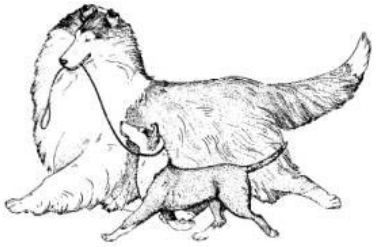

COLLIE HEALTH FOUNDATION

SUMMER 2014
Volume 27
Issue 2

"…TO FOSTER AND PROMOTE THE STUDY OF AND RESEARCH ON THE… PARTICULAR PROBLEMS OF COLLIES…

From the President, Gerrie Oliver
60 Columbus Ave, Closter, NJ 07624-2455
Phone: 201-768-1282/Email: gerrieoliver@hotmail.com

The CCA National in Springfield, MA was spectacular. Sincere thanks to Specialty Chairperson Laura LaBounty and the entire team for a job well done. CHF also did a great job with the traditional silent auction table, promos table, membership table and the Thursday night auction & dinner. Thanks to the many generous auction donors and to all the many CHF workers who gave up their time to help. Thanks, too, to everyone who supports CHF at these events!

CHF welcomed Dr. Leigh Anne Clark, Professor and Researcher, Department of Genetics and Biochemistry, Clemson University and her research assistant, Jacquelyn Evans who shared their findings on the Collie Whole-Genome Sequence in a special presentation on Thursday afternoon. Dr. Clark also provided interesting new information on gray collie syndrome. Be sure to check out CHF Member Kathy Moll's excellent account beginning on page 9.

With gratitude and appreciation, the 2013 President's Award was presented to Michele Brane. Michele has never refused a request to help CHF and has served in a myriad of jobs as far back as 2005 by handling Juniors' Certificates, advertising, creating the list of grants and the overview of tests and studies for the new website--not to mention writing an article on navigating the website for the Bulletin which became part of the Breed Ed Seminar in 2013. Michele also helps the CHF by sharing her artistic talents with us and donating beautiful hand painted items for the night auction each year.

August will be here soon and while searching to find something new to tell you about The Gathering, I went backwards in time to the 1998 article Nancy McDonald wrote for the Cornucopia (remember that?). Nancy's account of the second Gathering at Sunnybank reminded me of the wonder, mystery and romance that is still "The Place". Among all the wonderful weekend happenings that year, Nancy delighted in having Claire Leishman, who unselfishly dedicated a lifetime to collecting and preserving Terhune's treasures, as key speaker. How amazing is it that 15 years later we can still celebrate those treasures and Claire, too? In tribute to the "FABULOUS FEMALES" of Sunnybank, the story of this Quarter Century Collie Group Right Stuff Award Winner will be featured in a repeat of the original presentation. Come celebrate Claire and all the Fabulous Females of Sunnybank this August 16th & 17th and discover the wonder, mystery and romance for yourself!

continued on Page 2

In speaking of Right Stuff Award Winners, I last had the sad duty to report the passing of a great lady, the mistress of Deep South Collies, Helen Denton. Helen served in many capacities but most notably as President of the Collie Health Foundation, Chairman of the Grants Committee, worker at the early Gatherings and a fixture at every CHF Auction. Recently CHF was notified of a very generous $20,000 bequest from Helen's estate. I think her dear friend, Pati Merrill, said it best in Helen's Right Stuff Award tribute "The Foundation – she was there when it started and she continues to be there…" In recognition of her generous contributions to CHF, the Board voted to donate $25k of the $50k epilepsy initiative funding in honor of Helen Denton in order for her to be recognized the AKC/CHF "Millenium Founder" level donor.

Thanks for everything you do to help us grow! *- Gerrie*

Treasurer's Report
Nancy McDonald, Treasurer

Collie Health Foundation
Balance Sheet as of March 31, 2014

ASSETS			
Current Assets			
	Checking/Savings		
	Bank Of America Operating	$9,483.79	
	Bank Of America Money Market	$108,434.53	
	Paypal	$12,850.20	
	Wachovia - Hilda Rickenbaugh	$12,863.65	
	Total Checking/Savings		$143,632.17
Other Current Assets			
	UBS assets		
	UBS Money Market	$172,682.83	
	UBS accts	$332,799.57	
	UBS assets – Other	-$450.00	
	Total UBS Assets		$505,032.40
Total Current Assets			$648,664.57
Other Assets			
	Investment	$1,421.50	
	Promo Items Inventory	$10,867.38	
	Prepaid Expenses	$250.00	
	Veteran medallions	$2,100.00	
Total Other Assets			$14,638.88
TOTAL ASSETS			$663,303.45
LIABILITIES & EQUITY			
Current Liabilities			
	Other Current Liabilities	$100.00	
	Total Other Current Liabilities		$100.00
Total Liabilities			$100.00
Equity			
	Opening Balance Equity	$600,783.81	
	Unrestricted Net Assets	$77,711.79	
	Net Income	-$15,292,15	
Total Equity			$663,203.45
TOTAL LIABILITIES & EQUITY			$663,303.45

Anice, Bruce & Wolf

Grrrrrl Power!

