



**PURINA**  
**PRO PLAN**

# ***DACHSHUND*** Update

A NESTLÉ PURINA PUBLICATION DEDICATED TO DACHSHUND ENTHUSIASTS

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## **ANCIENT MUTATION DISCOVERED**

**Dogs' Short Legs & Abnormal  
Intervertebral Discs  
Are Linked**

# GENETIC DISCOVERY FINDS DACHSHUNDS' SHORT-LEG PHENOTYPE LINKED TO IVDD



**"Bonnie" (Tealdachs Sailor's Delight) was diagnosed with intervertebral disc disease (IVDD) at age 4 and recovered partially with treatment. Her dam was diagnosed with IVDD after producing the litter.**

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"Caring for a paralyzed dog is emotionally, financially and physically draining."

Tealdachs breeder MaryAnne Teal

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Dachshund breeder MaryAnne Teal of Williamsburg, Virginia, has been around the block more times than she would like dealing with dogs diagnosed with intervertebral disc disease (IVDD). Despite her efforts to study bloodlines and breed away from the debilitating disease known for its high mortality rate and high cost of surgical and veterinary care, Teal has not been successful.

An owner of Smooth Standard Dachshunds for 30 years, Teal adores the breed's big personality, its long-backed body and short legs. Her love for her Dachshunds is seen in the top-quality care she has given her dogs with IVDD. Decompression surgery and rehabilitation did not always help her dogs regain walking ability. When these efforts did not restore mobility, she outfitted her dogs with carts and her home with ramps and gates to keep them safe.

"IVDD has pretty much affected our lives in every possible way," Teal says. "We have stressed our own backs and knees lifting and carrying our dogs. It is absolutely heartbreaking when a dog never walks again. Caring for a paralyzed dog is emotionally, financially and physically draining."

Teal is not alone. Dachshunds have the highest occurrence of IVDD than any other breed, with an estimated disease incidence of 19 to 24 percent,<sup>1</sup> thus many breeders and owners can relate to what it's like to care for a dog affected by IVDD.

Although the cause of IVDD has been a mystery, a common theory has blamed the Dachshund's long back. [A recent breakthrough discovery at the University of California-Davis](#) identified a functional fibroblast growth factor 4 (*FGF4*) retrogene insertion on canine chromosome 12. The finding is key in helping to explain the causative variant attributed to the chondrodystrophy (CDDY) phenotype in Dachshunds, as well as many other breeds.

"Their backs are not so much long as their legs are short," says Danika Bannasch, DVM, PhD, the Maxine Adler Endowed Chair of Genetics at UC Davis, whose laboratory made the gene discovery.

Type I IVDD is most common in Dachshunds. It is an inherited disorder caused by CDDY, a condition of shorter legs and abnormal intervertebral discs in which the discs degenerate prematurely in young dogs, occurring in some dogs as young as 1 year of age. In contrast, Type II IVDD occurs in older dogs and is usually limited to a single intervertebral disc.

Having a gelatin-like core surrounded by a fibrous coating, the intervertebral discs, located between the vertebrae, protect and cushion the spinal column. In dogs predisposed to Type I IVDD, the discs calcify and harden, which can cause them to herniate into the spinal canal. As the discs press on the nerves of the spinal cord, a dog may experience



**“Hildie” was breeder MaryAnne Teal’s first Dachshund to have IVDD. Only 2 ½ years old when she developed the disease, Hildie was paralyzed for the rest of life despite surgery and rehabilitation.**

pain, nerve damage, loss of bladder and bowel control, and/or paralysis.

In Teal’s experiences, her first dog with IVDD was partially paralyzed after being diagnosed at 2 ½ years old. Her second dog, a show champion and Hound Group winner, was bred before being affected with IVDD. Although the dog recovered, she produced a daughter that developed IVDD at 4 years old and recovered partially with treatment though she struggled for the rest of her life with ataxia, or muscle incoordination.

“The *FGF4-12* retrogene insertion in the dog genome that is responsible for CDDY is characterized by short legs due to dysplastic, shortened long bones and susceptibility to Type I IVDD across several dog breeds,” Dr. Bannasch says.

An earlier *FGF4*-retrogene insertion discovery on canine chromosome 18 explains a short-legged

phenotype known as chondrodysplasia (CDPA) that also occurs in several breeds, including Dachshund, Basset Hound, Pembroke Welsh Corgi, Pekingese, Scottish Terrier, West Highland White Terrier, and Cairn Terrier. [The identification of the \*FGF4-18\* insertion was made in 2009 by a research team at the National Institutes of Health](#) studying breed sizes and morphology.

