

THE Irish Wolfhound Foundation



Focus

Summer 2013

The Irish Wolfhound Foundation, Inc.

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Focus

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Photo by Mary O' Malley

Challenge Grant Raises Money for Osteosarcoma Research

The Irish Wolfhound Foundation received a challenge grant for osteosarcoma research in December 2012 and not only met, but vastly exceeded our fundraising goal, thanks to the very generous people in the Irish Wolfhound community.

Help make this our best membership year ever! Form on page 7

Broad Institute Update

March 26, 2013



Project Update: Identification of genetic risk factors of Osteosarcoma in Irish Wolfhounds

Dear Members of the Irish Wolfhound Foundation,

This update is intended to provide a brief summary of work completed since our last update in August, 2012. Following, please find a brief review of the project's key objectives and a summary of work-to-date for each.

Task 1. Tissue collection from sick and healthy dogs

In an effort to strengthen the analysis discussed in our August, 2012 update we have collected and genotyped a total of 101 novel samples (this includes the 51 previously reported samples, as well as 50 new samples). Of the novel samples, 45 are from dogs diagnosed with osteosarcoma, and 56 are from older healthy dogs (i.e. healthy controls). These samples were recently run on the 170k Illumina SNP array.

This number exceeds our original goal of collecting 80 novel samples (40 healthy controls and 40 cases) for this round of genotyping; however, we would like to continue sample collection from both osteosarcoma-affected dogs and older, healthy dogs to facilitate further investigation into other regions of the genome that may also play a role in the disease.

One critical way that the Irish Wolfhound community can continue to support this and other canine health projects after providing a biological sample is to persist in submitting health update forms on an annual or biannual basis, even if there has been no change in the dog's health status.

Options for online and downloadable (i.e. paper) forms can be found at: <http://www.broadinstitute.org/doghealthupdate>

Reminders are sent to dog owners via email by our Dog Disease Research team members one to two times annually, however, we find it to be enormously helpful for breed clubs and associations to also remind their members to complete these health updates annually or biannually.

Again, we are not only looking for changes in health status -- updates that can confirm our healthy controls are also critical for the project!

Task 2. Increase genotyping to increase the power of the analysis

In our August update we reported finding two regions of association by including only cases < 6 years old (28 cases with mean age 4.5 years) and only controls > 6 years (62 controls, mean age 9.0 years). We are now preparing to submit a paper to a high profile journal describing these early findings. In this paper several risk factors are described.

Since osteosarcoma is a complex disease we would expect to find more regions that play a role in its development. Therefore, Task 2

aims to identify additional risk factors by genotyping additional dogs which will allow us to strengthen the analysis and provide a clearer view of additional genes that contribute significantly to the disease.

The basic quality control of the data has now been performed resulting in a total data set of 128 cases and 134 controls that are unique and of high quality. Analysis to identify additional risk factors will now begin.

Task 3. Find the mutations for the major genomic regions linked to disease.

This work is already in progress and will be further expanded upon completion of Task 2. For now we are examining previously associated regions in a total of 16 dogs with the disease and 16 without the disease to allow the identification of the specific disease mutations. This is an enormous task that will be ongoing throughout 2013.

We have found one actual mutation, from which we are beginning to learn about the disease mechanism.

We expect to generate more data soon based on the results from Task 2. Additional analysis of the sequencing data will be ongoing.

Tasks 4-6 are dependent on the results from tasks 2 and 3 and have therefore not started.

Task 4. Develop guidelines and a DNA test for risk prediction.

Task 5. Understand the function of the mutations to unravel disease mechanisms.

Task 6. In the long term, we would like to facilitate the development of new treatment options and help guide selection of treatment based on DNA predisposition.

Principal Investigator:

Dr. Kerstin Lindblad-Toh

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Professor, Comparative Genetics, Uppsala University, Sweden
Email: kersli@broadinstitute.org

Lindblad-Toh lab members:

Dr. Emma Ivansson, Uppsala University, Postdoctoral Fellow, Project Lead

Dr. Elinor Karlsson, Broad Institute, Postdoctoral Fellow, Computational Biology

Dr. Snaevar Sigurdsson, Broad Institute (Former), Postdoctoral Fellow

Dr. Cedric Howald, Broad Institute, Postdoctoral Fellow

Michele Perloski, Broad Institute, Sample coordinator

Collaborators:

Dr. Matthew Breen, North Carolina State University

Dr. Jaime Modiano, University of Minnesota

Dr. Guillermo Couto, Ohio State University

Dr. Mike Starkey, Animal Health Trust, United Kingdom

/update prepared for Kerstin Lindblad-Toh by Leslie Burke

Startle Disease Final Report

Professor Robert J Harvey London 27th March 2013

Final report: Startle disease: a new genetic disorder in Irish Wolfhounds

Principal Investigator: Professor Robert J. Harvey, PhD

Project contact email, mailing address, phone number:

