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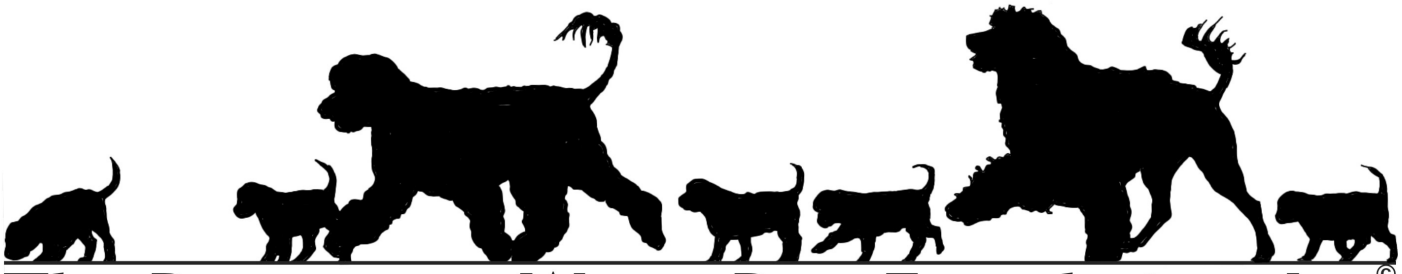

The Portuguese Water Dog Foundation, Inc.©

We are dedicated to funding canine medical research focused on issues that affect the health and well-being of Portuguese Water Dogs everywhere.

Inside this issue

Non-PRCD PRA Gene Located

A new early onset PRA mutant gene has been located by Dr. Gustavo Aguirre at the School of Veterinary Medicine, University of Pennsylvania. Optigen expects to have the gene test available at the end of October.

Five years ago a courageous breeder reported the occurrence of PRA at an earlier age than expected. Along with the stud dog owners, the breeders and owners made available to researchers dogs of interest for genetic testing and clinical exams.

Thanks to your generous support, the Foundation provided a grant to Dr Aguirre to perform gene sequencing and unlock the final answers needed to locate the gene responsible for this new type of PRA in our breed.

The Foundation contributed $9,400 for WGS on 4 different dogs [2 affected, 1 carrier, and 1 homozygous normal]. Samples were tested at the WGS platform at the University of Bern, Switzerland.

Look for news in the near future of test details and protocols.

Microphthalmia and Delayed Growth Syndrome

Margret Casal, DVM, PhD; University of Pennsylvania

Microphthalmia and delayed growth syndrome (aka "puppy eye syndrome") has been reported by Portuguese Water Dog breeders dating as far back as 1986. However, there is no information in the scientific literature and the majority of data concerning this syndrome has been obtained from records of breeders, which have anecdotal reports of the disease and little, if any, medical diagnostics. Affected dogs present with microphthalmia of varying severity, other eye abnormalities, short stature and other findings. To date, the investigators have been able to collect DNA from 24 affected dogs. Males and females can be affected, although females predominate (about 70%). Preliminary pedigree studies suggest an autosomal recessive inheritance. Human literature reports numerous syndromes associated with microphthalmia, and many genes have been identified as having a causative role. The goals of this investigation are to better characterize the clinical syndrome seen in Portuguese Water Dogs, confirm a suspected mode of inheritance, obtain additional samples for investigation into the genetic mutation, and develop a mutation based, genetic test for breeders to eliminate this syndrome from the Portuguese Water Dog breed.

In the past decade, the Foundation has supported early data gathering for PES, collaborating with researchers, veterinarians, breeders and volunteers. We greatly appreciate everyone who has supported this endeavor, which has led us to this research at the University of P Pennsylvania. A $10,000 matching gift challenge, offered by Peggy Helming and Milan Lint doubled the impact of your gifts. We not only reached but exceeded our goal of $10,000.

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AKC CHF Progress Reports

Enhanced Testing for the Diagnosis of Bartonellosis in Dogs

Dr. Edward B. Breitschwerdt, DVM
North Carolina State University

Bartonellosis, a zoonotic bacterial disease of worldwide distribution, is caused by approximately 10 different Bartonella species. Bartonella are transmitted to canines and humans by ticks, fleas, lice, mites, and sand flies.