Fabulous Females of Sunnybank

August 16-17, 2014

The 18th Annual Gathering at Sunnybank

381 Terhune Drive, Wayne, NJ 07470

SATURDAY, AUGUST 16th

9:00 am & 9:30 am

SunnybankWalking Tours

Guides: Marilyn Horowitz & Kathy George
Judy Leathers & Donna McKoy

Special Ladies Only Musical Ensemble
Susan Chandler, Keyboard

11:00am – The Gathering's Own Fabulous Females!

Kristina Marshall on Sunnybank Jean and her Kennelmates
Kathy George on Sunnybank in the Words of its Fabulous Females
Noralee Smiley on Marion Harland
Donna McKoy on Anice Terhune
Judy Leathers on Claire Leishman
& QCCG's Tribute to Claire

10:00a to 2:00p - Microchip Clinic @ Gazebo - $25

AKC CAR Including lifetime enrollment; no annual fees
24/7 support by dedicated recovery experts - Collar ID tags

1:00pm – CGC & CGCA Testing - $15

1:00pm Bright & Beautiful Therapy Dog Test - $25

Joanne Silver & Cindy Mauro, Evaluators
Entries Limited to 15 Dogs – Pre-registration Required
Call Sue Chandler 973-696-2506 or
greyskyes110@optonline.net
CGC Dogs must be 6 months old; Therapy Dogs must be 1 year

RALLY!

2:00p – Rally Demonstration
Cathie Sayre, Erin Byrne & Maria O'Boyle

Portobello's, 155 Ramapo Valley Road, Oakland
$40 - Advance Reservations or $45 at door
Send Your Check to Gerrie - Payable "CHF"

SUNDAY, AUGUST 17th

9:00 am

Collie Memorial & Bagpiper at Sunnybank

Complete order form below and mail together
with your check for $4 payable to "CHF" before August 1st
FMI: Sue at 201-391-9826 or
susiezo@aol.com

10:00 am - Virtues Match

* PROFILE * SKULL*MUZZLE*EXPRESSION*
* OUTLINE * FRONT * REAR * SIDE GAIT *
Moderated by Royal Rock's Leslie Canavan
Judges: Joan Kirkland, Kirkhaven
Lee Runnels, Kimberee
Marianne Sullivan, Millknock

The Gathering Juniors' Match
Judge: Joan Kirkland, Kirkhaven

SPECIAL GUEST: Samantha Wright, AKC/CHF

Lad of Sunnybank Memorial Match

"Lad of Sunnybank" Trophy Best in Match
Judges:
Dogs: Erin Blaisure, Tirnanog
Bitches: Robette (Johns) Ehrbar, Rowbar

Event Prices: $5/Virtue or $12/3
Juniors, Lad Match Entry & Rally Fun Run: $5
Microchip $25
CGC $15 TDI $25

BREAKFAST & LUNCH AVAILABLE
SATURDAY & SUNDAY
Courtesy of Boles' Bistro & CCNNJ

HOLIDAY INN EXPRESS, 303 Union Ave., Haskell, NJ 07420 - Call DIRECT 973-839-4405
LA QUINTA INN & SUITES,1850 Rte. 23 & Ratzer Rd., Wayne, NJ, CALL DIRECT 1-973-696-8050

FMI: Gerrie Oliver, 60 Columbus Avenue, Closter, NJ 07624 - (201) 768-1282 - gerrieoliver@hotmail.com
or Nancy McDonald, 2834 Cotten Road, Sanford, NC 27330-6994 - (919) 718-9347 - nancy@collieexpressions.com

T-SHIRTS, PREMIUMS, AUCTIONS *PAYMENTS WITH "SUNNY MONEY"* *SORRY, NO VENDORS ALLOWED*	All Proceeds to Collie Health Foundation Updates at www.colliehealth.org, *Collie Expressions* and colliesonline.com	*VISIT THE VAN RIPER-HOPPER HOUSE* *533 Berdan Avenue, Wayne, NJ 07470* *973-694-7192*

Collie Memorial Celebration at Sunnybank
Memorial Card Order Form

Name for (memorial) (celebration)_____
Any additional information (title, year of birth, etc.) (8-10 words only please)_____
_____

Your Name:_____
Street Address: _____
City State Zip:_____

Total number of cards ordered at $4.00 each _____
Total amount enclosed: $ _____
Please make your check payable to **CHF**.
FMI: Sue at 201-391-9826 or susiezo@aol.com

To: **Ms. Susan DeLorenzo**
22 West Park Avenue
Park Ridge, NJ 07656

If you wish to have your card(s) mailed after the Memorial, enclose a No. 10 SASE for every 2 cards ordered, or a SAS priority mailer if you are ordering a large quantity and send by August 10, 2014.

