



PURINA Pro Club

Update

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Ragdolls Are Second Breed to Have a Genetic Test for HCM

Breeder Sue Shorey of SuPurr Ragdolls in Millington, Mich., was delighted to have bred a litter in 2004 that produced a gorgeous Ragdoll male representing good breed type and great potential as a sire. Named "Snoops," the male Ragdoll is one of the most loveable cats Shorey has ever had.

"Snoops follows me everywhere I go. I can't do anything without him there," Shorey says. "He has the most wonderful temperament and loves everyone."

A conscientious breeder with more than 10 years' experience breeding Ragdolls, Shorey is vice president of Ragdolls of America and the Midwest regional director for Ragdoll Fanciers Club International. She and her husband, Bill, take extra steps to keep their cats healthy and happy. "The cattery is not a business to us," she explains. "We love all our cats."

As Ragdolls, along with many other breeds, are susceptible to the feline heart disease hypertrophic cardiomyopathy (HCM), Shorey took

Snoops at 8 months of age for a routine echocardiogram, a test that she has performed on all her cats used for breeding. She was horrified when Snoops was diagnosed with the

RAGDOLLS ARE NOT THE ONLY BREED AFFECTED BY HCM. OTHERS INCLUDE AMERICAN AND BRITISH SHORTHAIR, SCOTTISH FOLD, MAINE COON, DEVON REX, PERSIAN, SIBERIAN, NORWEGIAN FOREST CAT, TURKISH VAN, AND SPHYNX.

progressive heart condition that is the most commonly diagnosed feline heart disease.

"I was told that Snoops would live six months at best," Shorey recalls. "His mother had been scanned every

year to the age of 5, and she always scanned negative. His father also scanned negative."

HCM is a disease in which the heart's papillary muscles that anchor the mitral valve and the walls of the left ventricle become abnormally thickened. As the muscles thicken and the heart's chamber volume decreases, the heart pumps a reduced volume of blood. HCM is also a primary myocardial disease in humans that affects about one in 500 people.

Severely affected cats have breathing difficulties from the accumulation of fluid in or around the lungs, which usually progresses to congestive heart failure. Sometimes HCM causes sudden death, often with no prior noticeable signs. In other cases, the signs of HCM remain mild for most of a cat's life. HCM affects a wide range of ages, making it frustrating for breeders to determine which cats are safe to breed. Some, but not all, affected cats die from the heart disease.

Ragdolls are not the only breed

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Norwegian Forest Cat and Sphynx Breeders May Contribute to Research

Stored samples of feline DNA in Kate Meurs' research laboratory at Washington State University hold the key to helping investigators untangle the genetic causes of hypertrophic cardiomyopathy (HCM), a progressive and often fatal heart condition that is the most common heart disease in cats.

Already direct DNA tests are available for determining HCM in Maine Coons and Ragdolls. Ongoing research focuses on finding the mutations in Norwegian Forest Cats and Sphynx, two other breeds affected by the condition.

Meurs, D.V.M., Ph.D., DACVIM, the Richard L. Ott Professor of Small Animal Medicine and Research at Washington State University School of Veterinary Medicine, has been studying feline HCM since 1995. She began the research when she worked at The Ohio State University.

"We've been working on HCM in Norwegian Forest Cats for several years but so far haven't found the mutation," Meurs says. "It took us about a decade to find the Maine Coon mutation. We were lucky to find the Ragdoll mutation so quickly."

To help advance the research in Norwegian Forest Cats and Sphynx, Meurs needs more participants. DNA is needed from qualifying cats. Requirements include

documented cases of HCM by veterinarians and certified Sphynx or Norwegian Forest Cat pedigrees.

"What we really need are good DNA samples from cats diagnosed with HCM that have been confirmed with echocardiograms performed by veterinary cardiologists," Meurs says. "Otherwise, we spend time and money on samples that may turn out to be negative. These studies are very expensive. It helps when a couple of dedicated people spearhead the effort to provide quality samples and help with fundraising. That is the main reason the Ragdoll study was a success."

