

THE Irish Wolfhound Foundation



Focus

Summer 2012

IWF and IWCA Announce Gift Agreement for Osteosarcoma Study

The Irish Wolfhound Foundation (IWF), together with the Irish Wolfhound Club of America (IWCA) is pleased to announce an agreement to provide the Broad Institute a \$42,160 gift to support research by Dr. Kerstin Lindblad-Toh on genetic risk factors for early onset osteosarcoma in Irish Wolfhounds. This one year project will be part of an ongoing effort at The Broad to identify the primary risk factors in our breed. This knowledge is the first step in developing specific SNP chips that can be used for identification of wolfhounds likely to develop osteosarcoma. It will also aid in understanding the modes of transmission of risk factors and provide insights that could help improve clinical treatment for this disease that affects so many Irish Wolfhounds.

DNA samples of affected and control dogs are being pro-

vided from the Irish Wolfhound Foundation DNA bank to support this research project.

Thanks to the IWCA and regional clubs, a major portion of the funding necessary for this gift has already been obtained. Those individuals and organizations wishing to contribute to this effort will be acknowledged by both the IWF and the IWCA. Contributions can be sent to "Osteosarcoma Fund" c/o David Milne, IWF Treasurer, 150 Creek Rd, Phillipsburg, NJ 08865. The IWF is a 501-3(c) charitable organization. If the planned gift amount is exceeded, funds will be used for additional research on osteosarcoma in Irish Wolfhounds.

The researcher leading this effort, Prof. Kerstin Lindblad-Toh is a world-renowned researcher in comparative genomics and leads groups in both the United States, where

she is Scientific Director of Vertebrate Genome Biology at the Broad Institute and in Sweden where she is a professor at Uppsala University and Director of Science for Life Laboratory.

Prof. Lindblad-Toh leads the dog disease-mapping group at The Broad that has developed several specific DNA tests that are being used for testing for genetic diseases in dogs. Author of over a hundred papers, she is published in a number of journals, including Nature. She was recently elected to the Royal Swedish Academy of Sciences.

For further information on the study and where to send blood samples of affected dogs, contact: Frances Abrams, PhD, Irish Wolfhound Foundation Research Coordinator at frances.abrams@att.net.

The Irish Wolfhound Foundation, Inc. Officers and Directors

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The Irish Wolfhound Foundation is a 501(c)(3) charitable organization. Your donation is tax deductible to the full amount allowed by law.

Focus

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New Study on Startle Disease in IWs

The Irish Wolfhound Foundation is funding a new study to look at the prevalence of Startle Disease in Irish Wolfhounds, using DNA from our extensive DNA bank.

Irish Wolfhound Startle Disease

A new genetic disorder known as startle disease has recently been identified in Irish Wolfhounds from the USA. Dogs with startle disease have a low birth weight, muscle stiffness, tremor on handling and difficulty breathing. Professor Robert J. Harvey (UCL School of Pharmacy, London) and Prof. Diane Shelton (UCSC, San Diego) recently found the causative mutation for this disorder - a deletion in the gene encoding a glycine transporter called GlyT2. Carriers of the GlyT2 gene deletion show no discernable clinical differences from normal

animals. The Irish Wolfhound Society has recently funded a new study on this disorder. Prof. Harvey will apply a new diagnostic PCR test to screen the >400 archived DNA sample in the Irish Wolfhound DNA bank, held by Prof. Nate Sutter (Cornell University) to determine the frequency of startle disease carriers in these samples.

Irish Wolfhound Seizure Study Update,

April 11, 2012

All 96 samples that had been genotyped on Affymetrix chips have been reanalyzed during my sabbatical at Cornell University, College of Veterinary Medicine in Ithaca, NY under the guidance of their biostatisticians. The samples were composed of 36 affected IWs and 60 older IWs in which seizures have never been recorded. We have located three chromosomal regions associated with seizures and have begun fine mapping these areas of interest. Three genes are of particular interest, as their functions are related to one another. Because of the size of these areas and in order not to miss mutations, large scale sequencing will be performed of these areas. We expect to have these results by the end of summer.



