

PURINA Pro Club

Update

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Gene Discovery in Maine Coons is First Mutation Identified for HCM

CH Lunarcoons Ganymede is an award-winning Maine Coon cat, a prized sire and a goofy house pet. During a routine ultrasound, "Ganymede" was diagnosed with echocardiographic evidence of hypertrophic cardiomyopathy, a progressive heart condition that causes death in some, but not all, affected cats.

Breeder and owner Paul Huntley of Lunarcoons Cattery in San Jose, Calif., was devastated. "We screen our cats annually," he says. "Ganymede had received a total of five previous screenings. All showed normal heart function. This is perhaps the most tragic aspect of this disease — in some cats there are no outward symptoms for many years."

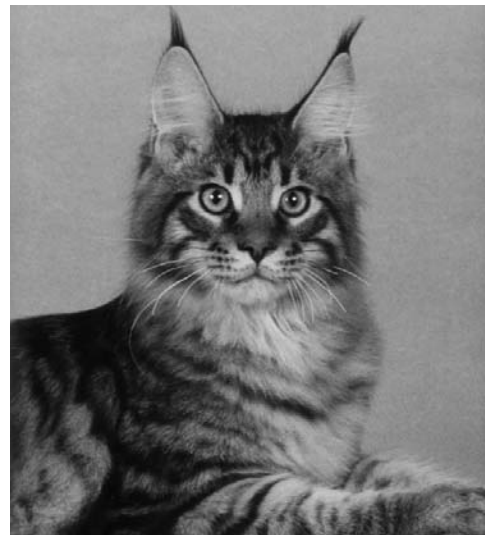
Gene Discovery Aids Breeders

Though hypertrophic cardiomyopathy (HCM) appears in different forms in different breeds, a recent research breakthrough has led to discovery of the genetic mutation that causes HCM in some Maine Coons. The finding is expected to lead to the availability of a direct DNA test in early 2006 to help breeders determine which Maine Coons are carriers and

thus should not be bred.

"This most likely is not the gene mutation that causes the disease in all cats, or possibly even all Maine Coon cats," says Kate Meurs, D.V.M., Ph.D., the Richard L. Ott Professor of Small Animal Medicine and Research at Washington State University School of Veterinary Medicine, who led the research team that discovered the genetic mutation. "This is exciting and we have worked on it for a long time."

HCM affects many breeds, with severity of symptoms varying by breed. HCM also affects as many as one in 500 people. No one knows the exact number of cats that develop HCM, but it is the most commonly diagnosed heart disease in cats. 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 accumulation of fluid in or around their lungs. For some cats, the first and only sign is sudden death. HCM affects a wide range of ages,



CH Lunarcoons Ganymede, bred and owned by Paul Huntley of Lunarcoons Cattery in San Jose, Calif., was diagnosed with HCM after testing normal in five previous screenings.

making it frustrating for breeders to determine which cats are safe to breed.

The discovery of the genetic mutation in Maine Coons is "the first step to allowing us to really understand all aspects of the disease, from the molecular basis to the clinical signs observed in the cat," Meurs says.

"However, we need to keep in mind that even though we have a DNA test for the identification of this Maine Coon mutation, there will be some cats that test negative that will still get this disease. This is because of the genetic complexity of HCM."

The direct DNA test can be performed on a kitten as young as 6 weeks old, which provides a great step forward in identifying kittens that could pass along the gene if bred. 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. Early detection will allow breeders to reduce the prevalence of HCM over time, without compromising genetic variability within the breed.

A Scientific Mystery

Hypertrophic cardiomyopathy is a disease in which the heart's papillary muscles that anchor the mitral valve

Medications Used to Manage Feline HCM

The most important things an owner can do for a cat diagnosed with HCM are to monitor them with regular checkups and follow his veterinarian's advice closely. Though there is no known cure for HCM, veterinarians often prescribe medications to treat various signs of the progressive heart disease.

Unfortunately, there is no proof that these medications are beneficial in cats with HCM, says Mark Kittleson, D.V.M., Ph.D., DACVIM, professor of cardiovascular medicine at the University of California-Davis School of Veterinary Medicine. Owners should not medicate their pets without the direction of a qualified veterinarian.

- Beta blockers may help slow the heart rate and decrease the severity of an abnormality that occurs secondary to HCM.
- Calcium channel blockers may improve heart function by reducing heart rate and myocardial oxygen consumption.
- ACE inhibitors should be used in cats that are in heart failure. Prior to that time, there is no proof they are beneficial, Kittleson says.
- Diuretics are the most effective agents for treating heart failure (pulmonary edema and pleural effusion).
- Medications also are used to help treat other conditions such as hyperthyroidism or hypertension (high blood pressure) that masquerade or worsen HCM in some cats.

