis and design.

After seeing the world nearly five times while serving thirty-nine years in the U.S. Navy, I decided to settle on 24 beautiful acres less than three miles from Gettysburg's Square. In the morning with the sun rising, I can look out of my kitchen windows and see the "Big Roundtop" and the Battlefield. Life is good and allows time to enjoy traveling with my bride, exploring and studying history and of course loving and showing our Boxers.

During my career, I served as a civilian senior staff officer for the Department of Defense working at the Defense Agency (DIA) in Washington DC. I retired from DIA in August 2015. Prior to DIA, I was the principal partner for Gettysburg Integrated Solutions, LLC (GIS). My firm provided consulting support to corporate, federal, non-governmental agencies, Department of Defense and various institutions of higher education. We employed 53 people and billed in excess of $10M per year.

Through the years I've been able to develop extensive government program management experience in the area of intelligence support to combat operations, systems integration, financial planning, programmatics and Congressional liaison. Before owing my own corporation, I retired for the first time in 2004. When I retired I was the Deputy Associate Director of Naval Intelligence (N2R) where I was responsible for overseeing a program in excess of $180M per year. In addition to my Naval Service, I've had over twenty-five years of experience in higher education as a University Administrator and educator.

Real Life Research- Theresa Garton's Experience with "Shine On"

By Theresa Garton

In July, I got a surprise call from Dr. Jaime Modiano. He is a very well known veterinary cancer researcher, who is studying a number of cancers, including hemangiosarcoma. It was pretty thrilling, and a little confusing to get a call, in which he left me his personal cell phone number! He was also very careful to repeat, several times, in the message, that there was no emergency, and that I shouldn't worry about my dog, which of course was not completely reassuring.

In the article below, hopefully I have summarized what Dr. Modiano told me on the phone correctly! Many of us have been participating in this study the phase 3 arm of his hemangiosarcoma study, known as "SHINE ON." Dr. Modiano and his team have been recruiting dogs that meet the following criteria:

• Must be an AKC-registered or pedigreed Golden Retriever, Portuguese Water Dog, or Boxer.

• Dogs must be at least 6 years old and in good general health

• Owners must agree to submit blood samples for re-testing according to the study guidelines

• Dog/Owner must live in the contiguous 48 states

Those of us participating sign up, and then are notified when they are ready for our samples. A LOT of people want to participate in the study, and they have limited capacity to process the samples. We then make an appointment with our local vet to have blood drawn, and samples shipped to MN expeditiously. As noted above, your dog may be called back for a second sample. Also, if you are a veterinarian, you must have another veterinarian draw the samples. The samples cannot be drawn by the dog's owner.

I have so far had 3 of my own dogs participating in the study, and at least one more of my breeding. My dogs participating are all related, either cousins, or siblings, full or half. 2 of the dogs of my breeding have been called back for a second blood draw, 2 have not One of my dogs, a cousin of my bitch Robin, passed away at the age of 12, about two months after his second sample, but I was also never contacted about his results being unusual. The two that were not called back for a second blood draw are siblings of Robin, either full or half brothers. Dr. Modiano had called me about my bitch, Robin, who is 10 years old, and to all outward appearances, extremely healthy, about a month after her second sample was drawn.

The purpose of the blood draws is to identify hemangiosarcoma cells in the blood. They are currently in Phase 3 of the SHINE ON study, which will investigate whether cells in the blood can help identify hemangiosarcoma in it's earliest stages, and also whether treatment with a drug called eBAT can prevent hemangiosarcoma tumors from developing, if administered before tumors have developed. They use an artificial intelligence program to randomly select some of the dogs who have volunteered samples, for a second blood draw. When certain criteria are met after that second blood draw, some dogs are "un-blinded" , and identified as potential subjects for the experimental part of the study.