Collie Memorial Celebration at Sunnybank
Memorial Card Order Form

Name for (memorial) (celebration)_____
Any additional information (title, year of birth, etc.) (8-10 words only please)_____
_____

Your Name:_____
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The Collie Health Foundation Joins the AKC Canine Health Foundation's Epilepsy Research Initiative as a Champion Sponsor

The Winter 2013 Newsletter included an announcement that the Collie Health Foundation had joined the AKC Canine Health Foundation's Bloat Initiative as a Champion Sponsor. In late May 2014, the CHF Board voted to again join with the AKC Canine Health Foundation and support their Epilepsy Research Initiative as Champion Sponsor pledging $50,000 toward the initiative. The following information came from the AKCCHF and has been edited and reformatted for our newsletter.

AKC Canine Health Foundation Launches Epilepsy Research Initiative

WHAT IS EPILEPSY?

Epilepsy is a general term for neurological conditions that cause seizures.

Epilepsy is among the most common neurological disorders in dogs. Any breed of dog and mixed-breeds can be affected by epilepsy. Epilepsy can be heritable and some breeds are believed to be predisposed to the condition. More information on seizures in dogs is available from the American College of Veterinary Internal Medicine.

WHY FOCUS ON EPILEPSY IN 2014?

Epilepsy research is an unmet need articulated by dog clubs, owners and veterinarians. Much more must be done to understand the causes of epilepsy and to develop additional treatment options. Approximately 30% of all dogs diagnosed with epilepsy are not able to achieve relief from seizures with the current drugs therapies available. The current drug treatment options also carry possible negative side-effects. Epilepsy is often a devastating diagnosis for a dog and his owner.

We must make a significant investment to make real progress in the fight against epilepsy.

Because little is understood about the causes of idiopathic epilepsy, more work must be done to define the underlying molecular mechanisms that cause the disease. The life-altering nature of epilepsy is of foremost concern to the AKC Canine Health Foundation and will require a major research effort. We need significant sponsorship from dog clubs as well as donations from individuals and corporations.

The Request for Proposals is written as a two phase effort. The recipient(s) of the Phase I grant(s) will be expected to deliver something demonstrable so that research on epilepsy moves forward in a substantial way. Collaboration among researchers is required to translate results from bench to bedside as rapidly as possible. The request for proposals released to the research community follows.

Epilepsy Initiative
Request for Proposals

Released to Researchers on February 20, 2014

The seizure-related syndromes collectively known as epilepsy represent one of the most common neurological disorders in dogs, and as such are a significant concern to the AKC Canine Health Foundation and our donors. In response to donor concern, CHF is launching a major, two phase research effort to better classify disease, understand the underlying mechanisms that predispose dogs to epilepsy, and finally, to introduce new drugs into the canine epilepsy treatment pipeline.

To insure success, the Epilepsy Research Initiative requires the formation of collaborative pre-clinical/clinical research groups who will work together to define the molecular basis of epilepsy and develop disease modification or prevention strategies. It is expected that formation of collaborative pre-clinical/clinical research teams will accelerate the discovery phase and thus the translation of research from laboratory bench to patient. Successful applications must demonstrate both a strong understanding of the clinical syndromes themselves and a rigorous preclinical research base.

Phase I: Discovery
As epilepsy has a wide range of severities, precipitating causes, comorbidities, and treatment outcomes, any major prevention/therapeutic target identification effort must include the goal of accurate disease diagnosis and phenotyping. In Phase I researchers are expected to focus on defining the underlying molecular mechanisms of disease within clearly stratified patient populations. While genomic studies can be a component of pre-clinical research, GWAS in the absence of complementary proteomic, epigenomic, metabolomic, transcriptomic or pathophysiology studies will not be considered responsive to this RFP.

Overarching 'Special Topics of Interest' include, but are not limited to:

- Discovery approach to define the pathophysiology of canine epilepsy. The focus of discovery research should be epilepsy prevention and/or identification of novel therapeutic targets.
- Overcoming the blood brain barrier to delivering potentially novel anti-seizure agents such as RNA therapies, genes, antibodies, or cell therapies to treat epilepsy.
- Identify and validate biomarkers that define a beneficial response to treatment.
- Define novel ways to image brain chemistry and function during seizures to better phenotype disease.
- Develop systems that anticipate epileptic seizures and deliver a therapy to halt them.

Milestones that will trigger submission of Phase II applications must be clearly defined in Phase I grant applications. Funding in phase I is expected to be up to $100,000 per award.