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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 hereditary and has been observed in several breeds, including the Devon Rex, Ragdoll, American and British Shorthair, Persian, Norwegian Forest Cat, and Turkish Van. Information from owners and breeders suggests that familial HCM exists in many other breeds as well.

Until now HCM has been a scientific mystery. Cats are usually middle-aged when clinical symptoms are first detected, but HCM has been found in cats as young as 6 months and as old as 13 years. Affected cats are at risk for the development of heart failure or blood clots that can result in cardiac distress or sudden death. Some cats have an aggressive form with early onset and severe physical signs.

The first signs owners may notice are 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. "If a cat has a heart murmur, it should be screened with ultrasound, especially if the cat is used in breeding," says Mark Kittleson, D.V.M., Ph.D., DACVIM, professor of cardiovascular medicine at the University of California-Davis School of Veterinary Medicine. "HCM has a characteristic dynamic heart murmur but this same type of heart murmur also occurs in a benign condition. Without ultrasound, we have no idea which is causing the murmur, plus not all cats with HCM have the characteristic heart murmur."

"One of our cats developed a heart murmur that was detected by a veterinarian during an annual physical exam," Huntley says. "This led to a cardiac workup and the HCM diagnosis. Another cat of our breeding simply died suddenly in the arms of his owner. Often, sudden death is the first and only sign that something is wrong."

Other cats, like Ganymede, do not demonstrate physical signs and HCM will remain mild for most of the cat's life. This can be problematic for breeders attempting to breed out genetic carriers. A male cat with no immediate family history of HCM might sire several litters before HCM is detected. Although that cat would most certainly be neutered, a gene mutation would most likely have already been passed on.

The best clinical test for HCM in breeds other than a Maine Coon is an echocardiogram, or ultrasound screening of the heart. Unfortunately, an echocardiogram can be problematic for a number of reasons. Veterinarians suggest that any cat with clinical

signs such as heart murmur or arrhythmia (abnormal heart rhythms) should be screened. However, an affected cat may have such mild evidence of HCM on the echocardiogram that it is difficult to tell if the test is normal or abnormal, or HCM may have progressed to fatal proportions before an ultrasound is performed.

Onset of HCM can occur at any age so a normal echocardiogram does not guarantee that a cat is HCM free. Ganymede had five normal screenings before HCM developed. 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.

Locating the Gene for HCM

Meurs, who recently moved to Washington State University from The Ohio State University, and Kittleson have studied and collaborated on HCM in Maine Coons for 10 years. Their research has taken countless hours and thousands of dollars. The research project that led to the identification of the HCM gene in Maine Coons was funded through the Winn Feline Foundation's Ricky Fund, the University of California-Davis Center for Companion Animal Health, as well as other sources, including many individual gifts.

The Winn Feline Foundation, which can be found at www.winnfelinehealth.org, is a nonprofit organization that supports studies into medical problems affecting cats. The Foundation's Ricky Fund for HCM research was established by Steve Dale in memory of his Devon Rex "Ricky," who died from HCM. Since 2003, the Ricky Fund has awarded about \$60,000 for HCM research.

Meurs and Kittleson determined that similar to humans, cats inherit HCM in an autosomal dominant fashion. This means the mutation is not inherited on the sex chromosomes, X or Y. Rather, it results from a mutation in one copy of a gene that codes for a structural protein from one parent, causing the autosomal dominant trait.

Prior to the discovery of the mutation, evaluation of several other genes that cause HCM in humans and Maine Coons had been ruled out in Meurs and Kittleson's research. However, Meurs discovered that the cardiac protein, myosin-binding protein C, is significantly reduced in Maine Coons. "It was a lengthy process," Meurs says. "First, we discovered an abnormal protein. Once we made this discovery, we looked at the gene and found the mutated gene." With the mutated gene pinpointed, a genetic test was created for HCM in Maine Coons and used in the colony at the University of California-Davis to verify that it was an actual mutation rather than a normal variant.

The genetic test will allow breeders to test Maine Coons for HCM as

kittens. Paul Huntley of Lunarcoons is thrilled. "This is huge," he says. "There is simply no other way to say it. HCM is without question the single most serious health problem the Maine Coon community faces. The potential for an early screening technique that is 100 percent accurate in predicting disease caused by this mutation will avert untold grief, and drastically reduce, if not completely eliminate, affected cats from the breeding population."

However, Meurs is quick to point out that this discovery is not the "end-all, be-all solution" to HCM. She explains that in human beings there are over 200 different mutations and 10 different genes that cause HCM. So far her research has isolated one mutation on one gene in one breed. Most likely other breeds will have a completely different mutation.