When Dr. Modiano called, he explained that Robin had been "unblinded" due to consistently high levels of the cells that seem to indicate a high risk for hemangiosarcoma. He explained I had 2 choices. I could engage in "watchful waiting", waiting to see if she developed hemangiosarcoma - or not. OR, I could attempt to get her enrolled in the experimental study, where she would receive the experimental drug, and hopefully have a better change to avoid, or postpone, development of hemangiosarcoma tumors.

He further explained what eBAT was. This is my understanding from my notes that I took on the phone while talking with Dr. Modiano. eBAT is a biologic chemotherapy that is an amalgamation of 3 proteins. These are 1- certain epithilial growth factor receptors 2 - urokinase 3- a toxin from Pseudomonas bacteria. The pseudomonas toxin is normally very toxic, but has been altered to make it less toxic. The drug has so far been very well tolerated by the dogs who have received it. The drug targets hemangiosarcoma cells and tumors, and attacks them, as well as the macrophages, or inflammatory blood cells that maintain the tumors. The hope is that this drug will decrease the hemangiosarcoma cells, and reduce the future risk of hemangiosarcoma tumors.

He also explained that the drug is very well tolerated. He reported that the most common side effect was hypotension, or low blood pressure. They have discovered this is less frequent if the infusion is done slowly. He said about 40% of the dogs receiving the infusion have hypotension, and that those who have it once are more likely to have it with further infusions. He explained that even if this developed, it should had been easily managed, and had not resulted in long lasting harm to the dogs. The other side effect they had noticed was elevated liver function tests. He explained that this was much less common than the low blood pressure. He said all dogs who had developed this, save one, had their liver function tests return to normal as they got further away from the infusion. The one dog who had maintained elevated liver function tests was being monitored, and had not had other problems at the time I spoke with Dr. Modiano, as I understood it.

Given my options, I chose the second route, to try to get her enrolled in the study. She had a large number of tests - X-rays, ultrasounds, blood work - to discover whether she already had hemangiosarcoma tumors we did not know about. None were identified. Therefore, we were cleared by the study to schedule a trip to MN. My husband and stepdaughter made a road trip from Oklahoma City to St. Paul. There, Robin saw another

oncologist who works with Dr. Modiano, and some of the tests were repeated. They still did not discover any hemangiosarcoma tumors. So, she was accepted into the study. They did determine that she had an asymptomatic UTI, and treated her for that.

We were offered a study to determine whether she had hemangiosarcoma tumors around her heart. However, this was not required. I had to pay for her tests at my local vet, but all of her care in MN was paid for by the study. The study of her heart would not have been paid for by the study, and we declined to do that. She had had several chest x-rays, and other studies, so we felt the risk of tumors around her heart was very low.

She received an infusion of the eBAT biologic, 3 times over a week. They only give the infusion Monday, Wednesday, and Friday. You must also have an evaluation prior to starting the infusions, so the travel commitment requires a stay over the weekend. Robin had her initial evaluation on Thursday. We did not receive word until very late in the evening that she was accepted for the infusions. On the day of the infusions, she was dropped off at 7:30 AM. They usually called to have her picked up in the early afternoon, from 1 PM to 3 PM She was released on the day of the third infusion, to return home. Dr. Modiano said that they do further evaluations, often on the day after the third infusion, but try to move through this expeditiously on the last infusion day for people who have to travel long distances.

Robin tolerated the infusions very well. She seems to have had no side effects at all, and appears completely normal, her usual self. She will have to supply blood tests a month later, and then 3-6 months later, pending results.

Hopefully this description of our experience has been instructive, and interesting. Most of all, here's hoping that this study will lead to a real solution for hemangiosarcoma!

Research Updates- Your ABCF Dollars at work!

