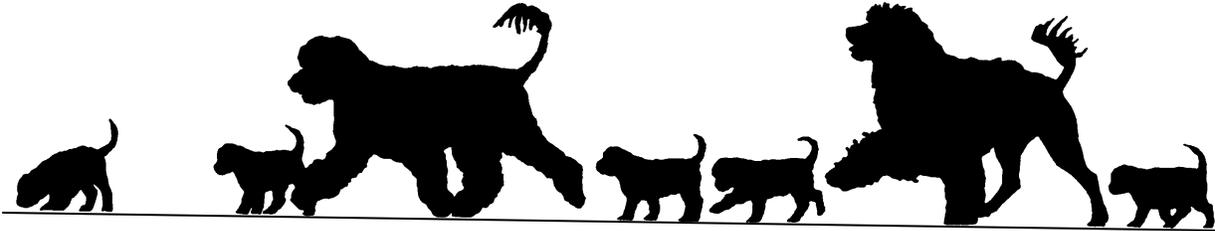


PORTUGUESE WATER DOG FOUNDATION, INC.



2006 MID YEAR UPDATE

LYMPHOMA RESEARCH UPDATE (CO-SPONSORED WITH MORRIS ANIMAL FOUNDATION)

Gene Expression Profiling of Relapsed Lymphoma in Dogs,

The Ohio State University, William C. Kisseberth, DVM, PhD D03CA-132

Lymphoma is one of the most common cancers in dogs. Breeds with a high incidence of lymphoma include boxers, golden retrievers, German shepherds and others. Lymphoma is one of the most treatable cancers-more than 90 percent of dogs treated with chemotherapy go into remission. Unfortunately, most dogs relapse and eventually die from the disease. The investigators are comparing gene expression patterns of tumors from chemotherapy-treated dogs that have relapsed, with tumors from the same dog obtained prior to treatment. Rather than spend more time and money constructing a cDNA library of canine lymphoma and with the dramatic progress of the canine genome, the investigators will use the Affymetrix® Canine GeneChip for the final stages of this project. This array should perform excellently and provide further information for

analysis of lymphoma samples in this study, thereby, helping investigators to classify canine lymphomas and identify genes of potential diagnostic and prognostic significance. They are currently enrolling patients to collect paired pre-treatment and first relapse lymph node biopsies from dogs with lymphoma treated with the same doxorubicin-containing combination chemotherapy protocol. The last phase of this three-year study will be to determine gene expression patterns and how those patterns may assist in prognosis of lymphoma patients and identification of potential new targets for therapy in relapsed lymphoma patients. They will use the information to identify important genes and different sub-types of lymphoma, which will help in the development of new and better cancer treatments. Because of the extended time it has taken to accrue patients, it is likely that this study will need a six-month, no-cost extension in the fall.

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IBD RESEARCH UPDATE (CO-SPONSORED WITH MORRIS ANIMAL FOUNDATION)

Mechanisms of Epithelial Injury in Canine Inflammatory Bowel Disease,

University of Pennsylvania, Peter J. Felsburg, VMD, PhD D04CA-108

Inflammatory bowel disease (IBD) occurs relatively frequently in dogs and can cause vomiting, diarrhea, anorexia and weight loss. Despite the incidence and severity of IBD in dogs, the underlying causes remain uncertain. Current theory suggests an interplay of genetic, environmental and immunological factors and how the epithelial cells (the cells that line the intestine) respond to these factors. The results of this study showed for the first time that probiotic bacteria can positively alter inflammatory cytokines - proteins which regulate the intensity and duration of immune responses - in turn reducing inflammation of the gut. Results obtained from this study helped to further understand the mechanisms of this dis-

ease and have opened up some promising leads to more specific strategies for treating and preventing IBD. Further studies, including probiotic bacteria studies, need to be done. This study opened the doors for such interest.

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NEW PUPPY PLEDGE!

Breeders! Are you looking for a way to introduce your puppy buyers to the PWDF and its mission? Do you want to spark their interest in the health of the Portuguese Water Dog?

We would like to introduce you to PWDF Puppy Pledge! What is a Puppy Pledge? It is an innovative way for breeders to introduce puppy buyers to the PWDF. You, the breeder, inform the puppy buyer about the PWDF and suggest that they consider a tax deductible donation to us to help support health research for the breed. If they would like more

information about the PWDF they can visit our website (www.pwdfoundation.org). We already have a number of breeders who have been doing this for the past few years. Some of them even make it (the donation) mandatory as part of the contract.

As an example, we have a participating breeder who has placed 4 puppies out of her current litter.