Dr. Breitschwerdt's laboratory demonstrated the first evidence for Bartonella infections in dogs in 1993. Bartonella species have been associated with an expanding spectrum of important disease manifestations including anemia, endocarditis, hepatitis, lymphadenitis, myocarditis, thrombocytopenia and vascular tumor-like lesions. Infections can be life-threatening. Due to a lack of sensitive and reliable diagnostic assays, definitive diagnosis of bartonellosis in dogs remains a significant problem. Because these bacteria invade cells and infect tissues throughout the body, this chronic intracellular infection is difficult to cure with currently used antibiotic regimens. This study will develop improved serodiagnostic tests for bartonellosis in dogs.

These assays can also be used for worldwide sero-epidemiological prevalence studies, and to establish early and accurate diagnosis.

Dr. Breitschwerdt's research group has described concurrent infection in dogs, their owners and veterinary workers; this allows for a One Health approach to this important emerging infectious disease.

The study is progressing according to our expectation. Preparation of antigen for IFA and WB for so many species of Bartonella is time consuming and somewhat contingent upon the ability of each species to tolerate the growth conditions imposed upon them and therefore unpredictable, but work is going well. The third specific aim is the most technically advanced and will take extra care in developing, but is expected to add significant information and advancement in serological modalities for diagnostics.

Discovery of Biomarkers to Detect Lymphoma Risk, Classify For Treatment, and Predict Outcome in Golden Retrievers

Dr. Jeffery N. Bryan, DVM, PhD;
University of Missouri, Columbia

Lymphoma strikes 1 in 8 Golden Retrievers, approximately one-third of the cases being B cell. While T cell classifications currently inform therapy choices for dogs, B cell classifications have been investigated little in Golden Retrievers. Epigenetic DNA methylation changes clearly underlie lymphomagenesis in humans, but have been evaluated minimally in dogs. Cancers con-tain tumor initiating cell (TIC) populations that resist therapy by expressing efflux pump and pro-survival genes that have not been identified clinically in lymphoma of dogs. We propose to improve diagnostic, classification, and prognostic ability using flow cytometry paired with biopsy to characterize the B cell lymphomas of Golden Retrievers. With these same samples, we will identify DNA methylation changes in lymphoma cells not present in normal cells to develop biomarkers of each class of lymphoma and identify new therapy targets for affected Goldens. More significantly, because DNA methylation changes occur so early in the process of cancer formation, we hypothesize that they could serve as biomarkers of risk, allowing medicine or diet to prevent lymphoma in Goldens before it develops. Finally, we propose to identify TICs in lymphoma biopsies to characterize stem-like cells by surface markers and DNA methylation changes. Identifying these cells will aid therapeutic strategy development. Each project advanc-es a current frontier of research. By performing them in parallel, the markers from each can be combined, correlated, and translated into biomarkers of risk, diagnosis, and prognosis to advance the prevention and management of lymphoma in Golden Retrievers.

Grant Objectives:
1. Characterize the types of B cell lymphoma in Golden Retrievers by flow cytometry.

2. Define the methylomes of B cell lymphomas in Golden Retrievers.

3. Identify and characterize subpopulations of cells within types of B cell lymphoma in Golden Retrievers with TIC phenotype.

Progress continues at all 3 institutions. The proposed immunohistochemical evaluations and flow cytometry techniques have identified that the population of B cell lymphomas appears to be a monomorphic group of diffuse large B cell variety (DLBCL) similar to the aggressive form in humans.

(continued next page)

Biomarkers to Detect Lymphoma Risk (Continued)

An immunohistochemistry panel is now functional to identify these and flow cytometry has being optimized, but does not clearly distinguish among them. Gene expression analyses are underway that we expect to further characterize these samples and better our understanding of the etiopathogenesis of the disease. Completed sequencing experiments have identified differentially hypermethylated genes in B cell lymphomas of Golden Retrievers that is similar to those in human lymphoma. A diagnostic PCR panel is in progress for methylation marks. We are beginning to add whole genome, exome, and transcriptome sequencing in a subset of cases to understand how mutation and DNA methylation interact. TAMU has successfully generated tumor initiating cell populations from cultured lymphocytes and has optimized the procedures to be performed on fine-needle aspirates of lymphoma nodes. It appears that multiple aspirates will be necessary to get all the material needed for characterization.

Sufficient TIC cells can be generated for sequencing with the protocol in place at MU. Because the lymphoma samples are so similar across the board, we have changed Aim 1 to evaluate gene expression in these tumors as it relates to the methylation profile.

