ichthyosis is inadvertently diagnosed or ignored. It also is possible that mild cases go undetected because it went away and never persisted into adulthood.”

ichthyosis is a diverse group of hereditary, usually congenital, diseases characterized by faulty formation of the outer layer of the epidermis, the stratum corneum, with resultant scaling. Skin biopsies have revealed two types of ichthyoses: epidermolytic ichthyosis (EI) and nonepidermolytic ichthyosis (NI).

Golden Retrievers develop the NI type, which also occurs in American Bulldogs and Jack Russell Terriers though in a more serious, yet not common, form. Among the breeds that develop EI are Norfolk Terriers, Rhodesian Ridgebacks and Labrador Retrievers. A University of Pennsylvania study of 46 Golden Retrievers diagnosed with ichthyosis from January 2004 to January 2007 found that all the dogs had mild to moderate dry scaling with variable hyperpigmentation on their abdomens. Large, loose scales ranging from soft white to gray were described as looking like snowflakes. “The dogs looked like walking snow globes,” says Elizabeth Mauldin, D.V.M., associate professor of pathology and dermatology at the University of Pennsylvania School of Veterinary Medicine. “We documented that the dogs suffered from a primary disorder of cornification, the process of making scale in natural skin turnover. We determined that a skin biopsy can be used to diagnose the disorder.”

The 46 dogs in the study consisted of 25 females and 21 male Golden Retrievers. Twenty-two dogs had skin lesions when they were younger than 1 year of age; three dogs developed the disorder between 1 and 2 years of age; and 13 dogs were older than 2 years of age. The age of onset was unknown for eight dogs.

The wide age distribution reflects the subtle nature of the phenotype. The challenge of determining an exact age of onset is difficult as mild scaling could have been overlooked. Hereditary ichthyosis is often present at birth, but it is not uncommon for signs to develop later in adulthood. “All the dogs had strikingly similar histopathologic changes consisting of mild to moderate hyperkeratosis, or thickening of the outer layer of skin, and an absence of epidermal hyperplasia, which is the proliferation of normal cells, and dermal inflammation,” Mauldin explains. “Environmental factors including nutrition, supplements, humidity, estrous cycle, and other skin conditions likely impacted the degree of scale formation.”

Electron microscopic analysis of the skin of five affected dogs compared with two normal control dogs showed crystalline structures in the outer layer of skin, the stratum corneum. Pedigree analysis of 14 dogs indicated that Golden Retriever ichthyosis is an autosomal recessive condition in which a dog inherits a copy of the mutated gene from both its sire and dam.

Not curable, ichthyosis is treated with moisturizers and emollients to provide palliative care. “Corticosteroids, such as prednisone, do not improve skin condition and actually worsen the skin barrier,” explains Mauldin. “This further impairs the body’s natural defenses and puts a dog at risk for secondary bacterial and possibly yeast infections.”

Breeders Can Test Golden Retrievers for Ichthyosis

A direct DNA test to help identify Golden Retrievers that are carriers, affected or normal for ichthyosis is available through Antagene, a diagnostic testing laboratory in La Tour-de-Salvagny, France. Ichthyosis is a scaling skin disorder with an autosomal recessive inheritance.

The $120 genetic test can be performed from a cheek swab or blood sample. Samples from Golden Retrievers in the U.S. should be sent to Optigen, a diagnostic testing laboratory in Ithaca, N.Y., which extracts the DNA and ships it to Antagene for DNA testing. Results are available in three to four weeks.

The GRCA Health & Genetics Committee recommends prebreeding testing primarily for dogs that have clinical signs of ichthyosis and for dogs that have close relatives known to be carriers, affected or have clinical signs.
Golden Retriever Ichthyosis
continued from page 1

Two other studies were simulta-
necessarily performed on ichthyosis in Golden Retrievers. The studies, which took place in England3 and France,4 concluded similar clinical and histo-
pathological results. Thus, the three studies led to the hypothesis of an autosomal recessive transmission mode.

DNA Discovery Aids Understanding

The discovery of the causative muta-
tion for Golden Retriever ichthyosis was made in 2010 by a group of French geneticists led by Catherine André, Ph.D., head of the Canine Genetics team at CNRS/University of Rennes. The project was funded by CNRS and the European Commission under the LUPA initiative that brought together genomic experts at university and pri-
ivate laboratories to study the genetics of dogs and learn more about human diseases. A genomewide association study of 460 and 40 unrelated healthy ones allowed them to identify a genomic region on canine chromosome 12. 