This breeder suggests a donation be made to the PWDF. The amounts we have received from these 4 puppy owners are \$50, \$100, \$100 & \$200. Those are typical amounts.

The vast majority of new puppy owners are deeply concerned in the health of their puppy and the rest of the breed. Naturally their name is listed as a donor in our Update. Along those lines we would like to have a separate listing of those breeders who make an effort to support the PWDF. Therefore, please ask your puppy buyer to put your name on the memo line. Should you not want to be listed, we can honor that request

HIP DYSPLASIA REASEARCH UPDATE (CO-SPONSORED WITH MORRIS ANIMAL FOUNDATION)

Mapping Refinement of Quantitative Trait Loci for Canine Hip Dysplasia,

Cornell University, Rory J. Todhunter, BVSc, PhD D04CA-135

Hip dysplasia is one of the most common inherited traits in dogs, with an extremely high incidence in some large breeds. It is caused by mutations in multiple genes. In previous studies, these investigators discovered the genetic markers that point to the chromosomal regions that harbor the genes that contribute to hip dysplasia. In

this study, they hope to narrow down these regions through additional genetic evaluation. Thus far, they have improved the marker coverage to exclude chromosomes from further investigation and have identified eight chromosomes that harbor significant quantitative trait loci (QTL) contributing to hip dysplasia traits. Because they have mapped initially in a small pedigree, parameter estimates are likely to be artificially elevated, thus, in order to confirm these results, the researchers are continuing to map these regions with more dogs. They are also in the midst of developing statistical models for hip

dysplasia association analysis. They have chosen a mixed model for the association analysis which integrates genomic tools, combining both phenotype (physical appearance) and genotype data.

By narrowing the regions that harbor hip dysplasia genes across breeds, these scientists hope to discover the contributing mutations and use that information to design genetic tests that can be used to prevent the propagation of dysplastic dogs.

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2006 Mid Year Update is a publication of the Portuguese Water Dog Foundation, Inc.
P. O. Box 790
Oaks, PA 19456-0790
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The mission of the
**Portuguese Water
Dog Foundation**

is to generate significant
resources for funding
research into genetic and other canine
diseases to improve the life and
health of all
Portuguese Water Dogs.

In Memory of...
In Honor of...

Looking for reasons (or excuses) to support the PWD Foundation and health research throughout the year? You can show your support and at the same time acknowledge a human or PWD friend or family member? Send a donation to honor that friend or a memorial donation in the memory of a departed friend. The PWD Foundation will send a letter acknowledging your generosity to the person or family you designate.

HEMANGIOSARCOMA RESEARCH UPDATE (CO-SPONSORED WITH THE PWDCA)

Detection of Circulating Canine Hemangiosarcoma Cells Using Multi-Parameter Flow Cytometry

Jaime F. Modiano, VMD, PhD

The main goal of this project, funded by the PWDF and the PWDCA is to develop a diagnostic test that can be used to detect hemangiosarcoma cells in blood samples from dogs. The rationale for the test is based on the fact that, as a tumor of cells that line blood vessels, hemangiosarcoma tumor cells are in intimate contact with blood and are likely to shed cells into the circulation. We can therefore use the identification of those cells to confirm a possible diagnosis in dogs that have clinical signs, and eventually to detect the disease before it becomes clinically evident (early stages when it may be more amenable to treatment) as well as to follow response to therapy (monitor remissions).

The language and results in this report are geared to a lay audience. Members of the PWDF or the PWDCA who wish to obtain additional details can contact Dr. Modiano at info@modiolab.org.

For this report, we would like to briefly review the disease, the need for this test, what we have accomplished, and what the future holds.

The disease. Canine hemangiosarcoma is an incurable tumor of cells that line blood vessels (endothelial cells). The disease occurs most commonly in the spleen, but it can also arise from the heart, liver, skin, bone, or other organs. Based on current estimates of the lifetime risk of cancer in dogs (approximately 1 of every 3) and the prevalence of hemangiosarcoma (about 7% of all cancers), we predict that of 65 million pet dogs living in the United States today, as many as two million may get this cancer and die from it. Although dogs of any age and breed are susceptible to hemangiosarcoma, it occurs more commonly in certain breeds including Portuguese Water Dogs. Hemangiosarcoma is extremely indolent – that is, it develops slowly and is essentially painless – so clinical signs are usually not evident until the advanced stages when the tumors are resistant to most treatments. Less than 50% of dogs treated with standard-of-care for this tumor (surgery and intensive chemotherapy) survive more than six months. Many dogs die from severe internal bleeding before there is an opportunity to institute treatment.