Final AKC CHF Report

Mapping Genetic Risk Factors for Canine Hip Dysplasia

Dr. Antti Iivanainen, DVM, PhD, Research Institution: University of Helsinki and the Folkhälsan Institute of Genetics

Original Project Description: Canine hip dysplasia is a common developmental disorder of the hip joint that severely affects a dog's quality of life. As the disease has several genetic risk elements and is influenced by environmental factors like diet and exercise, it is of paramount importance that genetic association studies are conducted using adequately-sized cohorts of genotyped diseased and healthy animals. Dr. Iivanainen will sample a large population of dogs (>300-400 dogs) so that contributing genetic loci can reliably be discovered. This research group expects that with such a strongly powered study all major genetic risk factors can be uncovered with a high statistical significance. Investigators expect that identified loci will be discovered across breeds. The identification of genetic risk elements will allow the development of genetic tests that can be used in breeding programs to control the disease incidence, as well as further studies regarding the possible role of diet and exercise in hip dysplasia development.

Grant Objectives:

1. To establish an accurately phenotyped primary study cohort for genetic studies. We aim to sample at least 300 cases and 300 controls.

2. To perform a GWAS for 144 cases and 144 controls using canine high density SNP arrays.

3. To replicate the associated loci in independent multinational cohorts of dogs in different breeds.

Report to Grant Sponsor: The overall objective of our study is to perform a genome wide association study (GWAS) of canine hip dysplasia (CHD) in German Shepherds using a large sample cohort (200 cases and 200 controls). CHD is a common problem in many breeds. The dysplasia phenotype is graded from radiographs. In this study, we use the standards of Fédération Cynologique Internationale (FCI) ranging from A (healthy) to E (severely dysplastic). Each hip joint is graded individually. As the disease progresses also the risk for hip joint arthrosis – a painful and incurable condition – increases. The identification of genetic risk factors would enable the development of genetic tests to aid the breeders in controlling the disease. Four hundred animals consisting of carefully matched pairs of healthy and affected individuals should provide enough power for the association study to uncover the major genetic risk factors for this degenerative disease. We have collected a large single-breed study cohort of 1141 German Shepherds including 411 cases and matched controls plus additional 319 controls. We have analyzed the association of CHD to a genome wide array of genetic markers using a subset of these dogs (N=497). The study revealed ca. 30 markers on eight different chromosomes that suggestively associated with the disease. Targeted replication studies using independent cohorts of dogs (German Shepherds N=244 and 11 breeds N=1767) have validated the findings from 3 chromosomes.

Publications

"Safe and Effective Sarcoma Therapy through Bispecific Targeting of EGFR and uPAR," February 13, 2017. Molecular Cancer Therapeutics, AACR Journals

Borgatti, A., Koopmeiners, J.S., Sarver, A.L., et. al. Grant 1889-G: Innovations in Prevention, Diagnosis, and Treatment of Cancer.

Abstract: Sarcomas differ from carcinomas in their mesenchymal origin. Therapeutic advancements have come slowly so alternative drugs and models are urgently needed. These studies report a new drug for sarcomas that simultaneously targets both tumor and tumor neovasculature. eBAT is a bispecific angiotoxin consisting of truncated, deimmunized Pseudomonas exotoxin fused to epidermal growth factor (EGF) and the amino terminal fragment (ATF) of urokinase. Here, we study the drug in an in vivo "ontarget" companion dog trial since eBAT effectively kills canine hemangiosarcoma (HSA) and human sarcoma cells in vitro. We reasoned the model has value due to the common occurrence of spontaneous sarcomas in dogs and a limited lifespan allowing for rapid accrual and data collection. Splenectomized dogs with minimal residual disease were given one cycle of eBAT followed by adjuvant doxorubicin in an adaptive dose-finding, phase III study of 23 dogs with spontaneous, stage I-II, splenic HSA. eBAT improved 6-month survival from <40% in a comparison population to ~70% in dogs treated at a biologically active dose (50 μg/kg). Six dogs were long-term survivors, living >450 days. eBAT abated expected toxicity associated with EGFR-targeting, a finding supported by mouse studies. Urokinase plasminogen activator receptor (uPAR) and EGFR are targets for human sarcomas, so thorough evaluation is crucial for validation of the dog model. Thus, we validated these markers for human sarcoma targeting in the study of 212 human and 97 canine sarcoma samples. Our results support further translation of eBAT for human patients with sarcomas and perhaps other EGFR-expressing malignancies.