The researchers used candidate gene sequencing in 12 affected and 12 healthy Goldens to identify the mutation in the PNPLA1 (papatin-like phospholipase) protein. They found a homozygous insertion-deletion, or indel, mutation in PNPLA1 that leads to a premature stop codon and then an altered protein in the affected dogs.

“We considered PNPLA1 to be a promising candidate gene,” André says. “This premature stop codon causes a loss of 74 amino acids in the C-terminal region, affecting enzyme activity and potentially lipid droplet binding, of the PNPLA1 protein.” 
The research was confirmed by sequencing 320 Golden Retrievers, consisting of 120 affected and 200 unaffected healthy dogs. All the affect-
ed dogs were homozygous for the mutation, about 30 percent, and the healthy ones were either homozygous for the normal allele, about 30 percent, or heterozygous, about 40 percent, which is consistent with an autosomal recessive mode of inheritance.

The mutation was not found in 180 healthy dogs representing the other four retriever types: Labrador Retriever, Flat-Coated Retriever, Curly Coated Retriever, and Chesapeake Bay Retriever. Nor was the mutation found in 300 healthy dogs of 25 other breeds.

“The data support the causative nature of the mutation in Goldens, as well as the specific founder effect in the breed,” André explains. “The indel introduces a premature stop codon in the open reading frame of the gene, which led to a loss of 74 amino acids in the highly conserved C-terminal region of the PNPLA1 protein.”

The geneticists applied information from the Golden genetic model to human research. “We screened the PNPLA1 gene in humans affected with ARCI,” says André. “The research translated well from Goldens to humans through collaborations with Dr. Judith Fisher, a specialist of human ichthyoses from the Institute of Human Genetics at Freiburg University in Germany. Mutations in the PNPLA1 gene were identified in two human families affected by ARCI. This was the first evidence for the involvement of PNPLA1 in ichthyosis in dogs and humans.”

Random sampling of 500 Golden Retrievers in France further supports the autosomal recessive inheritance and the mutation frequency as follows:

• Forty percent of dogs are carriers that inherit one copy of the mutated allele. Though they will not be affected, they transmit the mutated allele to 50 percent of their offspring.

• Thirty percent are affected, inherit-
ing two copies of the mutated allele and passing one mutated allele on to 100 percent of their offspring. Many affected dogs do not show signs of disease, while others develop mild to moderate disease.

• Thirty percent are normal. They inherit two copies of the normal allele, and their offspring cannot get the disease even if the other parent is affected or a carrier. André notes that thus far all affect-
ed Golden Retrievers have the same mutation. She believes the disease is less prevalent in Golden Retrievers in the U.S. compared to those in France and other European countries, where the frequency of the mutation now reaches about 50 percent.

She is hopeful that ongoing research will help identify and clarify the role of the PNPLA1 protein in normal and affected dogs. “This is a big concern for breeders,” André says. “Some dogs are so mildly affected they are considered clinically unaffected, but if they are bred, they will spread the disease.”

Realizing Breeding Implications

A direct DNA test now is available for determining if a Golden Retriever carries the PNPLA1 mutation or is affected by the scaling disorder, although the DNA test cannot predict which affected dogs will actually show clinical signs. Margret Casal, Ph.D., D.V.M., associate professor of medical genetics at the University of Pennsylvania School of Veterinary Medicine, cautions that a positive ichthyosis test should not discourage breeders. "Breeders should not remove affected or carrier dogs from the gene pool," she says. "This would reduce genetic diversity and create a super bottleneck." The best approach is to gradually reduce the mutation over six or seven generations, Casal advises. "You would consider the entire dog — all his or her qualities and characteristics. An affected or carrier dog that has much to con-
tribute should be bred, although you should avoid breeding two affected dogs. Instead, breed outstanding affected or carrier dogs to clear dogs. This provides a choice of dogs to progressively decrease the frequency of the PNPLA1 gene mutation.”

The GRCA Health & Genetics Committee endorses this approach. It also echoes Casal’s caution regarding unnecessarily reducing the genetic diversity that is so vital for long-term breed health, Hovan says.

Golden Retriever breeder Gayle Watkins of Cold Spring, N.Y., who breeds under the Goldie Pines kennel, says that she has not been too concerned about ichthyosis since it appears so mildly in most Golden Retrievers. A recent litter of seven affected puppies made her think twice.

“We had DNA testing performed on the dam when she was pregnant,” Watkins says. “Both she and the sire tested positive. After this happened, I realized how upset prospective buyers can become about buying puppies with a known flaw.”

Two of the puppies had moderate to severe flakies, or dandruff. Scales could be seen when the hairs on their coat were parted. “When the puppies were 19 and 20 weeks old, the signs had disappeared, and eventually, there were no clinical signs,” she says.