In Other News....

We have been very fortunate to be given the opportunity to run 150 more IW DNA samples on the more informative Illumina chips to examine other diseases such as rhinitis (primary ciliary dyskinesia), dilated cardiomyopathy, and lymphoma. This (~\$50,000) grant has been provided to Dr. Marta Castelhana (Cornell; DNA bank) and myself from Cornell's College of Veterinary Medicine. We are extremely excited to be able to run the Illumina chips and I am looking forward to analyzing the data. The findings should bring us closer to understanding the molecular basis of these complex genetic disorders. *Submitted by Dr Margret Casal*

The Irish Wolfhound Foundation

The purpose of the Foundation is to promote the appreciation, knowledge, and understanding of Irish Wolfhounds by raising and allocating funds for research, education, and rescue.

IWF Research Committee Members

Mariellen Dentino, MD, Chairman
 Janice M. Bright, BSN, MS, DVM, DACVIM
 Margret Casal, Dr. Med Vet, PhD, Diplomate EUCAR
 Anne Janis, MS
 Nathaniel B. Sutter, PhD
 Alice Timmerman, DVM
 William D. Tyrrell Jr., DVM, DACVIM
 Frances Abrams, PhD, Administrative Coordinator -
 Frances.abrams@att.net

Meet

Margret Casal

Dr med vet, PhD, Dipl. ECAR
Associate Professor of Medical Genetics,
Pediatrics, and Reproduction
School of Veterinary Medicine,
University of Pennsylvania

Margret Casal obtained her veterinary degree from the University of Zürich in Switzerland and her Master's in Virology from the University of Bern, also in Switzerland. After working in small animal reproduction for several years at the University of Zürich, she came to the University of Pennsylvania's (PENN) Veterinary School for a residency in Medical Genetics. After the residency, she stayed at the PENN and completed a PhD in Gene Therapy and Genetics. Dr. Casal is specialized in veterinary genetics, pediatrics and reproduction. She is board certified in theriogenology by the European College of Animal Reproduction. Her clinical interests lie primarily in pediatric diseases of the cat and she has been working in the field of canine and feline reproduction for the past 25 years. Her research interests are focused on the characterization, genetic basis, and treatment of canine genetic skin disorders that also occur in humans. She has also been working on discovering the genes involved in idiopathic epilepsy and primary ciliary dyskinesia in the Irish Wolfhound.



Dr Casal's dog Picasso enjoying his wheels.

IWF Sponsored Health Studies

Ongoing and open to new enrollment

The Irish Wolfhound Seizure Study

Study Start Date: 08-01-1995
Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): Margret Casal, Dr med vet, PhD and Paula Henthorn, PhD

Simultaneous EKG and Echocardiograms in the Mature IW

Study Start Date: 01-01-2003
Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): Drs. Henry Green DVM & William Tyrrell DVM

Blood Collection for Research - The Irish Wolfhound DNA Bank

Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): Margret Casal, Dr med vet, PhD

Standard Electrocardiographic Examination Versus Holter Examination in the Management of Atrial Fibrillation in The Irish Wolfhound

Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): Dr. Sarah Zimmerman

The Pathology of Irish Wolfhound Dilated Cardiomyopathy

Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): Dr. Philip R. Fox and Gaetano Thiene, M.D.

Primary Ciliary Dyskinesia/Rhinitis

Study Start Date: 07-09-2004
Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): Margret Casal, Dr med vet, PhD

Chronic/Recurring Pneumonia

Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): Margret Casal, Dr med vet, PhD

Progressive Retinal Atrophy

Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): Margret Casal, Dr med vet, PhD

Lymphoma

Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): Margret Casal, Dr med vet, PhD

VPC Arrhythmias in Irish Wolfhounds

Study Start Date: 01-01-2007
Study End Date: Ongoing
Enrollment Status: OPEN to new enrollment
Lead Researcher(s): William Tyrrell, DVM

Ongoing - Closed to new enrollment

Startle Disease: A New Genetic Disorder in Irish Wolfhounds

Study Start Date: 03-08-2012
Study End Date: Ongoing
Enrollment Status: CLOSED to new enrollment
Lead Researcher(s): Prof. Robert J. Harvey, PhD and Nathan Sutter, PhD

The Irish Wolfhound Lifetime Cardiac Study

Study End Date: Ongoing
Enrollment Status: CLOSED to new enrollment

(Continued on page 7)

A Word From the President

June 2012

We have a lot of exciting news to report so I will make this short.