Tidbits! From the 2017 AKC CHF Health Conference

Courtesy Janet Boyd

August 11, 2017. Day one at AKC Canine Health Foundation conference and the word for you is GENOMICS.

Definition-Genetics and genomics are two terms that are often incorrectly used interchangeably. Genetics is the study of single genes and their role in the way traits or conditions are passed from one generation to the next. Genomics is a term that describes the study of all parts of an organism's genes.

Roughly 12 years ago the project to map the canine genome was launched. The collaboration we have today is truly remarkable. Involving the World Health Organization (WHO)...various tissue biological databases that have tumor types categorized...Genome wide association study (GWAS) and on and on.

The study of genomics offers us better predictions of treatment success based on individual tumor characteristics. Accurate tumor sampling and diagnostics are key. Genomics study is providing us with better idea of what treatment to use and how successful it might be. Comparative research between human and canine is providing access to ever improving diagnostic and treatment options for our pets.

The AVMA has a database of clinical trials underway should you find your beloved pet in need and are interested in that route. We'll get that link on our website in the coming days.

Day 1: Epigenetics...some think it may have a greater role in disease than genetics. Dr. Jeffrey Bryan presented an update on his promising research looking at methylation biomarkers. Will it lead to the ability to predict future development of lymphoma and the ability to reverse the process preventing the disease?

Day 1: Dr. Matthew Breen shared an interesting statistic when discussing what moves things forward in the quest to get answers to canine cancer diagnosis and successful treatment. Great strides have been made in pediatric cancer treatment. Of pediatric cancers diagnosed, 75% patients participate in clinical trials...<15% of adult cancers diagnosed participate in clinical trials.

With the application of genomics to canine research and the world wide collaboration, clinical trials provide the fuel to move things forward.

Day 2: The remainder of this morning's lectures were dedicated to tick-borne disease (TBD). These are vector diseases and resulting in infections from the disease vector (tick, flea, and so on) bite. Discussion covered diagnostics and work to improve accuracy. The "map" of these infections is changing as our travel patterns have dramatically changed. Prevention via preventive is critical to control.

Day 2: One of the lectures this morning covered bartonellas, as a part of the tick-borne disease initiative. It was fascinating to hear Dr. Breitschwerdt detail the history of this bacteria to it's current distribution. It was eye opening to hear more about these infections and how their reservoir hosts have expanded over time and change of travel patterns.

He noted that WHO's most recent data says they believe 20% of cancers are attributable to infections. It was fascinating to hear of cases where treatment was underway for a cancer diagnosis and a bartonellosis diagnosis was made...treated...and there was resolution. Important research as these chronic infections can create so many issues. Exciting research that will improve quality of life in all mammals.

Dr. Breitschwerdt received the Asa Mays award at AKC CHF conference. For more on his research, funded by the Foundation, see page 2 and our website.

Day 2: This morning Dr. Baltzer shared results in TPLO surgery recovery, looking at omega-3 fatty acid rich diet and physical therapy. As you might expect the rehab/omega-3 diet dogs recovered faster. Interesting that they did better with omega-3 (high doses) than with NSAIDS. NSAIDS inhibit pain but do nothing to prevent arthritis. Omega-3 inhibit arthritis.

Interesting tidbit from her talk...women rupture ACL similar to canines...slowly over time. Her rehab program was modeled after that of female human ACL tear rehab.

Day 3: This morning was the final session focusing on reproductive topics. Dr. Arenas provided an update on testing and treatment of brucellosis canis and shared the emerging concern for brucellosis suis in dogs. Her work on a brucellosis vaccine is now entering the final testing phase.

Dr. da Silvia provided an update on his work looking at the role of E. coli biofilm in pyometra. In addition there was discussion of current treatment options/management of pyometra. His lab is working on a proposal to explore treatment options to address the production of biofilm.

What can we do for you?

Since 1998, the Foundation has approved $580,935 dollars in funding. We currently hold $518,000 in donations — perfectly positioning us to fund future breed-specific and joint research as it becomes available. As we identify research grant requests and consider which of these medical research projects we should fund, we greatly appreciate our donors input. What diseases/conditions are of most concern to you? Please contact us and let us know your thoughts:

EMAIL INFO@PWDFOUNDATION.ORG AND TELL US WHAT MATTERS TO YOU.