Phase II: Implementation
Using data from Phase I studies, researchers will design and conduct patient-centered studies that will lead to tangible outcomes in disease prevention and/or treatment. Funding in phase II is expected to be up to $250,000.

Research Deliverable: At the conclusion of Phase I and II of the Epilepsy Research Initiative dog owners and the veterinary community will have improved methods for preventing and treating Epilepsy in dogs.

Samantha Wright, AKC Canine Health Foundation Program Manager notified the Board that the AKC Canine Health Foundation received six applications in response for the RFP from the following investigators:

Hannes Lohi, PhD; University of Helsinki
Sam Long, PhD; University of Melbourne
Charles Lee, PhD; Louisiana State University
Ned Patterson, DVM, PhD; University of Minnesota
Jennifer Gambino, PhD; Mississippi State University
Holger Volk, DVM, PhD; Royal Veterinary College

The next step is to assemble their scientific review group; made up of experts in the field of neurology and epilepsy who declare that they do not have a Conflict of Interest (COI) with any of the applicants.

COLLIE HEALTH FOUNDATION

Donations in Honor/Celebration/Memory
General Donations
February 1, 2014 – June 30, 2014

Donor	In honor/celebration/memory of….
Patricia Schroder	In memory of Ed Bechtel
Mary Ellen & Roger Splinter	In memory of Sampson, beloved pet of David & Karen Steen
Joani & Sami Berg	In memory of GCH Highcroft Lode-Arks Roulette & Sashay Enchanter's Strutn' My Stuff (Belle)
Jean Coffey	In memory of Ed Bechtel
James S. & Irene C. Lackman	In memory of "Teddy" 9/6/01 - 1/10/14, Crispin Lord of the Dance CDX, RE, CGC, HIC, TDI
Erin Matthews & Rich Bellows	General Fund
Joan Scheulen	In memory of Ed Bechtel
Carol Brim	In memory of beautiful "Apache" loved and cherished by Johanna Lance of Cleveland
Lloyd Broggini	In memory of Martha Hoffman
Broggini Family	In memory of Martha Hoffman
Helga Kane	In memory of Janet "Jidge" Holbrook
Wendy Bush Lyons, Esq.	In memory of Lynne Dorsey
Andrea Moss	In memory of Cathy Toft
Kathleen N. Peters	In memory of Lynne Dorsey
Jack & Lorraine Santi	In memory of Janet Holbrook
Lawrence S. & Theresa M. Uzelac	In memory of Peter Kane
Jean A. Wasiak	In memory of ALL the collies I've had since I was a child!
Mary & Rose Robischon	In memory of Lynne Dorsey
Gerald & James Ardine & Danielle Fuller	In memory of Judith Ardine
Central New York Kennel Club, Inc.	In memory of Brady, beloved collie of Deanne Balutis
Collie Club of Georgia	In honor of Gail & Millie Meyer & their many contributions to the Collie Community
Jean P. DeGruchy	In memory of Lynn Dorsey
Nancy Jan Holbrook	In memory of Janet "Jidge" Holbrook
Judith D. Kirkeby	In memory of Rita Stanczik
Earl & Linda Rogers	In memory of Judith Ardine
Shirley Schaffer	In memory of Judith Ardine
The Hurricane Ridge Kennel Club	In Memory of Janet "Jidge" Holbrook
Jane Gumnit	In memory of Evelyn Honig
Suzanne Walsh	In memory of Maestro, owned and loved by Noreen Bennett
S. James & Janice Coppersmith	In memory of the lovely Evelyn Honig
Orville & Becky Crowley	In memory of Linden Lane Tough Tactics (Tad)
Orville & Becky Crowley	In memory of Rita Stanczik
Orville & Becky Crowley	In memory of Evelyn Honig
Helen K. Denton	Bequest
Joseph & Michele DiCarlo	In memory of Evelyn Honig
Karing K9's Therapy Dogs	In memory of V-CH U-GRACH5 U-ALCH BIMRS/BIS U-CDX FAITHFUL PROMISE KEEPER, CD, HSAsd, AX, AXJ, OAP, OJP, NFP, RAE, NAC, RS-N, THD, CC, BPDX, CGC, AWCA AOM I, II, III and Oklahoma Veterinary Medical Assoc. 2012 Hall of Fame Inductee - "Jackson"
Mary Lenertz	In memory of Evelyn Honig

COLLIE HEALTH FOUNDATION

Donations in Honor / Celebration / Memory
General Donations
February 1, 2014 – June 30, 2014
continued

Donor	In honor / celebration / memory of….
Kathleen N. Peters	In memory of Evelyn Honig
Mary H. Wells	In memory of Malcolm, the Proulx family collie
Mary H. Wells	In celebration of Audrey Proulx's Graduation from Stanford
Mary H. Wells	In celebration of Anna Diaz's Graduation from Loyola Marymount University
Nancy Van Note	In memory of Linden Lane Tough Tactics (Tad) and Linden Lane Butterfly (Kitty) beloved collies of Orville & Becky Crowley
Sean Devlin	In loving memory of Lynne Dorsey
Judith D. Kirkeby	In memory of Albemarles Lady (Allie) 2001-2014
Kathleen N. Peters	In memory of Dennis Day, Abbehurst
Maria Elwan Theriault	In memory of Evelyn Honig

Study Assistance Request!