Benefits of a Genetic Test

Although the genetic test can be used for early detection and management of HCM, the biggest reason to screen Maine Coons is to select breeding animals. Susan Little, D.V.M., DABVP, an Ottawa-based feline medicine specialist and president of the Winn Feline Foundation, cautions, "It will be essential for breeders to have a sound management plan and work with a geneticist so that all the good health qualities of the breed are preserved. A cat or a breed is a collection of thousands of good genes, and we must take care not to throw away good genes simply to target one bad gene."

There is also the possibility that older cats with previously normal ultrasounds will test positive for the genetic mutation. Huntley recognizes the need for breeders to appropriately handle an HCM diagnosis in order to make strides toward eliminating the disease from the breed. "It is the ethical thing to do to inform the owners of direct relatives of the change in the cardiac status of the cat," he says. "Oftentimes a cat diagnosed with HCM may have relatives that remain in breeding programs, and it is vital that those breeders be aware that their cats are at risk."

Though the test is not yet commercially available, Meurs is hopeful that it will be on the market by early 2006. Potentially, the test will be a simple swab kit that owners can use to obtain a cheek cell sample. Those interested in obtaining a test kit may contact Meurs via e-mail at meurs@vetmed.wsu.edu.

Meurs' team will inform owners of the results. If a Maine Coon is negative, it does not have the specific mutation that has been identified so far. It is possible there is another mutation in Maine Coons. For this reason, a negative diagnosis may not absolutely rule out HCM. If a cat tests positive, it does not necessarily correlate to the severity of HCM but does

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confirm the possibility of the cat passing the mutation on to offspring.

Little points out, "Simply having the gene for HCM does not mean that a Maine Coon will actually become ill from heart disease. Since many cats are so mildly affected, they never suffer ill health. We do not treat asymptomatic cats, but identification of the disease in a cat will allow 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."

For now, medical treatment for cats diagnosed with HCM will remain unchanged. Veterinarians recommend regular ultrasounds to track the progress of the disease. Several medications are used to treat signs, but doctors are limited in their efforts because there is no known cure for HCM. Identification of the gene does open the door for further research that could find better treatment options for the disease. Understanding the effects of the mutant gene may lead to new ideas about intervention.

The next step is to gather information in other breeds. As additional genes and mutations are discovered, there may be several genetic tests available to veterinarians to help diagnose HCM in more breeds. Huntley believes that research like Meurs and Kittleson's is paving the way for successful breeding programs.

"It is only through open communication about this tragic disease, and following smart sensible practices developed in partnership between breeders and the veterinary community, that we can hope to overcome this disease," he says. "We are nearly there, and it is a godsend." ■

Conditions of Membership: Purina Pro Club Reviews Program

Purina Pro Club, a loyalty program for breeders and owners of purebred cats, offers members benefits such as Kitten Starter Kits, checks good toward the purchase of Purina brand cat and kitten foods, and the Purina Pro Club Update newsletter. Here's how Pro Club works.

Member Eligibility

To be eligible for Pro Club, one must care for five or more cats and/or breed one litter of kittens a year. Additionally, only one membership per household is allowed. Providing false membership to become a member of Pro Club or receive Kitten Starter Kits will result in termination of Pro Club membership and potential legal action.

Pro Club members are eligible to earn Purina Points by redeeming weight circles from participating brands of Purina cat and kitten foods. Cat food bought by Pro Club members will be fed to cats owned or cared for by the Pro Club member. Pro Club members may not resell cat food with weight circles removed from the bags.

Point Redemption

Weight circles — the colored circles on packages of participating Purina brand cat and kitten foods — may be redeemed for Purina Points for checks good toward the purchase of Purina

cat or kitten foods. Only weight circles, not UPC codes, are valid for submission.

For every 600 Purina Points earned, you will automatically receive a \$6 check good toward the purchase of any 14 pound or larger bag of Purina cat and kitten food. Points are not "banked" except when totaling less than 600 points. Please allow three to five weeks for processing and delivery of checks.

When you submit weight circles, remember to include a Weight Circle Claim Form to help speed up the processing of the weight circles. A Weight Circle Claim Form will be issued to you automatically when weight circles are submitted.

In addition, you may go online to order or download claim forms on the Pro Club Web site. Forms also may be ordered by calling Pro Club at 1-877-PRO-CLUB (1-877-776-2582) between 7 a.m. and 5 p.m. CST Monday through Friday. Weight circles and claim forms should be sent to: Purina Pro Club, 1400 S. Highway Drive, Fenton, MO 63099.

When mailing your weight circles, be sure to send them by certified first class mail or some other traceable delivery method to ensure delivery in the event Pro Club does not receive your weight circles.

Keep in mind that Purina Points

do not have a cash value. There is no cap to the number of points a member may earn, and occasionally Purina offers opportunities to earn bonus points. However, Purina reserves the right to terminate membership or remove or disqualify earnings for any violation of account or program terms. Points expire three years from the date of last activity, and cannot be purchased and are not transferable. Members are responsible for any taxes that might be owed as a result of points earned and/or redeemed.