The Winn Feline Foundation has established funds for HCM research in Norwegian Forest Cats and Sphynx, as well as other breeds. For more information, see www.winnfelinehealth.org/pages/breedrelatedproj.html.

For information on participating in Meurs' research, please contact the Veterinary Cardiac Genetics Laboratory at Washington State University via e-mail at vcgl@vetmed.wsu.edu or by calling (509) 335-6038. Additional information on testing cats for HCM and breeding HCM-diagnosed cats can be found on the Frequently Asked Questions page of www.vetmed.wsu.edu/deptsVCGL/Ragdolls.aspx and at www.testyourcat.com.

HCM Mutation

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affected by HCM. Others include American and British Shorthair, Scottish Fold, Maine Coon, Devon Rex, Persian, Siberian, Norwegian Forest Cat, Turkish Van, and Sphynx. Though HCM affects many breeds, the exact number of affected cats is not known, and the severity of signs varies by breed.

In 2004, the same year that Snoops was born, researchers discovered the gene mutation causing HCM in Maine Coons. The discovery was made by Kate Meurs, D.V.M., Ph.D., DACVIM, the Richard L. Ott Professor of Small Animal Medicine and Research at Washington State University School of Veterinary Medicine, after nearly a decade of investigations. Meurs found that the cardiac protein, myosin-binding protein C (cMyBP-C), is significantly reduced in Maine Coons.

Meurs and Mark Kittleson, D.V.M., Ph.D., DACVIM, professor of cardiovascular medicine at the University of California-Davis School of Veterinary Medicine, collaborated on the Maine Coon research. They had determined that similar to humans, cats inherit HCM in an autosomal dominant pattern of inheritance, meaning that the mutation is not inherited on the sex chromosomes, X or Y. Rather, the disease results from a mutation in one copy of a gene that codes for a structural protein from one parent, causing the autosomal dominant trait.

The gene mutation discovery led to

a direct DNA test for HCM in Maine Coons, allowing breeders to test their cats and determine whether they are carriers, affected or clear. Cats could now be tested as young as 6 weeks of age, providing a way to identify kittens that could pass along the gene if bred.

Since breeding animals are often selected as young as 16 weeks of age, an age usually too young for HCM to be detected in traditional ways, the genetic test provided a way to screen cats early. Early detection means breeders can reduce the prevalence of HCM over time without compromising genetic variability within the breed.

The reality is that HCM is a complex disease that appears in different forms in different breeds and in individual cats. Though the research isolated one mutation on one gene in Maine Coons, most likely other breeds, and potentially other Maine Coons, would have a completely different mutation. What's more, some cats that test negative still get the disease due to the genetic complexity.

Pitfalls of Echocardiogram Testing

Saddened that Snoops had been diagnosed with HCM, Shorey began thinking about what she could have done differently. "I started having my cats scanned for HCM using echocardiogram testing in 1999," she says. "Cats used for breeding were scanned every year, yet I still ended up with HCM. Scanning can tell us if our cats are expressing HCM, but it cannot

tell us if they are carrying the gene. It wasn't the answer. We needed something better."

Echocardiography is effective in detecting moderately to severely affected cats, but it does not always detect the minimal heart changes in

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mildly affected cats. Simply having the gene for HCM does not mean a cat will actually become ill from heart disease. Many cats are so mildly affected, they never suffer ill health. Although Shorey didn't know it at the time, it was likely that Snoops' parents were mildly affected, explaining why their echocardiograms did not detect HCM.

Shorey had heard about the HCM genetic test that Meurs developed

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Understanding Feline Hypertrophic Cardiomyopathy

Feline hypertrophic cardiomyopathy (HCM) is a challenging and complex heart condition. Veterinary cardiologists struggle to treat cats with the disease because signs vary significantly from cat to cat and breed to breed.