Why do we need a blood test for hemangiosarcoma? The clinical signs of hemangiosarcoma are non-specific, so there are some diagnostic challenges. In most cases, the disease appears as sporadic episodes of weakness or simply “feeling tired.” This is due to internal bleeding from the tumor, resulting in anemia (reduced numbers of red blood cells that carry oxygen). Because this bleeding is not always life-threatening when the tumors are small, the body can respond by reabsorbing the blood and making new red cells, allowing the affected dogs will resume their normal behavior until the tumor bleeds again.

A clinical suspicion of hemangiosarcoma can be strengthened by laboratory and imaging tests, but confirmation requires a biopsy that can be examined under the microscope by a pathologist.

Sometime, biopsies can be difficult to obtain (for example, in tumors that arise from the heart), or the other processes like large blood clots and inflammation may obscure the tumor in the biopsy sample. One benefit of this blood test would be the ability to confirm the diagnosis without the need for invasive procedures.

What have we accomplished? Since the beginning of this project, we have validated the principle of the test. In a paper that will be published in the journal *Experimental Hematology*, we document differences between circulating (normal) endothelial cells in healthy dogs (there are very few, if any present) and circulating hemangiosarcoma cells in affected dogs (they are readily detectable with our assay and they appear “different” from normal cells). It is important to note that even though we have established this “proof-of-principle”, much additional development conforming to various regulatory processes will be required before the test can be made available to veterinarians in practice; unfortunately, the timeline for this development is unpredictable.

As mentioned above, there are additional applications for the test. In the same paper, we show that malignant cells disappear from the circulation shortly after dogs are treated with standard-of-care, and they remain low while the dogs are in remission. Thus, the test can then be used to monitor these dogs through the course of treatment and afterwards to determine if the tumor is coming back (called “relapse”). Detection of cells in the circulation could alert the owners and veterinarian to look for metastatic disease in the early stages when additional intervention may be possible, or when the patient could be eligible for enrollment in new clinical trials.

A major objective that we are presently working on is to determine the “sensitivity” of the test. In other words, what is the smallest number of hemangiosarcoma cells in the circulation that we can detect? This is important not only to monitor remission, but also to know how early the disease can be identified before clinical signs appear.

What does the future hold? There is a quandary associated with early detection. Because the disease can arise from several different organs, we cannot provide guidance for appropriate therapy based only on this test. For example, we cannot recommend surgery to remove the spleen when the tumor may lie in the heart or liver (but we just can’t see it!) It is similarly difficult to prescribe chemotherapy, since we do not know if this would be effective and the possible side effects may not offer a reasonable trade-off. That said, we are ahead of the curve. With independent support from the AKC Canine Health Foundation, our lab is working on an immunotherapy approach that could target tumor cells no matter “where they live”, and thus providing a possible way to treat and perhaps cure these cancers before they become a clinical problem. Other groups are using different approaches to hopefully reach the same outcome. It is important to remember that it takes time for science to mature to the point where it can be applied clinically, so no one should expect these treatments to be “right around the corner.” Nevertheless, with your help, projects like these will accomplish the goal to help future generations of dogs live healthier lives.

**The Portuguese Water Dog Foundation, Inc.
P.O. Box 790
Oaks, PA 19456-0790**

The Portuguese Water Dog Foundation, Inc. needs your help and support to fund breed-specific 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.

Donor levels are: Deck Hand (up to \$49); **Sailor** (\$50 to \$99); **Boatswain** (\$100 to \$249); **First Mate** (\$250 to \$499) **Captain** (\$500 - \$999); **Commodore** (\$1000 or more)

Yes, I want to do my part to help Portuguese Water Dogs.

Enclosed is my donation, in the amount of \$ _____, payable to PWDF, Inc.

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 Deb Bender / The Calimel Fund
 John Estes
 Friends of the Foundation
 Mimi Johnson & John Karlsson in memory of Herring Runs Wendell Scupper & Herring Runs Beauregard Skipper
 Senator Edward & Vicky Kennedy
 Linwood A. Kulp & Maryanne Murray
 JD & Ann Northway, in memory of UCDX Cassie CD AWD NA CGC ROM and Mr Splash a.k.a. HIT UCDX CH Seabreeze Baquerio Galante CDX WWD ROM and in honor of our new pup Polly
 Nutmeg Portuguese Water Dog Club, Inc.
 Mary and Douglas Preston in memory of Lands Ends White Water (better known as "Buddy" Orson) and in honor of Dyanne Brewster (Patchwork PWDs) & Christine Harris (ReelLife PWDs)