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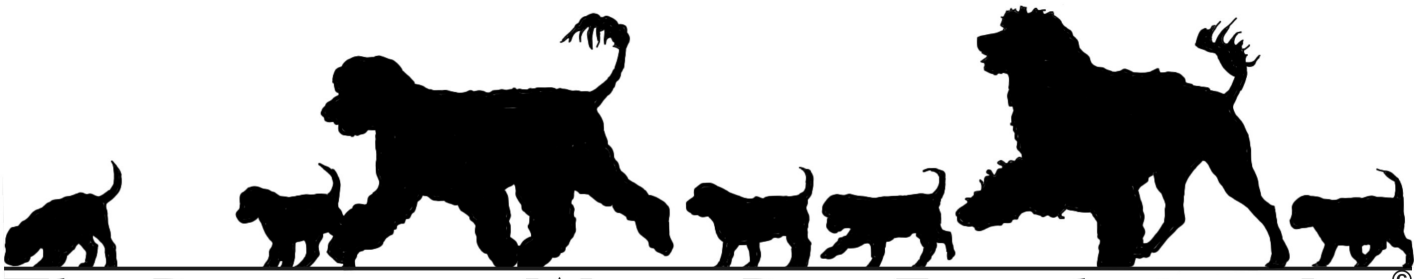

The Portuguese Water Dog Foundation, Inc.©

The Portuguese Water Dog Foundation, Inc.
P.O. Box 203
Parker Ford, PA 19457-0203
Tel 610-707-2589

The Portuguese Water Dog Foundation, Inc. needs your help and support to fund research to improve the quality of life and health of our Portuguese Water Dogs. Your tax-deductible donation, in any amount, would be greatly appreciated. In addition to personal donations, a donation may be made in memory or honor of a friend or loved one, whether human or canine. Donors' names will be kept anonymous upon request.

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Roberta W. Knight in loving memory of Pasha

Nutmeg PWD Club in honor and appreciation of all those PWD lovers that purchased the Nutmeg 2017 calendar

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United Sunshine States PWD Club in memory of our friend and mentor, Chuck Robinson

Victoria Trapanotto in loving memory of my Camie girl

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Verne Foster in memory of our dogs loved & lost

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Diane & John Burke, Jr. in gratitude for our new puppy, Bandit. We love him! Jake does too!

Janice Butler in loving memory of Angus, my sweet boy!

Janice Butler in memory of Jack, such a special boy whether sharing your heart relaxing at home or being a superstar in Agility, Water and Obedience. Loved all the years we got to hang out together and know how heartbroken Candi & Chuck without you! Thinking of you and Angus running together on the other side of the bridge – hope that there are balls and bumpers to retrieve!

Penny Diaz del Castillo in memory of my first PWD, "Fisher"

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Jane Freeman in loving memory of "Dutch" CH Freestyle Now And Forever CD. Loved and missed by Roberta Capuano & Tom Heffernan.

Barbie Geibert, SeaAngels in memory of SeaAngel's Gotta Love Morgan

Barbie Geibert, SeaAngels in memory of Scrimshaw's Simon Says

Vicki Goldberg

Vicki Goldberg in honor of the future Mr. and Mrs. Jodi and Mark Forkos

Great Lakes PWD Club in thanks for Lisa Arnett for conducting our Grooming Seminar

Ruth & Herb Henderson in honor of "SeaDog" CH Makitso's SeaDog At The Wire

Lewis & Casey Ingram

Stephanie Hertz & Caitlin Fitzgerald in honor of our new Karma PWD puppy "Halligan

Scott & Liz Kantor in memory of Moses Kantor

Nancy Kurkjian in memory of Jazz 11/22/2002 – 4/9/2009

Candace Lawhorne

Sarah Leatherman in memory of Rowdy Jack Tar - devoted companion to and stellar athlete for Chuck & Candi Bubert

Lou Ann & Robert Lindquist

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Susan Minkel in memory of Cocoa & Ceasar

Martha & David Murray in honor of our new Karma PWD puppy "Xavier"

Marilu Novy

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Lone Star PWD Club in memory of "Cocoa Puffs" Sapphire Cocoa Puffs

Lone Star PWD Club in memory of J.B.'s Saudade

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Gale Meadow in honor of the PWD PSG

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Don & Barbara Niemann in memory of "Gus" CH MACH2 Mariner NCO Gusto CD RA MXS MXF CWDX loved and missed by Carl & Susan Craig

Sandra Overton in honor of the PWD PSG

Julie Parker in honor of the PWD PSG

Kristi & Mike Portugue in memory of Chuck Robinson. A kind and thoughtful water trial judge, passionate and dedicated dog lover, and friend. We will miss you.

