



# We've Got It!

# CHONDRODYSTROPHY GENE MAPPED!

**A JOINT EFFORT BY THE BEAGLE COMMUNITY  
AND THE GENETIC RESEARCH COMMUNITY  
BENEFITS BEAGLES WORLDWIDE.**

by *Debbie Tissot*

The news is huge. In fact, the progress toward identifying the specific genetic mutation that causes dwarfism (chondrodystrophy) in Beagles, is on par with *any* history-making genetic or medical breakthrough, and the positive implications are enormous.

Though research continues, Mark Neff, DVM of UC-Davis says that they're 95 percent there. "The defect itself has been mapped, so now all that remains is to determine the precise mutation that *causes* the defect. Though

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that may sound as if there is much yet to be done, the heavy work is behind us and the fine-tuning can begin."

Thanks in part to the canine genome being mapped some years ago, the team at UC-Davis managed this feat of genetic research in a matter of months. But, when specific mutations are under examination, in order to generate accuracy, greater quantities

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## Directly from the Doc...

Thanks in part to the response to a previous *SBQ* article and swab distribution efforts by a number of dedicated breeders, researchers at the Center for Veterinary Genetics at UC Davis have announced an advance in research on the genetic basis of chondrodystrophy. This positive step forward is significant because it implicates a discrete region of the dog genome as harboring the causative gene for beagle chondrodystrophy. In addition, the result signifies that, despite variation in the expression of the disease, that it is likely a single gene of large effect is involved.

As many of you know, the complete genetic code for the dog has been deciphered. This means that we know each of the 2.4 billion letters that outline the basic blueprints of a dog. However, this sequence was obtained from a single Boxer dog (named Tasha), and so we know very little about the differences in the code that make the difference between a Great Dane and a Chihuahua. We also know little about which alterations to the code (mutations) contribute to hip dysplasia or epilepsy or cancer.

Access to the complete DNA sequence of the dog confers enormous power to genetic analysis, and this is partly why the success in chondrodystrophy has come now. (Many of the DNAs for this project were collected in the late 1990s!) The genetic region for chondrodystrophy was identified by assaying 800 DNA landmarks across the dog genome. To put this into context, AKC parentage uses 14 landmarks.

Mapping the defect has simplified the problem enormously. Instead of exploring 2.4 *billion* letters of code for the mutation, one now only needs to look at 1 million letters (although this sounds like a lot, it is a 2400-fold reduction in scale.) The next phase will be large-scale sequencing of the DNA from as many Beagles as possible, including both affected and unaffected dogs. The mapping results were obtained with just 24 affected dogs. At least twice that number will be needed to pinpoint the causal mutation with certainty. DNA from unaffected dogs is used to create a backdrop, against which the 'disease' DNAs are compared.

You can help by submitting DNA samples from your dogs (again, both healthy and affected dogs are needed). There is no cost to participate, and the sample collection process takes just a few minutes. A DNA collection kit will be sent to you by mail. The kit will contain 3 cheek swabs and a brief form for entering your information. The kit also contains a postage-paid envelope for returning the swabs to UC Davis easily and at no cost. The research team always assures complete confidentiality for all submissions.

If you would like to participate, please contact us by email or phone to request your DNA collection kit. With our help, the researchers believe a low-cost DNA test for Beagle chondrodystrophy should be available within 4-6 months *if* participation by the Beagle community is sufficiently strong.

As a final note — the researchers also note that they feel confident they could similarly resolve Chinese Beagle Syndrome (which they have re-named Musladin-Leuke Syndrome) if enough cheek swab samples can be obtained from affected Beagles. DNAs from healthy beagles submitted for the chondrodystrophy project can also be used for the Musladin-Leuke mapping effort, so your DNAs may be supporting two projects at once.

**Mark Neff - UC Davis**

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of genetic material are required. More samples of affected dogs are needed. "We can eradicate this!" Dr. Neff said. But, it will take several more months of research before a screening test can be developed, and it will take examining more affected and unaffected DNA samples to get to that point.

One of the problems with submitting samples of an affected dog is that many people don't know the symptoms. The degree of affectation varies from dog to dog, so those mildly affected may not be recognized quickly by their breeders or owners. There are, in fact, many finished champions in America – and we must presume elsewhere – who are, in fact, mildly affected with chondrodystrophy. They will almost certainly be identifiable as carriers, so it is important to actively evaluate even the most mildly suspect dog in the kennel; take a photograph just to be safe, swab his little cheeks, and submit that DNA to the project.