Kitten Starter Kits

Pro Club provides free Kitten Starter Kits to help ease the transition into a new home for kittens and new kitten owners. Each kit includes a comprehensive Kitten Care Guide, health record and a placeholder for breed-specific information, photos, pedigree, and more. Kitten Starter Kits resemble a file folder with tabs marking each section.

Kitten Starter Kits are available for Purina Kitten Chow or Purina Pro Plan. You may order Starter Kits in either of the two brands of Purina kitten food you feed and recommend. You also are provided a coupon for free kitten food so you may give new owners samples in a zip-lock bag that looks like the retail package. Additionally, the Kitten Starter Kits contain a savings coupon for kitten food for new owners.

You may order Purina Kitten Chow or Pro Plan Kitten Starter Kits online at the Pro Club Web site or by calling Pro Club toll-free.

Keep Your Address Current

It is important to keep your Pro Club address current to ensure the delivery of checks, Kitten Starter Kits and the Purina Pro Club Update newsletter. Pro Club is not responsible for packages sent to addresses that are not current. Rewards will be sent to your mailing address on file unless otherwise instructed. By requesting shipment of a program reward to a different address, you assume responsibility for receipt of the reward. ■

Purina Points Earned Per Pound of Purina Brand Cat Food	
Brand	Purina Points
Purina Pro Plan, [®] Purina ONE [®]	16 points per pound
Purina [®] Cat Chow, [®] Purina [®] Kitten Chow, [®] Purina Veterinary Diets, [®] and other participating Purina [®] brands*	8 points per pound
* Includes Kit N' Kaboodle, [®] Tender Vittles [®] and Happy Cat. [®] Excludes Dealer's Pride, [®] Cat Menu [®] and Deli Cat [®] brand cat foods; Tidy Cats [®] brand cat litter; and Purina [®] or Friskies [®] brand cat treats.	

Pro Plan Introduces New Senior Cat Foods Plus New Canned Entrées

Purina Pro Plan is helping to provide the nutrition senior cats need with the introduction of new Pro Plan Senior 11+ cat formulas.

Pro Plan Senior 11+ Chicken & Rice Formula and Senior 11+ Indoor Formula Turkey & Rice Formula both contain at least 43 percent protein to help sustain muscle mass for strength and to provide energy. Real chicken or turkey is the No. 1 ingredient, which provides high palatability to help keep older cats interested in eating.

Studies on aging cats show that at around age 11 cats begin to experience changes in weight and muscle loss. At about this age, cats' senses diminish and their ability to absorb key nutrients declines. Veterinarians report that nearly 20 percent of cats from ages 12 to 15 are underweight. By the time cats are 15 and older, the number that is underweight increases to 50 percent.

Pro Plan Senior 11+ dry cat foods are formulated with a special blend of nutrients to help facilitate digestion

of fat. Calcium, phosphorus and other nutrients help support strong bones and healthy joints. A small kibble is designed to be easier for older cats to chew. Pro Plan Senior 11+ cat foods will be available in stores beginning in mid-January.

Pro Plan also has Pro Plan Senior formulas for ages 7 to 11 to address the decrease in activity and risk for excess weight gain that occurs in cats at this age.

Pro Plan Senior 7-11 Chicken & Rice Formula, Senior 7-11 Indoor Care Turkey & Rice Formula, and Senior 7-11 Hairball Management Chicken & Rice Formula contain real chicken or turkey as the No. 1 ingredient.

Made with at least 41 percent protein, these senior cat foods help to maintain lean muscle mass and healthy weight. They also provide nutrition to help support strong bones and healthy joints, and contain antioxidants to help support a healthy immune system.

New Entrées for Adults

Pro Plan is introducing three new Pro Plan Canned Entrées for adult cats. Pro Plan Adult Cat Turkey & Rice Entrée, Adult Cat Tuna Entrée, and Adult Cat

Pro Plan is available in pet specialty stores, such as PetsMart and PETCO, at Farm & Fleet, and from veterinarians. For information, visit the www.proplan.com Web site or call 1-800-PRO-PLAN (1-800-776-7526) from 9 a.m. to 4 p.m. CST Monday through Friday.

Chicken Entrée offer exceptional palatability.

Adult Cat Turkey & Rice Entrée is made with real turkey in gravy; Adult Cat Tuna Entrée is made with real tuna in sauce; and Adult Cat Chicken Entrée is made with real chicken in a chunky form. All three Canned Entrée formulas provide complete and balanced nutrition for adult cats to help support a strong immune system. These cat foods will be available in stores beginning in mid-January. ■



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