Editors note: We received the following study assistance request from Animal Cell Therapies, Inc. This is not part of the work of the Collie Health Foundation.

Animal Cell Therapies is beginning clinical trials for using stem cell therapy to treat dogs who have osteoarthritis, laryngeal paralysis, ligament/tendon issues, Rheumatoid arthritis, liver disease, and burns. Our pilot studies have shown significant improvement with no adverse side effects. We are seeking funding to continue our studies, as well as volunteers who would like to participate in these studies. In addition, we are recruiting vets to administer our stem cells, as well as collect and donate umbilical cords from caesarian sections for the harvesting of stem cells.

Our primary clinical trial is taking place at the University of Florida, and we are recruiting further pilot studies across the country.

If your organization knows of any dogs who could benefit from treatment for arthritis (or any of the above-mentioned medical issues), please let us know, as we would love to assist in providing this ground-breaking treatment. As we are still in the clinical trial phase, we would be providing stem cell therapy at no cost.

Further information can be found on our website: www.actcells.com, as well as our YouTube channel: http://bit.ly/actvideos.

Kat Rheinbold
Executive Assistant
Animal Cell Therapies, Inc.
10054 Mesa Ridge Ct, #106
San Diego, CA 92121

ACTcells.com
Kat.Rheinbold@ACTcells.com
P: 858-678-8843
F: 858-678-0621

RESEARCH UPDATE FROM CLEMSON UNIVERSITY CANINE GENETICS LAB

THE SEARCH FOR THE ALLELES FOR DERMATOMYOSITIS IN THE COLLIE & SHETLAND SHEEPDOG AND THE MAPPING OF THE COLLIE GENOME

Presented by Dr. Leigh Anne Clark, Jacquelyn Evans & Dr. Allison Starr-Moss
Written by Kathy V. Moll

Reprinted with permission from the Collie Club of America *Bulletin* and reformatted for this newsletter. Because of space restrictions, four pie charts and one picture that were in the original article are not included here.

Introduction: It is my sincere wish that those who were not fortunate enough to attend the presentations sponsored by the Collie Health Foundation at the 2014 National study this article. The first presentation was Thursday afternoon and then was repeated at the CHF dinner and auction. Dr. Clark has provided me with suggestions and edits along with a few of the slides she and her colleagues used. Science isn't always spell-binding, but in this case, ***the presentation was excellent and contained information that is crucial for the future of our Collies!***

CHF President Gerrie Oliver introduced the speakers from Clemson University Canine Genetics, Dr. Leigh Anne Clark, Jacquelyn Evans – graduate student - and Dr. Allison Starr-Moss. All have been working on research projects concerning the Collie genome and specifically on the auto-immune disease, dermatomyositis (DM or DMS), occurring mainly in Collies and in Shetland Sheepdogs. The reason for the addition of the "S" in the abbreviation identifying dermatomyositis is to distinguish it from another canine disease called degenerative myelopathy, also abbreviated DM. These two diseases are not related to each other. To avoid confusion, we will use DMS to identify the Collie/Sheltie disease in this article.

Dr. Allison Starr-Moss introduced the new Clemson Genetics Counseling Service for Dog Breeders, a course for students of genetics with an interest in genetics counseling. She also handed out the pamphlet, ***Breed Healthy Dogs Through Understanding Basic Genetics,*** created by these students. Email Dr. Clark lclark4@clemson.edu or Dr. Starr-Moss astarr@clemson.edu to receive copies for use at club meetings and functions. Dr. Starr-Moss asked for suggestions that breeders would like to see included to improve the pamphlet, currently a work in progress. Please send your suggestions to her.

Background: Jacquelyn Evans spoke next about **chromosome 12** where immune system genes are located, including auto immune disease genes such as diabetes, hypothyroidism, lupus and dermatomyositis (DMS). Identification of the chromosome is a giant step toward finding the DMS alleles. The team made this important chromosome discovery.

Each puppy in a litter gets one copy of each chromosome and one copy of each gene on each chromosome from its sire and its dam. The pairs of each gene in the puppy are called **alleles.** If these pairs are identical, they are called **homozygous** for the trait the genes control. If they are different, they are called **heterozygous** for the trait. Taken together alleles (pairs) form the puppy's **genotype** (genetic makeup); the traits that are visible to the breeder in the puppy are called its **phenotype** (physical appearance).