Grant 01760-T: Use of Gene Therapy to Treat Dilated Cardiomyopathy

Principal Investigator: Margaret Sleeper, BS, VMD, University of Florida

Original Project Description: Dilated cardiomyopathy (DCM) is the second most common cause of heart disease in dogs, and medical management of the secondary signs is the only therapeutic option. The outcome for affected dogs depends on the stage of disease and the breed. Once diagnosed, dogs typically exhibit rapid and uniform progression to congestive heart failure (CHF), with most living less than 6 months. Previous research has shown that heart function is critically dependent upon calcium channel function. These gate-like channels found within the wall of cardiac muscle cells open and close, allowing calcium ions to flow into the cell. Calcium influx then regulates muscle contraction. Heart disease is strongly associated with malfunctioning calcium channels within cardiac cells. Gene transfer strategies to reduce calcium cycling abnormalities improve heart function in animal models as well as in human clinical trials. In this study, Dr. Sleeper will conduct a placebo-controlled, double blinded study to evaluate gene delivery approaches for treatment of Doberman Pinschers affected with DCM and CHF. If results show that the gene delivery slows progression of heart failure in Dobermans with DCM, the results will have significant ramifications for all dogs with heart disease, as calcium handling proteins are abnormally expressed in dogs with heart disease of varying causes.

Update: To date, 9 dogs have been screened for enrollment in this study, four dogs have undergone treatment (enrolled), one dog is scheduled for treatment (enrollment), one dog had a fatal arrhythmia while waiting for vector antibody titer results and three dogs have had vector antibody titers too high to safely treat. Data collection is therefore underway and as more dogs are treated interim statistical analysis will be performed to evaluate benefit or negative impact of treatment. We continue to advertise the clinical trial by various methods.

Grant 02502: Precision Medicine for Canine Lymphoma By Domenico Santoro, DVM, University of Florida Health Science Center

Principal Investigator: Nicole Mason, BVetMed, PHD, University of Pennsylavania

Original Project Description: The clinical response of dogs with lymphoma to multi-agent chemotherapy is highly variable. Although up to 85% of dogs respond initially, some relapse within weeks, while others enjoy remission times of two years. This heterogeneity in clinical response

is in part explained by the recognition that "lymphoma" is not a single disease entity, but consists of different subtypes that can be characterized on a molecular level by mutations in specific genes. As in human medicine, it follows that different lymphoma subtypes, driven by different molecular mechanisms, may respond better to therapies that are specifically selected to inhibit the driver mechanisms within that patient's tumor. Recent work using sophisticated genetic sequencing tools (next-generation sequencing (NGS)) has begun to shed light on the different molecular subtypes of canine B cell lymphoma, and specific therapies aimed at targeting patient-specific driver genes and pathways are being developed. To enable targeted therapies to move into the clinic, a personalized diagnostic tool must be developed that can rapidly and cost-effectively determine the mutational profile of a patient's cancer allowing selection of the most effective drug for that patient. The investigators aim to develop a NGS diagnostic test that can be employed on standard biopsy samples to identify molecular drivers of a patient's lymphoma (personalized diagnostics), enabling the most appropriate targeted therapy to be selected for that patient. In addition, they aim to determine whether specific mutational profiles within canine lymphoma identified by their NGS panel are predictive of clinical outcome.

Update: We have designed a next generation sequencing panel that aims to rapidly identify which genes are mutated in a patient's lymphoma. We are now in the process of validating this panel and optimizing the experimental workflow and bioinformatics associated with it. Once our panel is validated we will use it to determine the specific mutational profiles within canine lymphoma samples, determine whether profiling may predict patient outcome and ultimately whether specific therapies that target the individual patient's aberrant oncogenic pathway(s) provide superior treatment outcomes when compared with conventional, untargeted chemotherapy.