CAPTAIN (\$500-\$999)

Carole & Richard Allen
 Dyanne & Rick Brewster in memory of Emma
 Robert & Denise Buonaiuto in honor of Bella & Caicos
 Shirley Coleman & Allan Barnes in memory of our sweet Katie, gone too soon
 Pat DeVries
 William & Mary Harkins
 Theresa D. Herman in memory of "Lottie"
 Erin & Steve Mayfield
 Susan Helsel Myrick in memory of Am/Can/Int CH Pickwick's Dancar del Pacifica and CH Sun Joy's Guarda O'Mar Alto
 Donald D. & Barbara L. Niemann
 Barbara Paul
 Amy Haynie Phelan MD, DVM in memory of CH Windruff's Partytime at Driftwood "Partytime"
 Art & Martha Stern in memory of CH Misty Meadow Amigo Brigao and CH Regala's It's The Cha Cha Cha

FIRSTMATE (\$250-\$499)

Sigrid & Neil Bundy
 Colorado Portuguese Water Dog Club in memory of Colorado PWDs departed in 2005: Grand-Lares Showstopper "Sherman" loved by Mary Ewing; CH. DelSur's Commotion by the Ocean "Pepper" loved by Bea & Gordon Jennings; CH. Sunnyside Quiet Wind N Sails TT "Mariah" loved by Barbara & Jim Schmidt; Pinehaven's Rafiki AX,AXJ,WJD "Pago" loved by Leila Vale & Dave Walker: Del Sur Scylla's New Year Resolution "Nori" loved by Deb Keller.
 Phyllis L. Heintz & Misty Harbor's Ocean Girl in memory of Pennrico Knollkrest G. Taylor
 Carolyn M. Knutson
 Betsy Schimpff
 Charles & Margaret Schreiber
 Donna E. Shalala in memory of Cheka
 Art & Martha Stern
 Tom & Peggy Weissenborn in memory of "Baron"

BOATSWAIN (100-\$249)

Ken & Margit Amstutz in memory of Gretta & Heidi
 Ann & Jim Arens in memory of "Buddy" CH Pinehaven's Brigadoon TDI CGC Delta Pet Partner and in honor of "Sassy" CH Anji Elissa Deriva de Galvez TDI CGC Delta on her 12th Birthday
 Bryan Aumiller
 Strphan & Karen Begin in memory of all of our dogs at the Rainbow Bridge
 Samuel Bell Jr in honor of Prince Henry
 William Benjamin
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 Robert Candage
 Robert & Sandra Caruso
 Barbara & Roy Cawley -Makitso, In memory of Xena - our foundation
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 Carol Eisenberg & Bill Benjamin in honor of "Camper"
 Amanda Ford

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 Bea & Gordon Jennings in memory of Del Sur's
 Commotion By The Ocean "Pepper"
 Marion Krupka in memory of PWDs: Cully, Dinah and Lovey
 Haven & Allan Lane & Tejo in memory of
 "Willi" CH Sunnyside Veluda Baleia, 1994-2005 - So Loved & Accomplished
 Thomas E. Leather
 Karen A. Libutti
 Louann & Robert Lindquist in memory of Maggie Mae & "Bump"
 Carol Mattingley & Ann Bowley
 Andrew and Laura McCullough in honor of our PWDs: Stella, Sadie and Callie
 Lisa & Joe McGrath and Family in honor of Rugby
 Brian & Mary Ann McGunigle
 James & Patricia McLaughlin in honor of Morgon
 Claire McLean - Deewal reg., in honor of Am. Mex. Lux. Ger. Dutch Int. CH Deewal Intrepid
 Michael & Eugenie McNamee
 Doreen Mogavera
 Steve Monas & Maggie Megaw
 Norm & Jan Mosher
 Sandra Overton
 Pawtraits
 Sandy Pond
 Karen Rand in honor of Millie & Sophie
 Gary and Kathleen Rosen in memory of Robert Rosen
 Sagui Residence in honor of Rosiedog Sagui
 Robert & Virginia Santoli - Ginsan PWDs in honor of the PWD PSG
 Robert & Virginia Santoli
 Nancy & Roger Schlemmer in memory of Karen and Jim Fitzpatrick's "Monte" and "Rudi"
 Marge & Charles Schreiber in memory of CH Friendship's Woodrow
 Sheryl & Ted Shaker in memory of Calvin, Inka and "Dana"
 Geral & Janet Shipley in honor of Sergio
 Linda K. Shultz in honor of Ellie and her 8 beautiful puppies and proud Uncle Charlie
 Mary J. Shupert
 Southern California Portuguese Water Dog Club, Inc. in memory of the following members' dogs: Mary Ellen Kinnaman's Chewey; Sue Nelson's Noah; Janis Watts' Lida Rose; and Chuck & Susan Teasley's Lego
 Ronald V. Stoch in memory of CH Seawatch Mariners Star (Tillie)
 Jerry & Sharon Stugen in memory of Serra Jerry's little girl.
 Jane & Salo Suwalsky in memory of Magellan ("Jelly") died Dec. 27, 2004
 Mathew Thomsen & Adrienne Hall
 Leila Vale & Dave Walker in memory of Pinehaven Rafiki - "Pago"
 Bruce Young & Kristene Thompson in memory of "Bogie"
 Geri Zuckerman in memory of 'Champion of my Heart' - "Mica"
 M-HIT M-HC U-UD Questar's Little Dipper UDX PU NA WWD GROM