Immune System Alleles: When working properly, immune system genes produce proteins that allow the body to distinguish its own proteins from those proteins that come from outside sources such as bacteria. Thus, the dog's healthy immune system can mount a response to outside proteins that attack its body and overcome them. Heterozygosity for immune system alleles allows for maximum protection and a healthy immune system.

In recent GSD studies, the Clemson team discovered that 70% of the population was heterozygous for 11 immune system alleles. In Pembroke Welsh Corgis the percentage was even higher. So it appears that there are healthy genetic immune system choices in these two breeds.

Unfortunately, modern American Collies are not as fortunate; over time we have reduced our heterozygous immune system population. In the population studied, 100% of the Collies were homozygous for immune system alleles. Subjects varied widely in background and included rescues, pets and show Collies. Available pedigrees helped eliminate Collies that were closely related in the first two generations.

International Collies studied were slightly better off for heterozygous in 2 alleles identified in the breed. The same pedigree criteria were applied to European, Australian and a few South American Collies. None with American ancestry were included. Still, 87% of these Collies were homozygous, leaving only 13% heterozygous for the 11 immune system alleles. The team is still collecting genetic data to help widen the samples.

Driver/Passenger Effect & Bottlenecks: While the exact reasons for the loss of diversity are unclear, there are a couple of possible explanations. One may be that the selection for particular behavioral and physical traits, such as herding in past generations, have created **driver** and **passenger genes.** Unrelated genes exist together on DNA strands. In the past, breeders have systematically selected for particular traits. If most breeders are doing so for generations, then the **driver/passenger** effect takes over among genes in close proximity to each other on a strand. For example, the genes for a Collie physical trait may become the driver, carrying along the neighboring immune system genes that have now become passengers. Selecting for homozygous alleles for the physical trait might cause a reduction in the alleles of the surrounding genes.

Another possibility is that only a small number of imported Collies became the foundation for all early American Collie kennels at the turn of the 20th century, causing a **bottleneck** at that period in our breed's development. Bottlenecks vastly reduced the number of different genes in modern dogs. The first species-wide canine bottleneck happened when dogs were domesticated thousands of years ago, because only a small population of grey wolves contributed to the creation of modern dogs. The second overall bottleneck occurred when people began selecting for characteristics in temperament and appearance, creating different breeds for specific work. Individual breeds often have their own bottlenecks.

Genetic Mapping Process: Dr. Clark explained how the team narrowed the search for the location of the alleles causing DMS among the 40 canine chromosomes containing hundreds of thousands of genes that make up the Collie's genotype. Of the over 600 genetic diseases in dogs, 65% are **autosomal recessives**. For example, in Collies progressive retinal atrophy (PRA) is a simple recessive. This disease occurs when the dog has two recessive alleles for the disease which causes blindness. Collies that are heterozygous (only one recessive gene) are carriers of the disease, but have a normal allele that prevents them from having the disease. The genes that cause dermatomyositis are among the 35% that are not autosomal recessives, so finding the location and determining inheritance and then eliminating the disease is more complicated.

Next, Dr. Clark talked about the importance of ***single-nucleotide polymorphism (SNP, pronounced snip).*** *Letters are used to indicate the bases adenine, cytosine, guanine, and thymine; these instructions come in a chain designated with A, T, C or G. The order of these bases on the chain determines the meaning of the genetic message. A change in one chain or string is a SNP. SNPs are the most common type of genetic variation. Each SNP represents a difference in a single DNA building block, called a* ***nucleotide.*** *For example, a SNP may replace the nucleotide cytosine (C) with the nucleotide thymine (T) in a certain stretch of DNA. The team used these SNPs as road signs so that they knew where in the genome they were while searching for DMS genes and also to include or eliminate sites where the DMS gene(s) are or are not located. SNPs do not cause any genetic problems.*

DMS Definition & History: Dr. Clark showed slides of Collies affected with DMS. The disease presents with skin lesions, usually on the face, ears and bony prominences and may also include muscle atrophy, especially in the temporal and masseter muscles of the head. Severity varies widely from barely noticeable to severe. The affected dog can live a normal life span with few outbreaks or can die very prematurely. ***DMS auto-immune disease***

should not be confused with demodectic mange, which is not an auto-immune disease. The latter is likely a temporary T-cell disruption in puppies, is usually localized and typically goes away for good once the puppy's immune system is fully functional. The confusion of the two is understandable because both have a puppy onset. Unless mange is generalized and resistant to treatment, it is much less serious than DMS.