Grant 02234-MOU: A Novel Approach for Prevention of Canine Hemangiosarcoma

Principal Investigator: James Modiano, VMD, PhD, University of Minnesota

Original Project Description: Hemangiosarcoma, an aggressive form of cancer in dogs, is the cause of death for one out of every five Golden Retrievers in the United States. Portuguese Water Dogs and Boxers also have an especially high risk for this disease which is devastating for all dogs. Hemangiosarcoma is incurable partly because the cancer is detected at a very advanced stage when it is resistant to conventional therapies. Thus, an unconventional approach to improve outcomes for hemangiosarcoma patients will involve effective methods for early detection and for disease prevention. This project will pair two novel technologies consisting of a patented test to detect hemangiosarcoma cells in blood samples, and a treatment that attacks the cells that establish and maintain the disease. Three milestones will be met: first, will be to expand understanding of the performance and utility of the blood test for cancer in dogs with active disease; second will be to confirm the utility of the test to predict disease progression in treated dogs. And third will be to

establish the performance of the test in the "early detection" setting (dogs at high risk without evidence of active cancer), and thus measure hemangiosarcoma prevention through eradication of the tumor initiating cells with the targeted, investigational drug. This project will create tools to guide further development, licensing and deployment of these paired technologies against cancer, specifically hemangiosarcoma, with an ultimate goal for disease prevention in all dogs.

Funding for the research is provided through the collaborative efforts and generosity of the American Boxer Charitable Foundation, Golden Retriever Foundation, and Portuguese Water Dog Foundation. The AKC Canine Health Foundation supports the funding of this effort and will oversee grant administration and scientific progress reports.

Update: The hypothesis of our project was that identifying dogs at risk for the earliest signs of hemangiosarcoma, and using the drug eBAT (called BEAT in the original proposal) to target the cancer-stem cell compartment in these dogs, would create an effective means for prophylaxis. We proposed two aims and three milestones. The aims were that (1) our test could detect hemangiosarcoma cells in the circulation prior to the onset of grossly detectable disease, and (2) that eBAT would be safe to eliminate the incipient cancer cells. The milestones were to (1) confirm the sensitivity and specificity of the test in dogs with active disease and expand its predictive value; (2) confirm the utility of the test to monitor relapse; and (3) establish the performance parameters of the test in the “early detection” setting (dogs at risk without gross disease) and the potential to prevent hemangiosarcoma by eradicating the cancer stem cells using eBAT.

We have refined and improved the detection test, so we are confident that it can achieve clinically useful metrics for diagnosis. Our current estimates for sensitivity (can we find the disease if it is present?) and specificity (is it really the disease if the test calls it as such?) are close to 90% and 95%, respectively. We have evidence that the hemangiosarcoma-associated cells change over time in dogs receiving treatment. The dogs participating in this part of the study (prediction of relapse) are still being followed up and the results through the end of 2019 will be reported in the next and final progress report. In terms of early detection, it appears that about 50% of dogs at or over the age of 10 years have some pathology that can be detected by our test. This is consistent with the “textbook” expectation of 50% of dogs over 10 probably dying from cancer.

In the case of dogs that enrolled in phase-3 (early detection) and had a known outcome of death or tumor diagnosis, our test so far indicated the presence of an abnormality in 19 of 21 (91%). While we cannot yet say that the test matched the outcome in all these dogs, it does tell us that the use of the screening test to trigger more thorough diagnostic testing would benefit a large proportion of dogs. On the other hand, 98 of 99 (99%) dogs that were called “unaffected” by the test, and where at least six months had elapsed since the testing, had not developed disease in the interim time since the test was done.

As far as establishing the efficacy of eBAT as a tool for prevention, there is a very high bar for proof. Experiments done in parallel to this project (with funding outside AKC CHF) suggest that eBAT can delay or

prevent development of hemangiosarcoma or the associated terminal hemorrhage caused by hemangiosarcoma in mice harboring canine hemangiosarcoma tumors. These are not perfect models and the results are still preliminary. Nonetheless, combined with the remarkable safety of eBAT, they provide support to continue testing dogs at risk, and to eventually be able to formally test the hypothesis that fewer dogs in the population receiving eBAT prevention would develop hemangiosarcoma than in the population that did not receive it.

Regardless of the final result, we have introduced significant innovation in this trial that will be of interest to the biomedical and translational communities, and we remain excited to provide support for additional large-scale trials for early cancer detection in companion dogs.