Another minor problem has now been addressed as well. So he can remain on task with this important research, Dr. Neff has designated a single individual within his organization to process requests and distribute swabs to all in need. In the past, swabs have been available through *SBQ* but those supplies have been diminished. However, for those in her vicinity, JK Marten of Rowdy Beagles in Dallas, Texas, continues to maintain a supply and will be happy to provide them just as she has for the past many months. She can be reached at [rowdy65@hotmail.com](mailto:rowdy65@hotmail.com).

Another disorder is also of interest  
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get your **DNA SWABS**

**UC Davis Contact:**  
**Katy Robertson,**  
**DNA Collections**  
**(530) 752-3864**  
**[katy@ucdavis.edu](mailto:katy@ucdavis.edu)**

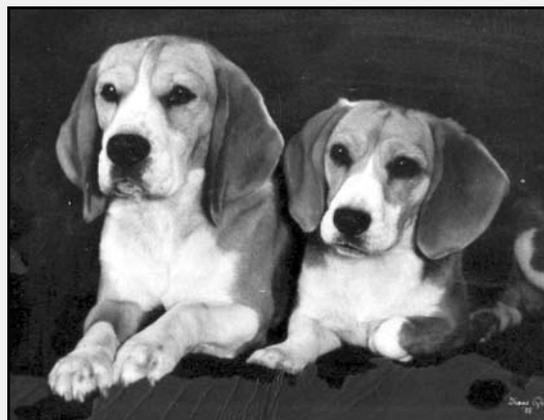
## Living With Sister

by Lynne Katusich

In 1985, a litter was born that I had planned for with great excitement. The sire and dam were from great lines, as well as both being very successful in the show ring. There were three puppies, 2 males, 1 female. They were all normal birth size and weight, with the girl being slightly smaller. The first sign that she was going to be small was the difference in the rate of weight gain between her and her brothers.

At the appropriate time, the boys were walking, but the girl (whom we had named Little

*Sister is sitting with her litter brother, Ch. Rancho Glen's It's A Snap, winner of the 1989 National Specialty. The third littermate was also a champion. Note the dramatic size difference.*



Sister) mostly stayed on her side in the pen. To help her along, I started filling the deep part of our kitchen sink with warm water and having her "swim" in it by holding her in the water while she made the instinctive swimming motions. To this day, I know that was what helped strengthen her legs and allowed her to learn to walk.

When the puppies were about 6 weeks old, I went to Utah for dog shows. When I called home after the first show, my husband delightedly told me that Sis had walked that day without any urging or assistance! He said that she had used her nose to help her balance. From then on, she made steady improvement, but was still not physically like her brothers.

I took her to our vet, who agreed with my guess that she was a chondrodysplastic dwarf. I was cautioned then that it was felt these dogs didn't live as long as other dogs. That was depressing, but Mike and I made up our minds that we were going to enjoy this little girl for as long we could have her – a decision we never regretted for a moment!

As Sister grew up, she became the Queen Mother of Rancho Glen Beagles. If she wanted to cross the exercise yard, the dozen other Beagles would part like the Red Sea to let her do what she wanted. They loved her, and she loved them. She never minded being kenneled when needed; always ate her dinner that was just like everyone else's, and traveled everywhere on show circuits with us in the motor home. When we set up at a show site, the exercise pens would go out, and Sis would go in happily. She made so many friends for our breed from the people who fell in love with her at shows!

In her whole life, she had no additional health problems, and she probably saw the vet less than the others who would have been considered normal. Sis was the perfect house pet or kennel dog. She and Mike were inseparable and watched football and baseball together all the time.

I would tell anyone that unless you are in the breed only for show wins or selling puppies, you could not do better than to have your own Little Sister as a beloved pet. These little Beagles seem to focus more on you than a more physically active dog, and the rewards are endless.

But, there are some twists to my story. Her brother, Hogan, won the National Beagle Club Specialty in 1989. That was quite a moment for us. However, living with Sister matched it in every way. I always worried about her life expectancy, but she lived to the ripe old age of 17+ years, outliving her brother by 2+ years. Don't give up on these special children! They are a delight and a gift.