Having just returned home for the National Specialty, I would like to send out a big thank you to the show committee for putting on a wonderful event. As always, the Foundation was there in force, providing two full days of health testing which resulted in performing over 70 echocardiograms. That information not only benefits the owners but provided much needed data for the active cardiac study. The Foundation's Gift Shop was once again shipped out and set-up thanks to Dick & Jane Staudt. I also would like to thank Sally White for taking on the daunting task of organizing the live and silent auctions. The Foundation receives a portion of the proceeds from the live auction and I much appreciate the relationship with the IWCA in this. Thank you to all that provided items for the auction and of course the bidders!

The Board of the Foundation is very excited to announce that we now officially have Jean Minnier aboard as our Rescue Coordinator (thanks Jean!). All grant requests will be submitted to and reviewed by Jean. Please visit the IWF web site for more information, including the Rescue Grant Application and a listing of the regional rescue contacts by state.

It continues to be an honor for me to be involved with the Foundation. I am humbled by the selfless efforts of so many people within our community. I look forward to continuing the positive relationship with the IWCA that has emerged, it takes a Village folks and the future of our breed depends on it.

Regards,

Doug Marx – IWF President



Reduced-cost Echocardiograms and EKGs

Once again the IWF will be sponsoring reduced-cost echocardiograms and EKGs at the 2012 IWADV Specialty this coming October. Further details will become available on both the IWADV and IWF web sites (www.iwadv.org, www.iwfoundation.org) later this summer. The heart testing information will also be included in the IWADV Specialty premium list.

Reminder

The Irish Wolfhound Foundation's membership year runs from July 1 to June 30. We have accomplished much this last year but there is much we still need to do. Please help make this our best membership year ever by joining or renewing today. Many people making this small gesture of support can accomplish a lot for our hounds! See page 8 for the membership form.

The Irish Wolfhound Foundation, Inc.

Treasurer's Report

Balances are as of 05/15/12

\$127,076.20 - Regular Account

(includes Research, Rescue, Educations, and General/Unrestricted)

\$90,137.38 - General/Unrestricted Endowment Fund

\$17,957.59 - Rescue Endowment Fund

Disbursements 12/01/11 - 05/15/12 = \$65,589.65

(includes Broad Institute Osteosarcoma Genetic Study grant &
Casal Epilepsy Study grant)

Receipts 12/01/11 - 05/15/12 = \$56,784.87

(includes donations directed to Broad Institute Osteosarcoma Study)

Something to be Aware of: Startle Disease in IWs

Written by Prof. Robert Harvey, PhD.

Startle disease or hyperekplexia is caused by defects in mammalian glycinergic neurotransmission, resulting in neonatal hyper-tonia and an exaggerated startle reflex triggered by noise or touch. Startle disease has been shown in humans and animals to be caused by mutations in one of three genes (GLRA1, GLRB, and SLC6A5) encoding glycine receptors or transporters. Humans with startle disease show good therapeutic responses to benzodiazepines such as clonazepam, which enhance inhibitory transmission mediated by GABA_A receptors (1). Recently, a litter of Irish Wolfhound puppies was identified (2) in which two puppies showed touch-induced muscle stiffness and tremor beginning 5-7 days post-partum (see Photo and view a video clip on the IWF website). However, the puppies are unable to stand and show rigid extended posture in all four limbs. Symptoms ceased when dogs were relaxed or sleeping. Based on these clinical signs, we screened the possible candidate genes and found a defect in the glycine transporter 2 gene in the two affected puppies. Other members of the litter and the dam were shown to be carriers. Thus, a new cause of startle disease in the Irish Wolfhound breed showing an autosomal recessive mode of inheritance has been identified. The Irish Wolfhound Society has recently funded a new study on this disorder. Prof. Harvey will apply a new diagnostic PCR test to screen the >400 archived DNA sample in the Irish Wolfhound DNA bank, held by Prof. Nate Sutter (Cornell University) to determine the frequency of startle disease carriers in these samples.