Grant 02318: Genetic and Environmental Risk for Lymphoma in Boxer Dogs

Principal Investigator: Lauren Trepanier, DVM, PhD, University of Wisconsin, Madison

Original Project Description: Lymphoma is a fatal cancer of the blood cells that can occur in any dog. Lymphoma is more common in Boxers, Golden Retrievers, and several other purebreds, which suggests involvement of inherited genes. Recent research has focused on gene mutations in the tumors of dogs with lymphoma. However, we do not understand why these mutations accumulate in certain dogs, and this understanding is essential for disease prevention. Canine lymphoma resembles Non-Hodgkin lymphoma (NHL) in humans, which is more common in industrialized countries and is associated with chemicals found in tobacco smoke, certain household products, pesticides, herbicides, and fungicides. Glutathione-S-transferases (GSTs) are enzymes that can break down toxic chemicals in the body and prevent tumor mutations. Inherited gene defects in the 3 major GST enzymes, GST-theta, GST-pi and GST-mu, each increase NHL risk, and simultaneous defects in more than one enzyme further increase NHL risk. The investigators have characterized two GST-theta enzymes in dogs, and both have defective gene variants. So far, their findings suggest one variant is a risk factor for lymphoma in dogs of varying breeds. However, the genes for canine GST-pi and GST-mu enzymes have not yet been explored. This research will determine whether defective GST genes along with certain household and yard chemicals are associated with lymphoma in dogs, with a focus on the high-risk Boxer breed. The overall goal of this study is to identify combinations of genes and environmental chemicals that contribute to the development of lymphoma in dogs, so that better cancer prevention strategies can be developed.

Update: GST genes defend against environmental chemicals that could cause cancer. Our study goals were to determine whether defective GST genes or specific environmental exposures were associated with lymphoma in Boxers. While GST variants were not more common in Boxers with lymphoma, we did find that household

proximity within two miles of specific industrial sites were associated with lymphoma in this population. Final analyses will examine interactions between genotype and exposures in lymphoma risk.

Grant 02510-T: Identification of Novel Synthetic Lethal Partners to Optimize PI3K Targeted Therapies in Canine Hemangiosarcoma

Principal Investigator: Cheryl London, DVM, PhD, Tufts University School of Medicine

Original Project Description: Hemangiosarcoma (HSA) is a cancer of the cells lining the blood vessels that is very aggressive and has nearly always spread by the time it is diagnosed. HSA accounts for 5-7% of all cancers in dogs resulting in approximately 25,000-50,000 new cases per year. The treatment of choice is surgical removal followed by chemotherapy administration. Unfortunately, despite aggressive therapy, the majority of dogs diagnosed succumb to their disease within 6-8 months. Virtually no improvements in outcome for affected dogs have occurred in the past 30 years despite multiple clinical trials and research efforts. More recently a new therapy has been developed targeting two receptors on HSA cells. However, the majority of dogs still died by 10-12 months after treatment. The molecular pathway known as the PI3K/AKT/mTOR pathway has previously been implicated in the pathogenesis of many forms of cancer including HSA. Indeed, inhibitors of PI3K/AKT/mTOR pathway have some activity against HSA cell lines in the laboratory. The investigators have generated data showing that a subset of canine HSA tumors possess genetic mutations in PI3K that are known to activate the pathway in cancer cells. In this study, they will fully characterize the expression and function of PI3K in canine HSA tumor cell lines and tumor samples. This information will then be leveraged to identify new ways to block the PI3K/AKT/mTOR pathway using a combination of small molecule inhibitors that are most effective at killing tumor cells. These data will then be used to design future clinical trials in dogs with HSA.