“The chondrodystrophy-associated mutation occurred a long time ago,” says Emily Brown, PhD, DVM, a genetics graduate student in Dr. Bannasch’s laboratory who contributed to the UC Davis research. “There are descriptions of short-legged dogs dating over 4,000 years ago. Both the *FGF4-12* and *FGF4-18* mutations occur concurrently in unrelated dog breeds from diverse breed groups and geographical locations.”

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“Both the *FGF4-12* and *FGF4-18* mutations occur concurrently in unrelated dog breeds from diverse breed groups and geographical locations.”

Emily Brown, PhD, DVM, genetics graduate student at the University of California-Davis

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## WHAT IS A RETROGENE?

The mutation that causes dogs' short legs and susceptibility to IVDD is a functional fibroblast growth factor (*FGF4*) retrogene insertion on canine chromosome 12. A retrogene results from the retrotransposition of processed mRNA (messenger RNA). All cells have an mRNA molecule that transcribes the DNA from the cell's nucleus to the cytoplasm, or ribosomes, where it is synthesized into protein. Only a small percent of retrogenes encode functional proteins, such as *FGF4-12*.

## DWARFISM & ABNORMAL INTERVERTEBRAL DISCS

A fascinating aspect of the domestication of the dog from the wolf is the subsequent variation in size and shape of purebred dog breeds that has transpired from dog breeding and selection. [One of the most extreme examples of dog breed differences is in limb length](#), with extremely short limbs defining many breeds.

Extensive examination of growth plates has been performed on many short-legged breeds, such as Dachshund, Pekingese, French Bulldog, American Cocker Spaniel, and Beagle, as these breeds also are prone to IVDD. [Histopathological analysis of the bones of puppies from these breeds has shown that their short stature is due to defects in endo-](#)

[chondral ossification](#), the process whereby cartilage is replaced by bone in the developing limb.

"Dwarfism caused by chondrodystrophy has long been known to be associated with abnormal intervertebral discs," Dr. Bannasch says. "A reduction of long bone growth occurs due to defects in endochondral ossification. These early changes in the structure of growth plates cause shorter legs and can also impact dogs through premature degeneration of the intervertebral discs."

The *FGF4-12* insertion mutation causing CDDY affects height phenotype in a semi-dominant inheritance, whereby dogs with two copies of the mutation are smaller than those with one copy. The mutation impacts the IVDD phenotype

with a dominant inheritance, thus dogs only require one copy of the retrogene insertion to be predisposed.

Interestingly, some, but not all, CDPA-affected breeds are at increased risk for IVDD. For example, neither the Cairn Terrier nor the West Highland White Terrier has IVDD. The autosomal dominant inheritance of the *FGF4-18* insertion means dogs need only one gene copy from a sire or dam to inherit CDPA. Notably, some dogs have both *FGF4-12* and *FGF4-18* mutations, which result in a more drastic reduction of leg length.

Similarly, in humans, mutations in the *FGF* family of genes (*FGFR3*) cause achondrodysplasia, the most common dwarfism in people and a type of chondrodystrophy that prevents bones from growing as long as they should. The disorder is linked to shortened limbs and abnormal vertebrae associated with intervertebral disc disease. *FGF* genes are involved in several embryological development processes in humans and are key for appropriate growth and development.

Odd though it may seem, a medium-legged breed, the Nova Scotia Duck Tolling Retriever, helped the researchers discover the *FGF4-12* mutation that predisposes Dachshunds, as well as many other breeds, to short legs and IVDD. The idea of using Tollers, the smallest of the retriever breeds, was because they are commonly affected by a form of skeletal dysplasia that causes short-legged individuals and abnormalities such as long-bone bowing, physal (growth plate) widening and joint incongruity.

“Using a genome-wide association study (GWAS), we compared 13 Tollers with severe skeletal dysplasia and 15 Toller controls without severe skeletal dysplasia,” says Dr. Bannasch. “To our surprise, we found the short-legged Tollers had an *FGF4* retrogene insertion on canine

## GENETIC TESTING FOR IVDD RISK & SUBMITTING SAMPLES FOR FURTHER STUDY

A DNA test is available for chondrodystrophy (CDDY) and chondrodysplasia (CDPA) at the University of California-Davis Veterinary Genetics Laboratory (VGL). The test can be ordered [online](#).

The VGL reports test results and their interpretations as follows:

### CHONDRODYSTROPHY (CDDY & IVDD RISK)

N/N	No copies of CDDY mutation
N/CDDY	One copy of CDDY mutation. Dog is at risk for IVDD. Mutation causes leg shortening compared to N/N dogs. When bred to an N/N dog, this will produce 50 percent of normal-sized puppies and 50 percent of puppies at risk for IVDD.
CDDY/CDDY	Two copies of CDDY mutation. Dog is at risk for IVDD. Mutation causes leg shortening compared to N/N dogs. Will produce 100 percent of puppies with shorter legs at risk for IVDD.