HCM causes thickening of the walls of the left ventricle and the papillary muscles that anchor the heart's mitral valve. As the muscles thicken and the heart's chamber volume decreases, the heart pumps a reduced volume of blood.

Affected cats are at risk for development of heart failure or blood clots that can result in cardiac distress or sudden death. Some cats throw a blood clot to their back legs causing acute paralysis and pain. Cats with severe disease usually go into heart failure and have problems breathing due to the accumulation of fluid in or around their lungs. For some cats, the first and only sign is sudden death.

Owners may first notice their cat having breathing difficulties, such as heavy breathing, rapid shallow breathing or open mouth breathing due to fluid in the lungs or chest cavity, indicating congestive heart failure. Many cats with HCM may have heart murmurs.

HCM affects a wide range of ages, making it frustrating for breeders to determine which cats are safe to breed. Cats are usually middle-aged when clinical signs are first detected, but HCM has been found in cats as young as 6 months and as old as 13 years.

The best clinical test for HCM in breeds without a direct DNA test is an echocardiogram, or ultrasound screening of the heart. In this test, high-frequency sound waves present an image of the heart. Echocardiography is a good way to detect moderate to severe HCM, but it

doesn't always detect the minimal heart changes in mild forms of the disease. Veterinarians suggest that any cat with clinical signs such as heart murmur or arrhythmia, an abnormal heart rhythm, should be screened.

Since HCM can occur at any age, a normal echocardiogram does not guarantee that a cat is HCM-free. Annual screenings are recommended for all breeding cats, but this can be challenging. Echocardiograms are expensive and many breeders may not have access to quality ultrasound services.

While no cure exists for HCM, cats diagnosed with the condition can be treated based on their signs. Thus, owners are encouraged to monitor their cats with regular veterinary checkups and follow their veterinarians' advice closely.

Among the medications used to treat cats with HCM are:

- Beta blockers, which help slow the heart rate and decrease the severity of an abnormality that occurs secondary to HCM;
- Calcium channel blockers, which may improve heart function by reducing heart rate and myocardial oxygen consumption;
- ACE inhibitors, which are used in cats that are in heart failure; and
- Diuretics, which are used for managing pulmonary edema and pleural effusion.

The good news is that identification of the disease in a cat allows veterinarians and owners to be more proactive using regular heart ultrasounds to monitor heart function. Early detection of problems associated with HCM, such as blood clot formation or heart failure, may make treatment more effective.

Getting the Most Out of Your *Pro Club* Membership

As a member of *Purina Pro Club*, you receive many benefits. Kitten Starter Kits, a subscription to the *Purina Pro Club Update* newsletter, and a point redemption program are among the benefits. To help you get the most out of your membership, here is a review of how *Pro Club* works.

Submitting Weight Circles

Weight circles are the colored circles on packages of *Purina* brand kitten and cat food that allow you to receive food rebate checks. When submitting weight circles, you should follow these recommendations:

- Use a Weight Circle Claim Form with your weight circle submission. You may download a form at www.purinaproclub.com, or you can contact *Pro Club* by calling toll free at (877) PRO-CLUB or (877) 776-2582.
- Do not use another member's Weight Circle Claim Form to submit your weight circles.
- Fill out the Weight Circle Claim Form completely. A completed form expedites the processing of your submission.
- Always put your return address on the weight circle submission envelope.
- Submit a minimum of 75 pounds' worth of weight circles in one submission. Submitting smaller amounts is not cost-effective for *Pro Club* and increases handling time for all members.
- Submit only weight circles, not UPC codes. Only weight circles are valid for submission and credit to your account.
- Do not submit torn and worn weight circles. These will not be credited as *Pro Plan* must be able to identify the five-digit product code on the weight circle.