Department of Pharmacology, UCL School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX, UK. Tel: (44) 207 753 5930; E-mail: r.j.harvey@ucl.ac.uk

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

Background: We recently identified a new genetic disorder known as startle disease or hyperekplexia in Irish wolfhounds from the USA. Clinical signs include low birth weight, muscle stiffness, tremor on handling and difficulty breathing. By sequencing the canine equivalents of human startle disease genes in key DNA samples, we found that a deletion in the gene SLC6A5 (encoding the glycine transporter GlyT2) caused this new disorder. Since carriers of the GlyT2 gene deletion show no discernable clinical differences from normal animals, we aimed to accomplish the following:

1. To raise awareness of this new genetic disorder - Prof. Harvey will work together with the Irish Wolfhound Foundation to create a lay language article for publication on the IWF website. This aim was achieved and the article has been posted at: http://www.iwfoundation.org/articles_detail.html?item_id=38&year=2012 http://www.iwfoundation.org/articles_detail.html?item_id=38&year=2012

2. To apply a new multiplex PCR diagnostic test to screen the >400 DNA samples in the Irish Wolfhound DNA bank, held by Prof. Nate Sutter at Cornell, to obtain an estimate of the population frequency of this new disease gene variant. This aim was also achieved as follows:

Methods: Despite initial quality issues with the archived

DNA samples, we successfully applied high-sensitivity KASPar assays for genotyping 390 samples received from Dr. Sutter at Cornell. KASPar technology uses allele-specific oligonucleotide extension and fluorescence resonance energy transfer (FRET) for genotyping. We validated this method by genotyping existing DNA samples from our previous startle disease study (Gill et al 2011, Neurobiol Dis 43:184-189). All samples typing as heterozygous carriers were double-checked using our existing multiplex PCR assay.

Results: We analysed a total of 392 samples from the Irish Wolfhound DNA bank using the KASPar assay. Of these DNA samples, 382 were confirmed as normal (+/+), 2 samples could not be typed by either the KASPar assay or multiplex PCR and 8 were found to be heterozygous carriers (+/-) of the GlyT2 microdeletion. As expected, there were no animals that typed as affected (-/-). The heterozygotes were then verified using a multiplex PCR approach to verify the KASPar assay results.

Conclusions: By genotyping samples from the Irish Wolfhound DNA bank, we have detected 8 heterozygous carriers out of 390 samples. This equates to a frequency of carrier animals of 2%, i.e. on random testing there is 1 carrier for every 50 dogs in the archive. Since Irish Wolfhound DNA bank samples were collected during the period 2006 to 2012, we can also conclude that: 1. Startle disease in Irish Wolfhounds is not a new disorder, but has been present in the population for some time; 2. Heterozygous carriers of the startle disease mutation are more common than might have been expected. This study highlights the importance of future vigilance and DNA screening via Laboklin ([HYPERLINK "http://www.laboklin.co.uk/"](http://www.laboklin.co.uk/))

Please Help Us Find the Genes That Cause Irish Wolfhound Bone Cancer

The Irish Wolfhound Foundation is working with leading geneticists to help identify the gene(s) involved with bone cancer. We know that cancer, whether hereditary or not, is a disease of genes. But we don't know which set of genes malfunction when an Irish Wolfhound gets osteosarcoma.

If you have a wolfhound diagnosed with bone cancer, we need a blood sample from your dog. We also need more blood samples from wolfhounds eight years of age or older who have never had any type of cancer.

This blood will go into our own Irish Wolfhound DNA blood bank, which the IWF established in 2004 in order to support research specifically designed to help our breed. This is NOT the same as CHIC, so if your dog's blood is in CHIC and you would like to help, you will need to give another blood sample.

You can donate blood any time using the forms associated with the IWF DNA Bank (links to the forms can be found at the IWF website).

The IWF is also supporting the Broad Institute's study of the genetics of osteosarcoma in Irish Wolfhounds. Blood from affected hounds is particularly needed.

Thank you for supporting the critical research that is our best hope for fighting osteosarcoma in our beloved hounds.

In Memory



Seeing life from puppy level.



Bill explains what it means to be an Irish Wolfhound.

Bill Deemer

Irish wolfhound community lost a mentor and friend in December 2012 when Bill Deemer died unexpectedly.

Soon after their marriage Bill and Betty Deemer got two Irish wolfhounds (1969) but in 1973 decided to become serious about establishing a breeding program. They were able to import two bitches from Ruth and Leslie Jenkins (Eaglescrag Kate and Eaglescrag Janine) and



Bill pretending to groom!

from this foundation established Fitzarran Irish Wolfhounds. There was much success in the show ring and at national and regional specialties in the US and in Canada. There were also some wonderful coursing times at the Ky farm.

One of his greatest contributions was the generous gift of his time as he tried to help others understand characteristics he so fervently believed had to be preserved in the Irish wolfhound.