Update: Hemangiosarcoma (HSA) is a cancer of the cells lining the blood vessels that is very aggressive and has nearly always spread by the time it is diagnosed. HSA accounts for 5-7% of all cancers in dogs resulting in approximately 25-50,000 new cases per year. The treatment of choice is surgical removal followed by chemotherapy administration. Unfortunately, despite aggressive therapy, the majority of dogs diagnosed succumb to their disease within 6-8 months. Virtually no improvements in outcome for affected dogs have occurred in the past 30 years despite multiple clinical trials/efforts. More recently a new therapy has been developed targeting two receptors on HSA cells. However, the majority of dogs still died, by 10-12 months. The molecular pathway known as the PI3K/AKT/mTOR pathway has previously been implicated as a key driver of several cancers including HSA. Indeed, inhibitors of PI3K/AKT/mTOR pathway have some activity against HSA cell lines in the laboratory.

The purpose of this study is to fully characterize the expression and function of PI3K in canine HSA tumor cell lines and tumor samples to identify new ways to block this pathway using a combination of small molecule inhibitors that are most effective at killing tumors cells. Over the past year we have characterized the expression of the 4 isoforms that make up PI3K family in HSA cell lines, have characterized sensitivities of the lines to individual isoform inhibitors, and have generated cell lines deficient in two of the isoforms. We have found that in some of the lines loss of the PI3K β isoform causes the cells to reduced migration suggesting that this isoform may play a role in tumor spread. Megan Gutwillig, a combined DVM/MS student, finished her MS work and has returned to complete the last 3 years of her veterinary training. A new student will begin working on the project in the lab this fall.

Grant 02164-MOU: Determining the Genetic Contribution to Boxer Corneal Ulcers

Principal Investigator: Kathryn Meurs, DVM, PhD, North Carolina State University

Original Project Description:

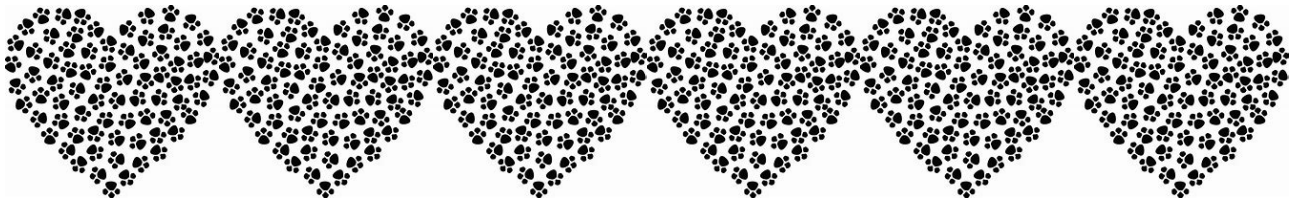
Spontaneous chronic corneal epithelial defects (SCCEDs) are chronic corneal ulcers that fail to undergo normal healing that are commonly observed in Boxers. The predilection for Boxers suggests that SCCEDs is inherited in this breed. Affected dogs develop spontaneous corneal ulcers that are often exceptionally painful and persist for weeks to months. Most dogs require surgical therapy to heal the corneal ulcer and experience corneal scarring as a result. The impact on the quality of life for dogs during episodes of ulceration has led to increased interest in disease prevention. However, since SCCED is an adult onset disease, many dogs are selected for breeding before they are diagnosed. A blood test that could identify affected animals before they are used for breeding would greatly decrease the prevalence of SCCEDs. In a previous study funded by the AKC Canine Health Foundation, Dr. Meurs and colleagues collected samples from adult Boxers with and without SCCED and performed a genome wide association study. In the study proposed here they will perform whole genome sequencing (GWAS) on a subset of affected and unaffected dogs and use the data from the GWAS to focus in on important variants. They will then more closely evaluate variants of interest to determine the gene and ultimately the causative genetic mutation. They hope that the identification of a genetic cause for SCCEDs in the Boxer can be used to reduce the prevalence of this disease in this breed but also to provide information for other affected breeds.