Once the genetic test was offered, Williamson tested the sire and dam of a recent litter that produced a puppy with lightly, flaking dandruff. Both the sire and dam came back as carriers. "The dam was bred three times before the DNA test was available,” she says. “What’s more, all three sires were carriers. I’ve always placed puppies with dandruff into pet homes, so while I don’t have any affected dogs at my kennel, I have plenty of carriers.”

 Watkins worries that as DNA tests become available for milder conditions, breeders will be forced to avoid pro-
ducing dogs with any diseases. “We are going to be pushed into making poor decisions for the breed, such as removing dogs from the gene pool for minor conditions,” she says. “Fortunately, ichthyosis does not affect a dog’s ability to hunt, retrieve, swim or participate in all kinds of dog shows, so I don’t think people will not lose dogs with great qualities. A DNA test can be helpful as long as we use smart breeding.”


Purina appreciates the support of the Golden Retriever Club of America and particularly Rhonda Hovan, the GRCA research facilitator, in helping to identify topics for the Purina Pro Club Golden Retriever Update newsletter.
Purina ONE beyond brand dog food, the super-premium natural food plus vitamins and minerals introduced in 2011, now includes Weight Circles on the packaging. Starting in January 2013, Purina Pro Club will no longer accept UPC codes for Purina Point credit.

Purina ONE beyond has a value of 11 points per pound, the same as other Purina ONE products. The Purina ONE beyond portfolio includes: Chicken & Whole Oat Meal Recipe, with real white meat chicken as the No. 1 ingredient and accented with carrots, tomatoes and apples, and Lamb & Whole Barley Recipe, with real lamb as the No. 1 ingredient and accented with blueberries, sweet potatoes and spinach. Both have a 26 percent protein to 17 percent fat ratio and are made without corn or wheat, added fillers or artificial preservatives. They offer complete and balanced nutrition for adult dogs.

Pro Club Dog Food Checks Change to Match New Packaging Sizes

One of the benefits of being a member of Purina Pro Club is receiving dog food checks to offset the costs of Purina brand dog food. The $7 dog food checks now can be used toward the purchase of any 14-pound or larger bag of Purina brand dog food. New packaging sizes for Purina brand dog foods prompted the change.

Purina Points accrue when members submit Weight Circles, the colored circles on packages of Purina brand dog food. Weight Circle submissions are processed as Purina Points that can be redeemed for items from the Purina Pro Club Rewards Brochure, online at www.purinaproclub.com, or for Purina dog food checks. Members should submit a minimum of 250 pounds worth of Weight Circles in one submission.

Pro Club members may order any quantity of checks in multiples of 10 checks, using their Purina Points. A set of 10 Purina brand dog food checks can be ordered for 7,000 Purina Points.

11th Annual National Dog Show Will Be Broadcast on Thanksgiving Day

The National Dog Show Presented by Purina, hosted by the Kennel Club of Philadelphia, will be broadcast on NBC from noon to 2 p.m. Central time on Thanksgiving, Nov. 22, following the “Macy’s Thanksgiving Day Parade.”

In its 11th year, The National Dog Show, which features Group and Best in Show judging, has become an American Thanksgiving Day tradition with about 20 million people tuning in. Co-hosts John O’Hurley, of “Seinfeld” and “Dancing with the Stars” fame, and David Frei, of the Westminster Kennel Club and an expert analyst, have provided commentary since the program began in 2002. Held at the Greater Philadelphia Expo Center at Oaks, The National Dog Show is filmed during the Saturday, Nov. 17 Kennel Club of Philadelphia Dog Show.

Purina ONE beyond dog food comes in 3.5, 15 and 26 pound package sizes. Purina ONE beyond is sold at pet specialty, grocery and mass retail stores. For information, visit www.purinonebeyond.com. To talk to a pet adviser, call 1-866-PURINA (1-866-787-4621) from 7 a.m. to 7 p.m. Central time Monday through Friday.