Janice Reilly in honor of the PWD PSG

Mary Salvary in honor of the PWD PSG

Bryan & Jeanne Sandeno

Nanci Z. Shelton in memory of "Keeper" Cold Harbor's Best Kept Secret

Heather Shilo in honor of the PWD PSG

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Bill & Elaine Trendler in memory of Tobie

Butch Tretter in thanks to Linda K. Hunt

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Janet Warnsdorfer, Galaxy PWDs in memory of "Guga" CH Galaxy's His Nobs Gustavo OA AXJ CXWD BROM

Catherine Waters in honor of the PWD PSG

Janis Watts in memory of "Leyna" Legado Morena Com Melena

Janis Watts in memory of "Colton" Legado Lempejo De Highbid

Janis Watts in memory of "Molly" Legado Hilariante Moli Morena

Janis Watts in memory of "Mira" Legado Graciosa Dama Mira

Charles White & Cathy Cates in memory of Beverly Rafferty

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Jerry Wolcoveick in memory of Alice Vicha and all the Norvic PWDs

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Ann Marie & Thomas Howe

Katie Katinas

Cynthia Kongorski

Sandra Novicki

Southern California PWD Club in memory of Voyager Angel of Knoxville

Val, JP, Sydney, JoJo & Bart Tangen in loving memory of "Bella" CH Stargazer's Astrud Isabella CD RA TD CWDX GROM November 23, 2001 to March 13, 2017. Best Sister Ever!

Debbie & Scott Totten in memory of the Murray's wonderful boy, "Stormy" MACH BenHil's Calm Before The Storm

Alan Urkowitz

Janet Warnsdorfer, Galaxy PWDs, in memory of "Kiki" Galaxy's Mountain And Sea Time

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Friends of Rhonda, Gale and Triton in loving memory of "Triton" GCHB CH Cutwater Trumpeter of the Sea CD BN RN AX AXJ OF RATN WWD, owned and loved by Rhonda Levinowski and Gale Erskine

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Linda K. & Krista K. Hunt, Kalista in congratulations on your new titles to "Hydro" CH Kalista To Splash-N-Dash BN RN MX MXJ TD CGC for his MX and MXJ!

Linda K. & Krista K. Hunt, Kalista in memory of Chuck Robinson

Linda K & Krista K. Hunt, Kalista in congratulations on your new titles to "Beamer" GCH Kalista's Ultra Black Magic Water RN AX AXJ for his AX AXJ!

Linda K. & Krista K. Hunt, Kalista, in congratulations on your new titles to "Titan" SunJoy's Back In Time At Kalista NA NAJ for his NA and NAJ!!

Sarah Leatherman in memory of Louie – gone too soon.

Up to $49.00

Linda K. & Krista K. Hunt, Kalista in congratulations on your new title to "Marley" MACH2 PACH Kalista's Harley Marley BN RA MXS MJG MXP2 MJP2 MJPB OF T2B THDX CWD for his PACH!

Linda K. & Krista K. Hunt, Kalista in congratulations on your new title to "Y" MACH2 Kalista's Now What BN CD RA MXG MJC MXP MJP MXF T2B CAX CWD for his CD!

Linda K. & Krista K. Hunt, Kalista in memory of "Bandit" Kalista's Partner In Crime loved and missed by Gary and Jeanette Stang

Linda K. & Krista K. Hunt, Kalista in honor of "Ducky" Can CH Kalista's Vixen AWD for her Canadian CH!

Linda K. & Krista K. Hunt, Kalista in memory of "Moxie" Kalista Hitherandthithering CGC CD RAE MX MXJ MJB OF AWD SROM

Linda K. & Krista K. Hunt, Kalista in congratulations on your new title to "Ducky" Can CH Kalista's Vixen RN AWD for her Canadian RN!

Linda K. & Krista K. Hunt, Kalista, in congratulations on your new title to "Sunni" Am/Can CH Kalista's Sun Star Traveler RE OA OAJ AWD SROM for her Canadian RE!

Linda K. & Krista K. Hunt, Kalista, in memory of "Major" CH Kalista's G Major