Update: FIRST, we demonstrated that Boxers with corneal ulcers have a deletion mutation in an important corneal gene that has a role in cell proliferation and regulation of genes involved in cell fibrosis and cell immune health.

SECOND, we demonstrated that dogs with the deletion have reduced levels of this protein in the cornea.

THIRD, we knew that several important ocular proteins are regulated from this protein. We demonstrated that certain corneal protein levels are increased in eyes from dogs with the deletion, suggesting that dogs with the deletion have decreased ability to regulate important corneal proteins. The increase in these proteins is thought to delay wound healing. Since our last report we did a more specific analysis to pinpoint the proteins altered in response.

Finally, the genetic mutation that we identified appears to be very common in the Boxer population and we think it would be hard to remove by selective breeding. However, we think that this mutation is likely only a problem for the dog when it has an eye injury, since it appears to be associated with ability of the corneal to heal properly. It is likely to be important even with a very minor injury that could be associated with common daily eye insults (sand, sticks, scratches) since a small injury may become prolonged by an inability to heal properly. Since we believe that this would be a difficult mutation to breed away from given the frequency in the population, our research may suggest that it may be very possible to apply replacement levels of this gene product (protein) to an injured eye to increase healing. This will be the next area to address through research.



ABCF Membership Chair Update

I realize that this is the time of year when you're inundated with requests from charitable organizations. All good causes, to be sure, however, I hope you'll consider this one because it concerns the future of the breed we love, our boxers. In case you haven't joined the ABCF for the calendar year 2019, this is your last chance!!!! Of course, if you're super-organized, you may also join for the calendar year 2020. **Just make sure to state the year clearly when sending your check!!!**

As I'm sure you're aware, the Foundation was created to fund research into the problems that affect our beloved breed and that goal remains our sole mission. To date, the ABCF has raised more money for health research than any other breed club. The money raised by the foundation has funded studies in boxer cardiomyopathy, sub-aortic stenosis, thyroid disease, degenerative myelopathy, and cancer, including lymphoma.

For as little as $25.00, the cost of ONE show entry, you can become a member of ABCF. By clicking on the following link, http://abcfoundation.org , then hitting Online Membership Form on the left side, you can print the form and send your check or card number by email, snail mail or by fax. But PLEASE take the time NOW to join the ABCF and help our boxers to lead longer and healthier lives. **I'd also like to add that cost of membership has remained the same since the inception of ABCF. How many organizations can say THAT?**

A huge thank you to the individuals and clubs who have already joined ABCF **for the calendar year 2019**!!!!!

Bobbi Compton

Membership Chairman

AMERICAN BOXER CHARITABLE FOUNDATION

ABCF Annual Support Membership form

1. Select your membership level:
_____ $25 _____$50 _____ $75 _____ $100 _____ Other

2. Select how you want to receive the ABCF Newsletter:
_____ Online _____ Via US Mail (There is an additional fee of $10 annually)

Pay by check or money order payable to the American Boxer Charitable Foundation or use MasterCard or Visa to join or renew your membership. You can also join, renew or pay online via our website.

Amount: _____ Method of payment: ____ Check ___ Money Order ____ MasterCard _____Visa

Signature:_____

Account Number:_____Expires:_____CVC:_____

Name:_____

Mailing Address:_____

City:_____ State:_____ Zip:_____

Country: _____ Phone:_____

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Complete form and mail to:
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2019 ABCF Members