SAILOR (\$50-\$99)

Linda & Steve Kelly in memory of Lida Rose
 Carol & Michael Pleskoff in memory of Lida Rose
 Dick & Judy Seibert in memory of Lida Rose
 Pam Barnett & Janet Shirreffs in memory of Lida Rose
 Kathryn Adams
 Morgan Ackerly
 Rae Lynn Ambach in memory of Cutter and Estee
 Anonymous
 Andrew & Shari Barden
 Marianne Beesley
 Joan C. Bendure
 Leon S. Benson and family in honor of "Oreobay I Wanna Talk About Me"
 Ed & Denise Brewer in memory of Porter and Nina
 Brinks Home Security - Matching Funds on behalf of Linda Kelly
 Virginia Brown

Jean Combs
 Julie Conger
 Phyllis Crane in honor of my Porty Jiggs
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 Christa Heinze - Southern California PWD Club in memory of
 Geri Zuckerman's Mica and Michael Bono & Valerie Zim's ZB
 Christa Heinze-Diamant in honor of Roseknoll's Winston
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 Cortereal - Nadine Hunter in memory of "Sailor" & "Margo"
 Nadine Hunter
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 Barbara Livieratos
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 The Manassas Museum Staff in memory of Brisa
 Mavis McClintock
 Susan McMahan
 Helen & Stephen McNelly
 Roni & Keith Merbler
 Kathy Monroe
 Diane Moore
 Linda Motta
 Suzanne Nelson
 Kelley O'Brien in honor of Halley
 Shirley Ochs
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 Julie Sanchez
 Charles & Marge Schreiber in memory of Chance
 Debora and Michael Sear, in memory of Nala
 Nanci Shelton in memory of CH Questar's Leao de Estrella - "Jerry Bear"
 Nanci Shelton in memory of Jim Potts
 Mike & Cheri Silva in memory of "Buzzy" Goin as fast as I can
 Bob & Bee Souza in memory of "Gus"
 Mary Sparks
 Wendy Diane Spradlin
 Ruth Steen in memory of Boa Vista Do Mar
 Mary Steve
 Kurt & Lore Tesnow
 Linda Trahan
 Walter & Sands Ward in memory of Chaucer and Dancer
 Cristi Fagus Wetherholt
 Dr. Jeffrey Wisch & Cynthia Crofts-Wisch,
 "Curly" & "Catie" Wolcoveick in memory of "Fargo"
 Bob & Charlene Wolfe in honor of "Rainy"
 Penny Yamamoto, Maggie and Sabrina in memory of Halley and Capri
 Phyllis Zusman

DECKHAND (up to \$49)

Kathy Adams, in honor of Steve Bergerson - my favorite
 photographer - Love, Marcell
 Kathy Adams, in honor of Peg Thomas - Mo Doherty - Thanks for
 giving our pups a great beginning! Love, Marcell

Kathy Adams in honor of Chuck Weiss - Love Coco
 Anonymous
 Douglas Beck
 Marion Beith
 Barbara Bekker
 Joan C. Bendure in honor of the PWD PSG
 Karen Berggren in honor of the PWD PSG
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 Susan & Stephen Rosenstein
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 Serry A. Sands, MS, MFT in honor of the PWD PSG
 The Schnell Family in memory of Bem (Bemparcido)
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 Gerald & Janet Shipley
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 Audrey Wallock in honor of Marley Wallock
 Nancy Wentworth in memory of Maritimo Ebbtide Tyler CDX, AWD, AD,
 AX, AXW, EAC, EJC
 Don & Gail Young in memory of Noah
 Aviva Zigelman
 Geri Zuckerman in memory of "Chance" CH Brieah's Mississippi Gambler