Bill enjoyed many generations of Fitzarran Hounds.....walking in the fields at their farm in Richmond Ky so he could watch his hounds move was a favorite activity. He loved picking puppies and each generation excited him anew....of course he depended on Betty for most practical things about raising the hounds- like feeding and grooming etc.

He is greatly missed.

All of you who knew him well have an Irish toast to Bill and his hounds.

Bill and Betty Deemer
Fitzarran Irish Wolfhounds

photos are provided by
"Mariellen Dentino"



In Memory

Diana Powers

April 30, 1918 - February 14, 2013



Many of you will remember Diana Powers for the great Irish Wolfhounds from her famous Powerscourt Kennel. Some will remember her as a popular judge of both the Hound and Herding Group. She served the dog community in many capacities, including being the AKC delegate from the Plainfield Kennel Club.



Photo by Mary O' Malley



Photo by Mary O' Malley

Presidents Message

Summer 2013

Another National specialty has come and gone. This being a very special one for me, my wife Amy handled this year's Best of Breed winner, CH Hound Hill Valley of Aerie who we bred and co-own with Donna Brown. This is truly a dream come true and something that all breeders should aspire to.

There are so many volunteers that are involved in putting on an event like this it's impossible to mention them all. I would like to single out a few, first, Dick and Jane Staudt who go above and beyond hauling the gift shop inventory to North Carolina. Thanks to Frances Abrams, Mariellen Dentino, & Bill Tyrrell for their tireless efforts to provide health testing and blood collection for the breed. To Joe & Donna Pitt, Judy Simon, & Sally White for the huge effort that is the auction, a big congratulation! This year's auction generated over \$20,000.00 which benefits both the IWCA & the IWF. Also, a big thank you to Show Chair, Bambi Rabe along with all her committee members that made this National a memorable one, a job well done!

In closing, I would like to mention the continued relationship that Irish Wolfhound Club of America and the Irish Wolfhound Foundation have nurtured over the past years; it is so important that we work together! I thank the IWCA for including the IWF every year at the National, I hope they feel the same way towards the Foundation; we can do so much more for the breed if we stick together.

Always thank your volunteers; a few words go along way.

Respectfully submitted,
Doug Marx – IWF President

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

The Irish Wolfhound Foundation, Inc.

Treasurer's Report

Balances are as of 4/08/13

\$159,003.76 General Account Balance

\$91,857.55 General Endowment Fund

\$21,061.62 Rescue Endowment Fund

2012 Disbursements total \$86,035.26

2012 Receipts total \$100,229.30

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.

The Irish Wolfhound Foundation gratefully acknowledges contributions from the following supporters

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IMO Tiarnan and Travis
 Lynn Wright
IMO Maegan, Darcie, Mollie & Dara



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 the membership form below

Thank You Anne!

Anne Janis retired from the board of the the Irish Wolfhound Foundation in April of this year. Few people in the history of Irish Wolfhounds in this country have made contributions as lasting and as important to the breed as Anne Janis. Her dedication to scientific inquiry into the health issues of Irish Wolfhounds has been long-standing and selfless.

Beginning in the mid-90's, when Anne was asked to submit pedigrees to the University of Pennsylvania study and to create a questionnaire to help determine the extent of seizures in our breed, Anne has been hard at work gathering vital information. Since even good work is never free, Anne and a dedicated group of IW owners initiated fund-raising projects, which ultimately raised over \$128,000 for the study. Finally, gene sequencing began in 2009. Currently, blood samples and data collection continue through the Irish Wolfhound foundation.

In addition to her work on the seizure issue, Anne was gathering data on other health issues facing the Irish Wolfhound, including recurring pneumonia, primary ciliary dyskinesia (PCD) and fibrocartilaginous embolism (FCE). Beginning in 2004, Anne offered risk analysis on any prospective breeding with information available only to the owners of the possible sire and dam. Since then, hundreds of Irish Wolfhound breeders have availed themselves of this service as a tool in determining health risks in a given combination of pedigrees. And through the years, Anne gave of her time and expertise to the Irish Wolfhound Foundation.

Her contribution to the health and overall condition of our breed, today and in generations of dogs to come, is incalculable, as is our gratitude.

Thank you, Anne.



THE Irish Wolfhound Foundation
www.iwfoundation.org

2013-2014 IWF Membership

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Payment information (US dollars only, please):

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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>.

Thank you for helping to fund IW research, education and rescue!

The Irish Wolfhound Foundation, Inc.

Focus

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Lititz, PA 17543

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Photo by Mary O' Malley

THE Irish Wolfhound Foundation



You Can Count on US ---- Can We Count on You?

With your donations the IWF is taking steps to insure your hounds will have a healthier future.

Please use my contribution for the following:

Research Education Rescue Wherever it's needed most

Name: _____

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David Milne, Treasurer — 150 Creek Rd — Phillipsburg, NJ 08865