Photograph of one of two affected puppies demonstrating a hyperextended posture and rigidity in the hindlimbs.

Genetic testing: A diagnostic polymerase chain reaction test is now in place for detection of carrier animals, which are asymptomatic and impossible to identify by other methods. Veterinarians and breeders can access the test directly via Laboklin (3).

References:

1. Rees MI, Harvey K, Pearce BR, Chung SK, Duguid IC, Thomas P, Beatty S, Graham GE, Armstrong L, Shiang R, Abbott KJ, Zuberi SM, Stephenson JB, Owen MJ, Tijssen MA, van den Maagdenberg AM, Smart TG, Supplisson S, Harvey RJ (2006) Mutations in the gene encoding GlyT2 (SLC6A5) define a presynaptic component of human startle disease. *Nat Genet* 38: 801-806.
2. Gill JL, Capper D, Vanbellinghen JF, Chung SK, Higgins RJ, Rees MI, Shelton GD, Harvey RJ (2011) Startle disease in Irish wolfhounds associated with a microdeletion in the glycine transporter GlyT2 gene. *Neurobiology of Disease* 43: 184-189. <http://eprints.pharmacy.ac.uk/1962/>
3. Laboklin startle disease test link: <http://www.laboklin.co.uk/laboklin/showGeneticTest.jsp?testID=8191DD>

Project contact: Prof. Robert J. Harvey, Ph.D., Department of Pharmacology, UCL School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX, United Kingdom.

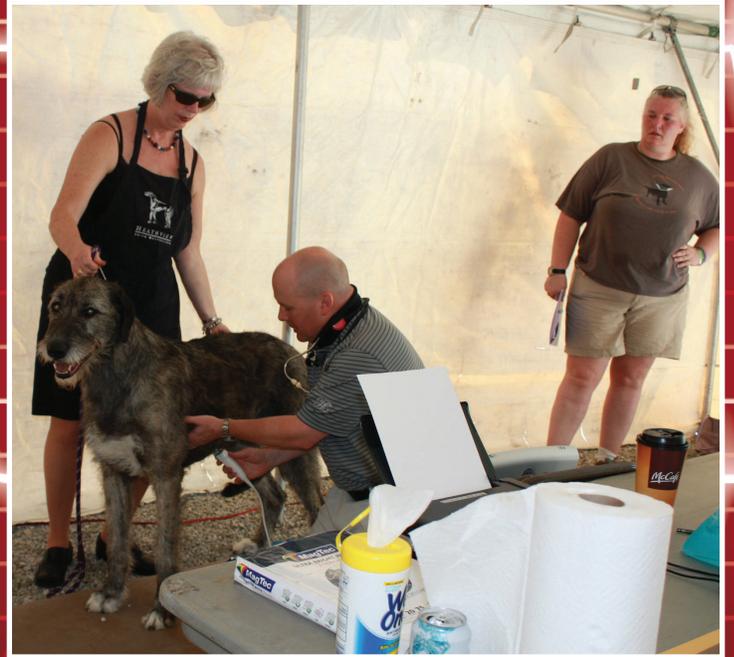
Co-Investigator: Nathan Sutter, Ph.D., Assistant Professor of Medical Genetics, Cornell University, College of Veterinary Medicine, VMC C3-179, USA.