### CHONDRODYSPLASIA (CDPA)

N/N	No copies of CDPA mutation
N/CDPA	One copy of CDPA. Mutation causes leg shortening compared to N/N dogs.
CDPA/CDPA	Two copies of CDPA. Mutation causes leg shortening compared to N/N dogs.

Thus far, 44 Dachshunds have been tested, says Cecilia Penedo, PhD, VGL associate director. “Genotype homozygosity is about 93 percent for CDDY and 98 percent for CDPA in these tested Dachshunds, though this is an area in which we need to learn more and collect a broader sample size.”

Danika Bannasch, DVM, PhD, the Maxine Adler Endowed Chair of Genetics at UC Davis, whose laboratory made the *FGF4-12* gene discovery, says, “We would love to get research samples from Standard Dachshunds and in particular senior and geriatric dogs without disc disease. Most of our samples have some from hospital cases, which possibly biases the CDDY frequency.”

If you are interested in submitting a research sample, please contact Dr. Bannasch at [BannaschLab@ucdavis.edu](mailto:BannaschLab@ucdavis.edu) using “IVDD” in the email subject line.

chromosome 12 similar to the one found previously on chromosome 18 in some short-legged breeds.

“Since the skeletal dysplasia phenotype is not uncommon among dog breeds, we investigated haplotype sharing across breeds and saw that a portion of this haplotype,



**Dr. Danika Bannasch of the University of California-Davis is shown with her 2-year-old Nova Scotia Duck Tolling Retriever, “Genes” (Aqueus Wild Type JH). A Toller enthusiast, Dr. Bannasch recognized the breed’s short-legged phenotype and growth plate abnormalities, which helped her team discover the *FGF4-12* retrogene that affects Dachshunds and many other breeds.**

or genetic variance, was shared with Beagles and American Cocker Spaniels, two breeds considered classically chondrodystrophic.”

In order to determine if the same region was associated with IVDD, the researchers performed a second GWAS for Type I disc disease across breeds including mixed breeds and found, indeed, the same region was associated.

To pinpoint the causative variant for skeletal dysplasia and IVDD, they sequenced the genomes of one

skeletal dysplasia-affected Toller, one IVDD-affected Dachshund and 83 unaffected controls.

“We found that this second *FGF4* retrogene insertion in the canine genome is not only responsible for skeletal dysplasia in Tollers but also for chondrodystrophy, including the predisposition to Type I IVDD across all dog breeds,” Dr. Bannasch continues.

The research team looked at other breeds that are considered chondrodysplastic and found the same mutation on chromosome 12 in the Dachshund, Beagle, American Cocker Spaniel, a short-legged Coton de Tulear, French Bulldog, Maltese, Pekingese, Pembroke Welsh Corgi, and a short-legged Miniature Poodle. Some of the breeds, such as Dachshund, had mutations on both chromosome 12 and chromosome 18.

The chromosome 12 mutation that causes CDDY is found in more breeds than the chromosome 18 mutation that causes CDPA. Other breeds with the *FGF4-12* retrogene insertion are: Basset Hound, Bichon Frise, Cardigan Welsh Corgi, Cavalier King Charles Spaniel, Chesapeake Bay Retriever, Chihuahua, Dandie Dinmont Terrier, English Springer Spaniel, Jack Russell Terrier, Nova Scotia Duck Tolling Retriever, Toy Poodle, Portuguese Water Dog, Scottish Terrier, and Shih Tzu.

“We realized that the long-held belief that all short-legged ‘dwarf’ dogs result from the same chondrodysplasia condition is wrong,” says Dr. Bannasch. “There are two independent genetic mutations caused by separate mutations of the same retrogene that cause slightly different types of dwarfism. It may have to do with the surrounding chromosomal region that drives expression in the developing disc. Chondrodysplasia is due to the *FGF4-18* insertion mutation, and chondrodystrophy is caused by the *FGF4-12* insertion.”

## IMPACT ON BREEDING

Dachshund breeders may wonder whether it is possible to select against the CDDY mutation that predisposes dogs to IVDD, while keeping the CDPA mutation and the breed's desirable short legs.

"The most important factor is how widespread the *FGF4-12* mutation is in the gene pool, as there must be sufficient variation at that locus in order to breed away from IVDD," explains Dr. Bannasch. "I think it is important for breeders to understand that the *FGF4-12* mutation is very common in most of the predisposed breeds."