*Editor's Note: Photos of Sister are featured throughout this article, courtesy of Lynne Katusich. These photos were taken for the specific purpose of publication in The New Beagle by the Drs. Musladin and Ada Leuke. Sister's DNA was one of the first samples submitted to the project in the 1990's.*

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est to the project and is next on the agenda. Formerly known as *Chinese Beagle Syndrome*, and recently re-named for those who first identified it as a distinct anomaly, *Musladin-Leuke Syndrome* is another form of possible dwarfism which may be confused with chondrodystrophy. However, one of the differences between the two is that

not all Musladin-Leuke sufferers is tiny, while being small is inherent to chondrodystrophy.

The Beagle world has become more aware of MLS (Musladin-Leuke Syndrome) in the past several years, and in *SBQ's* quest for photographs of chondrodysplastic Beagles, we discovered that the disorders are often confused. Indications are that MLS is more com-

mon than before thought, and it may be just as identifiable as chondrodystrophy is proving to be. But, it is important to know the differences. We suggest readers compare the photos provided so that when they submit DNA samples to UC-Davis they suggest the correct disorder. Providing photos along with samples and the required form is highly

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## MUSLADIN-LEUKE SYNDROME



7-week littermates



Clockwise from top left: 1. The faces of an unaffected (left) and its affected littermate demonstrate the oddly shaped skull, high ear placement and oval eyes that are typical of MLS puppies. In this case, note that the affected is much smaller than the unaffected. 2. The tricolor puppy struggles to stand because of the rigid, outward facing leg bones and the inability to bend its feet. Note the ear leathers. 3. The red and white demonstrates the same issues from a different angle making it very easy to see the lack of flexion in the ankles and feet. 4. The tricolor adult below is not small, unlike the other two models, but is clearly suffering similar problems. Unlike chondrodystrophy, MLS does not usually result in extremely short legs.



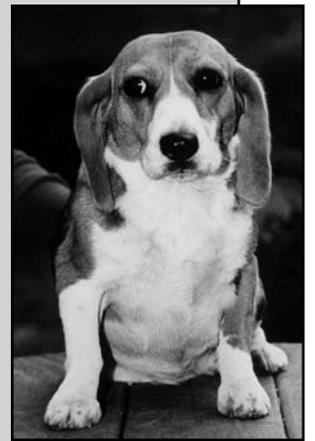
Among the interesting features is a rigid ear leather, often with extreme erectile power, and often featuring folds such as those shown on the puppy below. The ear is not being held that way, nor is it flapping about in the photo of the same 15 week puppy shown above. Bottom left photos show high toes and typical movement.



## CHONDRODYSTROPHY



The typical dwarf is, above all, very tiny. Sister matured to a whopping 10 3/4 inches. Also typical are the short, bowed front legs, heavy shoulders and overbuilt chest, deformed topline/spine and more often than



not, high outside toes. High toes are also common in MLS. However, chondrodysplastic Beagles do not exhibit the oddly shaped head and eyes which were the source of the original term for MLS, *Chinese Beagle Syndrome*. Both disorders often present with heart murmurs, and both result in difficulty moving, although the nature of the difficulty is quite different as the structural flaws are equally different. Chondrodystrophy was first officially identified in Denmark in the 1970s, but was almost certainly not new at the time, nor did it probably originate there. It has been identified in Beagles in many countries.

## GENETIC BREAKTHROUGH *continued from page 22*

encouraged. Images can be either digital files on disk or hard copies.

One of the questions often asked is why must DNA swabs be sent to Dr. Neff when their dog's DNA is on file with the AKC. Not the same thing at all! The profile generated by the AKC is just enough to determine parentage should the question arise, and would not be of any real use for genetic research even if UC-Davis had access to it – which it does not! Samples are

not routinely shared among different institutions, as ownership of both the knowledge and its source can become important later.

So, the other obvious question is, “Will UC-Davis share information with the *provider* of a sample identified as a carrier?” The answer is “sort of.” Dr. Neff indicates that owners of dogs identified as possible carriers will be notified that further testing is recommended. At that point, there should be a definitive screening process available, and those who receive such a letter are urged to take advantage.

The second examination of suspect DNA is handled by a different division of genetic science, and must be performed both differently and separately in order for a dog to be either cleared or identified as a definite carrier. Though this may seem redundant, it is the way of genetic research and is in place to protect all involved from liability in the case of dispute or blame. It is expected that such a program will be in place within a matter of months following final results of current chondrodystrophy research, and will hopefully become similarly available after the Musladin-