*A Special Thank You
to the following Individuals and Organizations for
Contributing to the Broad Institute Osteosarcoma Study*

Pam Bowman
Irish Wolfhound Association of the
Delaware Valley
Irish Wolfhound Association of the
Garden State
Irish Wolfhound Association of the
Greater Smokey Mountains

Irish Wolfhound Association of the
New England
Irish Wolfhound Association of the
West Coast
Irish Wolfhound Club of America
Rocky Mountain Irish Wolfhound Association
Mr and Mrs Ron Winters

Heart Testing at the IWCA National Specialty



Thanks to everyone who participated in the Irish Wolfhound Foundation heart testing at the IWCA National Specialty. Special thanks to Mariellen Dentino and Dr. William (Bill) Tyrrell who did so much of the testing and to Beth Chastain, who helped with blood sampling and Karen Frederick who helped with EKGs. Thanks to everyone who helped us with holding dogs and to those who brought food and water for the testing crew. The conditions were less than ideal and we appreciate the patience of those who had to wait, especially when they came at the appointed time and found a line in front of them. Your dogs were great. In spite of the heat, the tent and the jumble, they were patient and kind to those people poking, prodding and pinching them.

Everyone who brings their dog to be tested is helping the breed in several ways. First, they are providing data to the Irish Wolfhound Foundation study that Dr. William Tyrrell (Chesapeake Veterinary Cardiology Associates) and Dr. Henry Green (Purdue University) are doing. This study provides a simultaneous electrocardiograms and echocardiograms to evaluate the relative utility of the two diagnostic techniques in evaluating the hearts of our hounds. We need to get 500 Irish Wolfhounds and are well on our way to that goal.

In the process of doing this study, we are also learning more about the health of our hounds and defining the ranges of “normal” for the Irish Wolfhound breed. We are learning more about the progress of heart disease and collecting data on other diseases that affect our hounds.

It was particularly wonderful to test so many veterans. It is known that the incidence of heart disease, especially atrial fibrillation, increases with age in Irish Wolfhounds. Testing at shows

tends to skew the data towards the younger dogs and, while the objective of the study is to determine the best methods for detection as early as possible, it is necessary also to get some older dogs in order to validate the study.

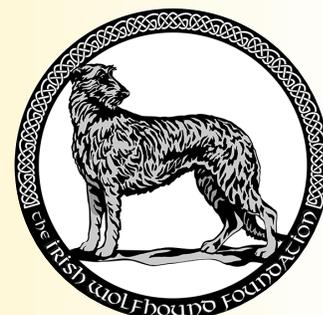
At the same time you are doing your dogs a favor by giving them a valuable check-up. How good can it get? Don't know about you but I am holding out for air conditioning next year!

Here is a brief summary of the statistics for the two days.

Irish Wolfhound Nationals Echo Clinic 2012: Eureka, MO			
Age	Male	Female	
<2	1	1	
2-3 yrs	14	14	
3-4 yrs	1	3	
4-5 yrs	2	4	
5-6 yrs	0	2	
6-7 yrs	3	5	
>7yrs	10	11	
Totals	31	40	71
Normals	15	16	
Degenerative valve disease/incidental findings (normal)	13	17	
Lone AF	0	1	
DCM	2	2	
VPCs	1	2	
Pericardial effusion/aortic tumor		1	
Equivocal aortic stenosis		1	
	31	40	71

The Irish Wolfhound Foundation gratefully acknowledges contributions from the following supporters