In the Dachshund, the *FGF4-18* retrogene insertion is fixed, which means all Dachshunds have this mutation, she says. However, only those that also have the *FGF4-12* mutation are affected with IVDD or at increased risk for IVDD. Thus, some dogs can have short legs and normal discs, while others may have short legs and abnormal discs.

"Although this finding is exciting, it is premature to think it will quickly solve the problem of IVDD in Dachshunds," Dr. Bannasch says. "We are not sure how common or genetically set chondrodystrophy

is across Dachshund sizes, so selection against it should be done very slowly and may not even be possible if CDDY is homozygous."

Given the high mortality rate of IVDD combined with the high cost of care and surgery, the *FGF4-12* retrogene insertion discovery provides important insights, though more research is needed to better understand its impact on a breed-specific level. Dr. Bannasch and her team are eager to collect more genetic samples and continue the work.

"We are optimistic that someday there will be more hope for Dachshunds and an ability to breed away from IVDD," Teal says. "This has been a difficult, heartbreaking journey for us, but our love for our dogs has carried us through." ■

<sup>1</sup> Ball MU, McGuire JA, Swaim SF, et al. Patterns of Occurrence of Disk Disease Among Registered Dachshunds. *Journal of the American Veterinary Association*. 1982;180:519-522.

Purina appreciates the support of the Dachshund Club of America and particularly Charlotte Borghardt, chair of the DCA Health Committee, in helping to identify topics for the *Dachshund Update*.

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## RECORD YEAR FOR NATIONAL SPECIALTIES AT PURINA FARMS

A record 38 National Specialties will be held this year at Purina Farms. The versatility of the Best in Class show and trial venue combined with its prime location in the middle of the country appeal to parent clubs, with many returning year after year. Custom-built for the dog fancy, the Purina Event Center offers a spacious indoor exhibition space complete with a separate benching and grooming area, dog bathing room, conference rooms, banquet rooms, Checkerboard Café, and numerous other amenities. The 346-acre property includes facilities for herding, tracking, coursing, diving dog, earthdog, and many more activities. Purina Farms is in Gray Summit, Missouri, about one hour from St. Louis.



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## PURINA PRO PLAN INTRODUCES SAVOR WITH PROBIOTICS FOR DOGS

*Purina Pro Plan* is introducing *SAVOR* formulas for puppies and adult dogs made with guaranteed live probiotics to support digestive health. *SAVOR* Shredded Blend Chicken & Rice Puppy Formula, made with chicken as the No. 1 ingredient, contains DHA from omega-rich fish oil to help nourish brain and vision development and is rich in antioxidants to help support a puppy's developing immune system. The complete and balanced puppy food also has calcium, phosphorus and other minerals to help build strong teeth and bones.

The adult dog foods now with probiotics are: *SAVOR* Shredded Blend Small Breed Chicken & Rice Formula and *SAVOR* Shredded Blend Large Breed. This small-breed food is high in protein, including chicken as the No. 1 ingredient, to meet the needs of highly active

small dogs, as well as calcium, phosphorus and other minerals to help maintain strong teeth and bones.

Vitamin A and linoleic acid, an omega-6 fatty acid, nourish healthy skin and coat.

The large-breed formula contains high-quality protein, including chicken as the No. 1 ingredient, plus EPA and glucosamine to help support joint health and mobility. Optimal protein and fat levels help maintain lean muscle and ideal weight and body condition.

Both of these adult formulas also have a natural prebiotic fiber, sourced from wheat bran, to help support digestive health. *Purina Pro Plan* Shredded Blend formulas feature a crunchy kibble combined with tender, shredded pieces for delicious taste and texture.

Look for probiotics coming to other *SAVOR* formulas later this year.



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## DEADLINE IS JULY 31 FOR PRO CLUB MEMBERS TO SUBMIT WEIGHT CIRCLES

Don't miss the cutoff of July 31, 2018, for mailing in weight circles. After this date, weight circles will no longer be accepted, as *Purina Pro Club* is introducing a new receipt submission program that will allow you to get your Purina Points into your account faster by taking a picture of your receipt from purchases of eligible *Purina* dog food on your smartphone or scanning the receipt into your computer and submitting it online. Your Purina Points will show up in your account by the end of the day in most cases if

uploaded correctly. You can start submitting receipts now, though once you submit receipts, you will not be able to mail in any more weight circles. To get started, click on the link below that will take you to helpful tools — instructions and a video — and then log on to your *Pro Club* account, register and begin submitting receipts.

[GO TO HELPFUL TOOLS](#)