Send Weight Circles By Certified Mail

P*ro Club* recommends that you mail your weight circles by certified first class mail or some other traceable delivery method to ensure proof of delivery verification in the event *Pro Club* does not receive your weight circles. *Pro Club* is not responsible for weight circles not in its possession.

- Avoid taping multiple weight circles together.
- Check your Weight Circle Claim Form or go online at www.purinaproclub.com to view participating cat food weight circles. *Pro Club* is unable to credit weight circles from brands that do not participate in *Pro Club*.



Ordering Kitten Starter Kits

Pro Club members can order Kitten Starter Kits for new owners that contain important information on caring for new kittens. Space also is provided for adding breeder information and veterinary records. To order Kitten Starter Kits, keep in mind you should:

- Only order Starter Kits for the kittens you currently have on the ground. Ordering annual amounts or multiple orders is not cost-effective for *Pro Club* and increases handling time for all members. Starter Kit information and coupon expiration dates are continually updated, so make sure you have only the most current Starter Kit information and offers available for your new kitten owners.
- Check your Starter Kit shipment upon receipt for kit materials. Multiple box shipments may have baggies and coupons in only one of the boxes.
- Contact *Pro Club* on non-delivery of orders, rather than reordering, so delivery issues can be corrected.

Redeeming Purina Points

Weight circles turn into Purina Points that are automatically redeemed for *Purina* cat food checks. When redeeming points, keep in mind:

- *Purina* cat food checks are good only toward the purchase of any

14-pound or larger bag of *Purina* brand cat food.

- Weight circle redemption points are automatically redeemed for \$6 checks good toward the purchase of any 14-pound or larger bag of *Purina* brand cat food. Points are not "banked" except when totaling less than 600 points. Points totaling less than 600 will remain in the member's account until the next weight circle submission. Six hundred points equal a \$6 check good toward the purchase of any 14-pound or larger bag of *Purina* brand cat food.
- Your *Pro Club* account address should be current as *Pro Club* is not responsible for packages sent to addresses that are not current.
- When requesting an alternate address shipment for rewards, you assume sole responsibility for the receipt of the reward.
- *Purina* cat food checks have a one-year expiration and cannot be reissued if a member allows them to expire.
- Rewards are like cash and should be protected. *Purina* is not responsible for replacement in the event of loss, theft or destruction after issuance.

Using Member Services

When communicating with *Pro Club*, be sure to observe the following:

- A name change request on an account number must be submitted in writing for review. The *Pro Club* account is the named member's account only. *Pro Club* will not be involved in disputes over account ownership.
- Protect your password for accessing your account on the *Pro Club* Web site. It is the responsibility of the *Pro Club* member to monitor who has access to account information. *Pro Club* will not be involved in disputes that are beyond the limitations of the program.
- When contacting or corresponding with *Pro Club*, please supply as much information as possible. This includes member number, name, dates, amounts and issue details. ■

Send Us Your Questions

Have questions about your Purina Points or how to redeem weight circles for rewards and rebate checks? Contact *Purina Pro Club* at (877) PRO-CLUB, or (877) 776-2582, between 7 a.m. and 5 p.m. CST Monday through Friday. You also may visit www.purinaproclub.com to review and redeem Purina Points.

Want to Reach the Editor?

Have comments about *Purina Pro Club Update*? Send them to us at: *Purina Pro Club Update*, c/o Editor, Nestlé Purina PetCare, 2T Checkerboard Square, St. Louis, MO 63164 or via e-mail at today'sbreeder@purina.com.

HCM Mutation

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for Maine Coons. She talked to Linda Kauffman, former president of the Ragdoll Fanciers Club International and owner of Kauffman Kats cattery in Wisconsin. "I told Linda that echocardiogram screening alone wasn't working," Shorey says. "We had to do something else."

Together, they contacted Meurs and asked if she would be willing to try and find the genetic mutation for HCM in Ragdolls. They were delighted when she agreed. Shorey, Kauffman and other dedicated Ragdoll breeders got busy fundraising and collecting DNA samples for the research.