Nancy King Aiken	Jocelyn Gagne <i>IMO: CHF Karontra Starkeeper Fantom 07/27/2003 to 03/18/2012</i>	David and Margie Milne	Judith L Snyder
Liz Barningham	Heather Gerry	Pamela Murphy	Robert Stokes
Gloria Barrick <i>IHO: Phillipa, and all you who work so hard who support the well being of Wolfhounds</i>	Tom and Margo Gilliland	Rana Murphy	Edward Storm
Jordan Bellish <i>IMO: "Gone but never forgotten. RIP Blue"</i>	Julia Green	National Fuel Gas Company Foundation	Akiko Tatsuki <i>On behalf of the 8th annual Irish Wolfhound Meeting in Japan, October 2011</i>
Gretchen Bernardi	Heather Haines	Frances and Fionna Norton	Peter and Margaret VanBrunt
Louise Bouchat-Laird	Joseph Hendricks <i>IMO: Riley</i>	Linda R Olsen	Brian Valente
Brendan Brannigan	Marilyn Hochstetler	Ernest Petrey <i>IMO: Donny and Corky</i>	Diana Vreeken & Doug Henry
Linda R. Breidenstein	Janet Howard	Bruce and Cynthia Pitsinger	Darlene Walker
Donna, Eugene and Vada Brown <i>IMO: Mike Pline</i>	Christina Kallay	Jeanie Pitzenberger	Howard Wittels
Jill Bryson	Mel King	Susan Rafacz	Anne Worthmann
Phyllis Buck <i>IMO: "Albert"</i>	MB Kinsella-Topping & Jack Topping	Gabriele Schneidman	
Peg Carty <i>IMO: Donna DiStephano</i>	The Kneller Family	Katherine Schowalter <i>IMO Krough, Sean, & Bailey</i>	
Cynthia Felice	Jane Liess <i>IMO: Claire- "She loved to take you on walks."</i>	Lynn Seaton	
Anne Flanigan	Anne Linden	Monique Seguin	
Michael Fullwood	Debbie Love and Les Jones <i>IMO: "Katie-Sweetest IW ever!"</i>	Paul and Dodie Seymour <i>IMO: Blanny Schreiner</i>	
	George and Jeanette Luther <i>In Remembrance of Kelso and Suvie</i>	Mary Ellen Shriver	
	Tracey and Leonard Luty	Carole Silverthorne <i>In Celebration of Nate, the Velcro hound</i>	
	Judy Mazurkiewicz	Constance Smalley <i>IMO: Vera Chaffee IMO: Mike Pline</i>	
	Elaine McMichael	Donna and David Smith	



(Continued from page 3)

Changes in Hormonal Measurements in Irish Wolfhounds with Atrial Fibrillation

Study End Date: Ongoing
Enrollment Status: CLOSED to new enrollment
Lead Researcher(s): Dr. Dan Hogan and Dr. Henry Green

An Evaluation of Heart Rate in Irish Wolfhounds Digoxin as a Sole Means of Providing Heart Rate Control

Study End Date: Ongoing
Enrollment Status: CLOSED to new enrollment
Lead Researcher(s): Janice Bright, DVM, MS, Diplomate ACVIM

Clinical and Immunological Outcomes in Dogs with Osteosarcoma Treated with Intratumoral Interleukin-12 Microspheres

Study End Date: Ongoing
Enrollment Status: CLOSED to new enrollment
Lead Researcher(s): Dr. Stuart Helfrand

Studies Ended

The Irish Wolfhound Osteosarcoma Treatment Study: Alendronate (Fosamax) for Palliative Treatment of Irish Wolfhound Osteosarcoma

Study Start Date: 11-01-2001
Study End Date: 10-31-2005
Enrollment Status: CLOSED to new enrollment
Lead Researcher(s): William Dernell DVM, MS, Diplomate ACVS

Reminder

The Irish Wolfhound Foundation's membership year runs from July 1 to June 30.

We have accomplished much this last year but there is much we still need to do. Please help make this our best membership year ever by joining or renewing today.

Many people making this small gesture of support can accomplish a lot for our hounds!

See page 8 for the membership form.

The Irish Wolfhound Foundation, Inc.

Focus
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Lititz, PA 17543

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Photo by Leigh St. Clair



THE Irish Wolfhound Foundation
www.iwffoundation.org

2012-2013 IWF Membership

Member name(s) and address:

Name(s):	
Street Address:	
City:	
State:	
Postal Code:	
Country (if outside US):	
Phone (optional):	

Please supply us with your email address so we can spend less money on postage and more on our mission in future:

Payment information (US dollars only, please):

Dues donation:	\$20.00
Additional tax-deductible donation:	
Total enclosed:	

Please complete and return to:

The Irish Wolfhound Foundation
David Milne, Treasurer
150 Creek Rd
Phillipsburg, NJ 08865

Alternatively, you may remit payment using our online Gift Shop at
<http://www.iwfgiftshop.com/minsc/index.php>.