A study conducted in the 1980s test bred DMS affected Collies to Labrador Retrievers, a breed that does not have any recorded cases of DMS. When the two affected Collies were bred to each other, the resulting litter produced 6 puppies; all of which were affected. When the same affected Collie sire was bred to a Lab, four puppies resulted; three of whom were affected. This tells us that DMS is not caused by a simple recessive. Instead it is **dominant**; only one copy from one parent is needed to produce the disease. Factors controlling the severity of DMS may include **incomplete penetrance**. If a mutation in the gene responsible for DMS has 80% penetrance, then 80% of those with the mutation will develop the disease, while 20% will not. Another possible factor is **variable expression**, which occurs when a phenotype is expressed to a different degree among individuals with the same genotype. It is possible that some dogs with DMS have such a mild case that it goes undetected. Environmental triggers such as bacteria and viruses may also be involved. Once the DMS alleles are identified, the exact factors that control inheritance may also become clear.

Specific Criteria & the Mapping Process: The team used SNP's and a technique called **association mapping** to start tracking down the culprit alleles. One group of DMS affected Collies and one control group of Collies with no DMS family history were used. The object was to compare regions in the DMS group that were different from regions in the control group. The selection criteria for these groups were as stringent as possible.

All affected Collies had been diagnosed by pathologists as probable DMS. Probable is the closest to definitive as anyone can get since other auto-immune diseases, such as lupus, read very much like DMS, so other criteria are used by pathologists to determine which disease is most likely. The controls were Collies 8 years or older that had no history of any type of skin disease and no closely related familial ties to skin disease.

In addition, checks for **population balance** were utilized. For example, Collies in the DMS group and control group varied in coat color, creating balance. Collies in both groups were all American bred, also creating balance. The team used **principle component analysis** to plot for balance and eliminated individuals that created imbalance.

The team genotyped thousands of SNPs to discover whether there is an allele of a SNP that occurs more frequently in DMS affected Collies than in non-affected. The goal was to sort through the SNPs to determine those with no association to DMS from those with a possible association. A tool called a **bead chip** was used to obtain individual Collie genotypes; it has the capability of identifying 173,000 SNPs.

In the next research stage, the team began preliminary mapping for dermatomyositis with surprising results. The region in which DMS occurs was narrowed down more quickly than expected, so research began on the genotypes in that region. Of the Collies that had 2 copies (homozygous) of the suspect DMS region, 92% exhibited the disease. Of the collies that had one copy (heterozygous) of the suspect DMS genes, only 18% exhibited the disease. It may be that the small percentage (8%) of homozygous Collies without signs of DMS never encountered a trigger that activated the auto-immune response, or that the disease signs in these Collies were too mild to be noticed by the owner or that symptoms were not going to appear until well into old age.

The team has narrowed thousands of genes to just over 100 suspect genes in a specific region of the genome. The goal now is to identify the DMS genes that are the driver genes from the many passenger genes along for the genetic ride.

Additional Funding, Research & Breeding: Because DMS also occurs in humans, the team applied to The National Institute of Health and received $300,000 to continue working. Their research in Collies benefits DMS research in human medicine. The next step in narrowing the number of genes further is to do a parallel study in

Shetland Sheepdogs that also have DMS. The aim is to use this study to locate DMS in the same region in affected Shelties and narrow further the region identified in Collies. In both breeds the genes are very likely to be the same. The team has already done much of the preliminary work on both the affected Sheltie group and the control group.

Dr. Clark's suggestion to breeders is that once a reliable test for DMS genes is created, breeders carefully attempt to breed first for Collies that are heterozygous for DMS. ***Any attempt to eliminate all Collies from the gene pool with only one copy of the gene would likely result in destructive bottleneck.*** Collies have had bottlenecks in the past, and our breed cannot afford another one. Very slowly eliminating heterozygous Collies is the only prudent approach since they have an 18% or less probability of having the disease. Further reducing genetic diversity in the Collie is far more dangerous.

The Collie Genome & Selective Sweeps: In addition to all the research that has been done to identify DMS, the team has also mapped the entire **genome** of 5 Collies in the study. This was a tremendous undertaking because the dog genome contains 2.5 billion base pairs. Of these Collies, two had no common ancestors for 4 generations, and 3 had none for at least 7 generations. The resulting gene chart from such mapping revealed **selective sweeps** in all 5 Collies. Remember, as breeders select over generations for a trait, the allele of the gene that causes that trait becomes more common in the breed. Alleles of other genes that are close by become more common, too. A "sweep" is a region with little genetic variation due to selection.

Dr. Clark showed slides of those results. What they reveal are sweeps in which breeders have consistently selected for a trait, for example, length of head. This multi-generational selection process becomes a driver/passenger effect in the genome. The gene for the selected for trait becomes the driver, and other genes on the same chromosome come along as passengers. These selective sweeps were evident on some Collie chromosomes, including chromosome 12 where the immune system genes reside. The driver genes in our breed have not yet been identified.