Purina-Sponsored Dog Shows* | November 2012 to January 2013

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<tr>
<td>Bulldog Club of America National Specialty</td>
<td>Nov. 19-24</td>
<td>Costa Mesa, CA</td>
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<tr>
<td>American Brittany Club National Specialty</td>
<td>Nov. 19-25</td>
<td>Fort Smith, AR</td>
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<tr>
<td>Lone Star Winter Classic &amp; Texas Kennel Club Dog Show</td>
<td>Dec. 6-9</td>
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<td>Holiday Cluster &amp; Malibu Kennel Club Dog Show</td>
<td>Dec. 7-10</td>
<td>Costa Mesa, CA</td>
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<td>Cleveland Crown Classic Dog Shows</td>
<td>Dec. 13-16</td>
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<td>Kennel Club of Palm Springs Dog Show</td>
<td>Jan. 3-6</td>
<td>Indio, CA</td>
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<td>Land O’ Lakes Kennel Club Dog Show &amp; Cluster</td>
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<td>Florida Gulf Coast Cluster</td>
<td>Jan. 10-11, Jan. 13-15, Jan. 18-20</td>
<td>Ocala, FL</td>
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* This table lists some, but not all, upcoming Purina-sponsored dog shows.
Westminster Best in Show Dogs Remembered for their Achievements, Ambassador Roles

The recent passing of three Westminster Kennel Club Best in Show winners has left a void in the hearts of their owners and dog enthusiasts around the world. "J.R.,” "Stump" and "Rufus” will be remembered for the records they set but also for how they endeared all who knew them.

Owner-handler Scott Sommer of Houston lost his beloved house dogs, J.R. and Stump, over six days in September. J.R. (CH Special Times Just Right), the Bichon Frise who won the Garden in 2001, died Sept. 20 at 15 years of age. On Sept. 26, Stump (CH Clussex Three D Grinchy Glee), the Sussex Spaniel who at age 10 became the oldest Westminster winner in 2008, passed away at 13 years of age.

After retiring as show dogs, J.R. and Stump had a daily ritual of taking a 10-minute ride with Sommer to the boarding/show kennel where they lived when they were being campaigned. Stump would get out of the car, walk into the kennel and take his place in the first run — the same that was his when being shown. J.R. liked to sit on a grooming table, where he would bark hello to all who entered.

The top-winning Bichon in breed history, J.R. won the Garden as a 3-year-old. Sommer continued to show the Bichon at select shows, and J.R. captured his 101st show at the first AKC National Championship. Best known for his bouncy, energetic temperament, J.R. also had a calm, empathetic side that came out when Scott took him to visit patients at children’s hospitals.

Stump, the 2004 Sporting Group winner at the Garden, came out of retirement to win Westminster, his 51st Best in Show and a first for the rare English breed. Though Stump was entered for Westminster, it was not until the Wednesday before that Sommer decided to bring him due to concerns that he was older and would have to fly in the cargo section because he was too large to meet the size requirement to fit under the seat. On the return trip from New York, Stump flew first class with Sommer.

Barbara and Tom Bishop of Holmdel, N.J., lost their beloved Rufus (CH Rocky Top’s Sundance Kid), the 2006 Westminster winner, Aug. 9 at 12 years of age. The first Colored Bull Terrier to win the Garden, Rufus accumulated 35 Bests in Show, including “The National Dog Show Presented by Purina” and the Morris and Essex Top’s Sundance Kid), the 2006 Westminster winner, Aug. 9 at 12 years of age. The first Colored Bull Terrier to win the Garden, Rufus accumulated 35 Bests in Show, including “The National Dog Show Presented by Purina” and the Morris and Essex

Rufus was commemorated with a special event held at the Purina Event Center at Purina Farms in Gray Summit, Mo., in August 2010.

Along with “Una,” the Beagle and “Sadie,” the Scottish Terrier, helped christen the Purina Event Center at Purina Farms in Gray Summit, Mo., in August 2010. Along with their owners and handlers, these Westminster Best in Show winners walked the red carpet and were the first dogs to enter the facility. Their names are engraved on brick pavers lining the Walk of Champions going into the building.

Purina joins the owners of these special dogs in commemorating their lives. Their accomplishments and their shining personalities will be remembered for many years to come.

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<tr>
<td>NGSFA Pheasant Championship</td>
<td>Nov. 1-10, Queenstown, MD</td>
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<td>Kentucky Open Shooting Dog Championship</td>
<td>Nov. 1-6, Richmond, KY</td>
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<td>Retriever National Open Championship</td>
<td>Nov. 10-17, Montgomery, TX</td>
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<td>English Springer Spaniel National Amateur Championship</td>
<td>Nov. 12, Ogden, UT</td>
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<td>Southern Championship</td>
<td>Nov. 12-17, Miami, FL</td>
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<tr>
<td>American Brittany Club National Championship</td>
<td>Nov. 18-25, Spokane, WA</td>
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<tr>
<td>English Springer Spaniel National Open Championship</td>
<td>Nov. 24-28, Pinckneyville, IL</td>
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<td>UKC Battle of the Breeds</td>
<td>Dec. 7-8, Ada, OK</td>
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