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Maryjane Alencewicz
Vera Anderson
Steven G. & Ann B. Anderson
Teresa Archer
Connie Back
Candy Bartos
Bill and Tina Bates
Susan Bell
Susan and Barbara J Blue
Jonathan and Norah Bonwit
Dean Brenner
Joyce Baker Brown
Claudine Burgess
Mary Frances Burleson
Joyce Campbell
Mary Lou Carroll
Michelle L Chevrier
La Relle Clark
Bob and Bobbi Compton
Lynn Cooch
Barbra Cotton-Beatty
Jennifer Crane
Sharon Darby
Kathleen and Tim Delany
Tom and Donna Doane
Mary Dohm
Jewell Dunning
Kimberley Dye
Karen Emerson
Linda Ennis
Bob Erickson
Jeannette Everett
Mark and Janet Ewing
Jacqueline Fabrizzio
Claire Fallon
Heidi Finley
Gyleen Fitzgerald
Sharon and Randy Fosseen
James & Anita Franzi
Renee Fulcer
B Thomas Fuson
Deborah Gagnon
Donna Galante
David & LuAnn Gardner
Kathryn Garrity
Roger George
Becky Gilchrist
Glenn Glass
Rhoda Goselin
Pam and Greg Gordon
Derick and Brenda Grice
Bob and Lyn Grimm
Jean Hale
Debora Hall
Robert & Grace Hallock
Cynthia Halloran
Jane Hamilburg-Guy
Heidrun D Hardy
John and Nanette Hauprich
Connie Haywood
Patricia Healy and Butch Engel
Dawn Heath
Mary Hickey
Jill Hootman
Linda and Jerry Huffman
Laurence & Marion Hughes
Jack Ireland
Theresa Janzen
Stephania Jenks
Linda Johnson
Sandra Johnson
Mandy and Ricky Justice
Myrna Kahlo
Audrey and Dave Kamphenkel

Gail. S. Karwoski
Joan Kenney
Priscilla Killman
Kelly Klingbeil
Cindy Knox
Phillip Koenig
Eugenia (Gena) Koshiol
Nadine Kuhlemeir
Melodee Lasky
Thomas and Carol Latta
Julie Lawrence
Valerie Lillibridge
Jill L. Lines
Patty Livingston
Mary and Tony Louwerse
Melissa Mathers
Jean H. Mattheiss
Lori McClain
Shelli McGregor
Carol McGuire
Lee (Mary L.) Morris
Jessica Murphy
Mary Myers
Carol Novak
Bette Jo and Dwight Nunn
Sandra and Steve Orr
Peggy Otto
Barbara Palmer
Loretta Parolisi
Sallie Peters
Susan Peters
Jeri Poller
Donna Purichia
Pat and Karen Quagliana
JoAnn Reinolds
Tom and Erin Rezmer
Delma Robinson
Michelle Rocca
Vickie Rounsaville-Millard
Jennifer Rumping
Patricia Russell
Scottie & Bethany Russell
Sally and Gary Ryan
Leila Sahni
Lynn Schaefer
Donna Schafer
Debbie Schlesinger
Ginny Shames
Dennis & Susan Simon
Rob and Phyllis Snyder
Sharon Steckler
Carole Stein
Cheryl Stevens
Larry and Susan Stogner
June Sutherline
Sue and Guido Tafur
Sue Ann Thompson
Thomas Tomaszewski
Ann Tomhave
Jane Tully
Lauri Travis
Bill and Tina Truesdale
Terri Underhill
Korinne Vanderpool
Robin Vaughan
Kathy Veglahn
Darlene Vickers
Allison Thomson Vicuna
Susan Wilkinson
Shirley and William Williams
Barry Wyerman
Mark Young
Linda Zazula
Allegheny Boxer Club
Blue Grass Boxer Club
Bluebonnet Boxer Club
Boxer Club of Colorado
Boxer Club of Long Island
Boxer Club of Milwaukee
William Brenner
Boxer Club of Southern California
Central Indiana Boxer Club
Connecticut Boxer Club
Connecticut Boxer Club
East Tennessee Boxer Club
Georgia Boxer Club
Greater Cincinnati Boxer Club
Heart of America BC
Houston Boxer Club
Middlesex Boxer Club
Mid-West Boxer Club
Minnesota Boxer Club
Missouri Valley Boxer Club
New York Boxer Club
Northwoods Boxer Club
Pacific Northwest Boxer Club
Potomac Boxer Club
Southeast Florida Boxer Club
Upstate New York Boxer Club