Normal Grey Coat Genetics in Collies: As a side product of the Collie Genome research, Dr. Clark was able to sort out the mystery of normal grey Collie coat color (no relationship to lethal greys). In testing the DNA from several different normal grays, she discovered that these Collies are actually blue merles with an additional mutation that eliminates the visible spots and produces a nearly solid grey coat. Normal blue merle littermates to a normal grey have no more chance of producing normal greys than any other blue merle. Also, no health related problems are associated with the mutated merle gene that produces solid greys than with any other Collies. Dr. Clark cautioned breeders against euthanizing these normal greys because they will be the same as any other Collie without the mutation, except for their coat color. However, these normal greys when bred reproduce their grey color. If breeders do not want to propagate this color, they should not breed greys.

Harlequin Pattern Coat Genetics in Collies: The subject of harlequin coat pattern came up. Dr. Clark believes harlequin in Collies results from a change in DNA within or close to the merle gene. It is not the same gene that produces harlequin coats in Great Danes. Dr. Clark and her colleagues found the harlequin gene in Danes a number of years ago. This separate allele does not exist in Collies. Most harlequin merles in breeds other than Danes reproduce a preponderance of harlequin blue merles, but can occasionally produce non-harlequin blue merles. Contrary to what some mistakenly believe, ***harlequin patterned Collies are not defective, and no additional health problems have been associated with the pattern***.

Conclusion: All of us who love the Collie owe Dr. Clark and her colleagues a huge debt for the massive amount of work they have done on our behalf. How we use the knowledge they provide will literally determine the inheritance we leave to our beloved Collies. ***Much more vital information is already in the Clemson Genetics' pipeline and will be available as soon as it has been verified by this dedicated team.*** It's our job to learn as much as we can about how to use genetic information wisely. It's a crucial part of what we create for future generations!

MEMBERSHIP BENEFITS!

You know the Collie benefits when you join the Collie Health Foundation as your dues help fund health research. Indirectly you benefit when the dog you love is able to live a longer and healthier life because of genetic testing available to breeders or increased knowledge on how to prevent/treat disease or other health issues. This is just a **reminder that YOUR MEMBERSHIP OFFERS YOU A DIRECT BENEFIT** in the form of **rebates for select DNA tests**.

Rebates are offered to CHF members only for Optigen's PRA test, Optigen's CEA test, Washington State University's MDR1 test, and Canine Cyclic Neutropenia (Gray Collie Syndrome) testing through either Health Gene or VetGen. These rebates for testing are only available through the end of 2014 so do your testing soon! See the Winter 2014 newsletter or visit the Collie Health Foundation's website at www.colliehealth.org/announcements.asp for more details.

Grant Approved for a Pilot Trial of Stem Cell Treatment of Dermatomyositis

In March, the Board approved a grant of $18,000 for a 12 month pilot trial of stem cell treatment of dermatomyositis. This amount will be only to cover the evaluation and follow-up of the patients. The Tufts University Laboratory of Regenerative Medicine will supply the stem cells. The following information was provided by the researchers in their letter of intent.

Project Description (Background):
1. Dermatomyositis is a prevalent and severe disease that specifically targets Collie dogs. Some of them have a poor life quality.

2. There is not a good, effective treatment for this condition. Some treatments are effective but have severe side effects (especially on the long term: steroids). Management is very difficult.

3. The disease is only partially understood. According to the most accepted pathomechanism an immune mediated reaction is the main pathogenic mechanism. Stem cells have proved to have immune-modulatory properties.

4. The equivalent condition in humans has been treated successfully with stem cells.

Project Description (Design):
Prospective, open pilot trial. Six dogs affected by dermatomyositis would be treated with canine embryonic cultured and well-characterized stem cells (IV, 1 M stem cells/kg). The severity of the lesions will be assessed with an objective scoring system. If good results are obtained in this pilot trial, a larger study could be developed to establish the best treatment, dose scaling, selection of the most adequate patients and concomitant therapy.

Researchers:
Lluis Ferrer, DVM, PhD, Dip ECVD. Professor of Dermatology. Dermatologist and dermatopathologist. Experience in stem cell therapy in canine skin diseases.

Andrew Hoffman, DVM, DVSc, DACVIM. Director of the Laboratory of Regenerative Medicine. This is the leading laboratory in veterinary regenerative, stem cell and nanomedicine. The Laboratory is funded by the NIH and several Foundations and private companies.

Research Institution/Affiliation:
Department of Clinical Sciences / Laboratory of Regenerative Medicine /FosterHospital for Small Animals. Cummings School of Veterinary Medicine. TUFTSUNIVERSITY (MA, US).

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