"In order to help Dr. Meurs find the mutation, we had to provide families with documented cases of HCM," Shorey says. "I went to breeders seeking relatives of affected cats. Even if the relatives were negative, their genetic information was necessary for the study. I contacted owners who I had given cats as pets. It took everybody to provide the genetic information needed."

Ragdoll breeders sent to Meurs' laboratory at Washington State University buccal swabs containing DNA, pedigree information and echocardiogram reports. Meurs analyzed the data, and then requested blood samples from certain Ragdolls. She designed a research program and sent out grant proposals hoping to receive funding for the study.

"The objective of the study was to evaluate the DNA in both affected and unaffected cats in search for the causative mutation," Meurs says. "The Ragdoll breeders worked very hard at helping acquire samples. We received about 100 samples."

Meurs received funding from the Winn Feline Foundation (www.winnfelinehealth.org), a nonprofit organization that funds and supports studies that focus on feline health and medical

problems and the same organization that funded much of the research that led to the HCM gene mutation discovery in Maine Coons. Additionally, Ragdoll breeders raised over \$50,000.

"Breeders were very aggressive at fundraising," Meurs says. "HCM is a severe problem, and I wanted to work on it, but it's important for people to realize that funding for this type of project largely has to come from grants and donations. Fundraising by breed clubs and organizations help to make these studies possible."

Financial support also came from the Ricky Fund, established by pet expert and journalist Steve Dale through the Winn Feline Foundation in memory of his Devon Rex "Ricky" who died from HCM. Since 2003, the Ricky Fund has raised over \$70,000 for feline hypertrophic cardiomyopathy research.

As good luck would have it, Meurs discovered the mutation causing HCM in Ragdolls in 2007, about one year after the research had begun. The mutation was on the feline cardiac myosin binding protein C (cMyBP-C) gene, the same gene but in a different location as in Maine Coons with HCM.

"We tested Ragdolls for the Maine Coon mutation and didn't find it, so we looked at other locations on the gene," Meurs explains. "We found it was not the same mutation, but it was located on the same gene. This occurs similarly in humans where about 90 different mutations in the same gene can cause the disease."

By last May, Meurs and her research team had developed a direct DNA test for HCM in Ragdolls. "The test is a good tool, particularly for breeders," Meurs says. "It allows them to make educated decisions about which cats to keep in their breeding programs. I don't think all cats that test positive should be removed from breeding programs, as long as breeders have a good understanding of the disease and know how to evaluate cats for breeding.

"As a geneticist, my advice if a cat is heterozygous positive for the mutation but shows no signs of disease and has lots of wonderful breed traits is to consider breeding him to an HCM-negative cat. Then, test the kittens to determine the best ones to keep for the breeding program. It's a mistake to remove all mutation-positive cats because you will create a negative effect on your gene pool."

"Having the genetic test is wonderful," Shorey says. "With this test, we can work toward a time when the disease is eliminated from Ragdolls."

Meurs cautions that the test does have limitations. "Even if cats test negative for the mutation, that doesn't mean they cannot develop HCM," she says. "Other mutations not yet found may also cause the disease."

Meurs continues to study HCM in Ragdolls to determine whether other mutations exist. She hopes that with tests currently available for HCM in Maine Coons and Ragdolls, breeders of other affected breeds will be encouraged to organize and support HCM research in their breeds.

As for Snoops, the cat who instigated the HCM research in Ragdolls, he continues to thrive at home with Shorey. At almost 3 1/2 years of age, Snoops has not only outlived his prognosis, he also is an example of the success that sometimes occurs with dedicated health care.

"Snoops takes four pills twice a day and has one injection," Shorey says. "I believe he's here for a reason. He motivated me to get involved. He's getting thin, and I know his time is coming, but he still enjoys life. Every day we have him is a gift." ■

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PURINA Pro Club Update

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