Ichthyoses are 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.2,3 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.2 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.
DNA Discovery Aids Understanding
The discovery of the causative muta-
tion for Golden Retriever ichthyosis was
made in 2010 by a group of French
clinicians 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-
vate laboratories to study the genetics
doing and learning more about human
diseases. A genomewide association study
of 400 dogs 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
Golden Retrievers to identify the mutation in the
PNPLA1 (pataxin-like phospholipase)
protein. They found a trinucleotide
insertion-deletion, or indel, mutation in
PNPLA1 that leads to a premature
stop codon and then an altered protein
in the affected dogs.
“Considered PNPLA1 to be a promising candidate gene,” André says.
“Premature stop codon causes a
loss of 74 amino acids in the C-
terinal region, affecting enzym e 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
Reiver. Nor was the mutation found in
300 healthy dogs of 25 other breeds.
“Data support the causative
nature of the mutation in Golden’s,
as well as the specific founder effect in
the breed,” André explains. “The indel
insertion-deletion, and thus 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 Golden 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
inherited 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 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, cauinion that a positive ichthyosis test should not
discourage breeders. “Breeders should
not remove affected or carrier dogs
on the dam when she was pregnant,”
Wattcns says. “Breeders should stop
undeing 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 activities. It is so important
to not lose dogs with great qualities. A DNA test can be helpful as long as we use smart breeding.”

1 Grill A, et al. PNPLA1 mutations cause auto-
somal recessive congenital ichthyosisis in golden
2 Maulin EA, et al. The clinical and morphologic
features of nonneoplastic ichthyosis in the golden
retriever. Veterinary/Pathology. 2008;Mar;
3 Cadiergues MC, et al. Clarification defect in
the golden retriever: clinical, histopathological,
ultrastructural and genetic characterisation.
4 Guazzone E, et al. Clinical, histopathological
and genetic data of ichthyosis in the golden
retriever: a prospective study. Journal of Small

Purina appreciates the support of the
Golden Retriever Club of America
and particularly Rhonda Hispan, the
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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 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 Pro Club Member 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.

A limit of one check can be used per bag. Members should allow three to five weeks for processing and delivery of checks.

**How to Reach Purina Pro Club**

To view your Purina Point balance, Pro Club members should visit www.purinaproclub.com or call 1-877-PRO-CLUB (1-877-776-2582) between 7 a.m. and 5 p.m. Central time Monday through Friday.

Purina dog food checks expire in one year and cannot be reissued. Members should protect dog food checks like cash. Purina is not responsible for replacement in the event of loss, theft or destruction after issuance.

When submitting Weight Circles, Pro Club recommends that you mail them by certified first-class mail or other traceable delivery method. This helps to ensure proof of delivery in the event Pro Club does not receive your Weight Circles. Pro Club is not responsible for Weight Circles not in its possession.

**Reminders from Pro Club**

Pro Club members should be aware of the following:

- Purina Pro Club is not a program for institutional organizations, such as rescue groups, humane societies or animal shelters.
- Any retail sale or purchase—including Internet transactions—of Purina and Purina Pro Club materials is a violation of program terms and conditions. This includes, but is not limited to, the selling or buying of Puppy Starter Kits and weight circles.
- Pro Club is not responsible for fraudulent weight circles. Submitting fraudulent weight circles is a violation of the Pro Club program terms and conditions.
- Purina reserves the right to terminate membership or remove or disqualify earnings for any violation of account or program terms.
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 Clussexx Three D Grinchy Glee), the Sussex Spaniel who at age 10 became the oldest Westminster winner in 2009, 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.

冬奥会的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 in Westminster, his 35 Bests in Show, including “The National Dog Show Presented by Purina” and the Morris and Essex Kennel Club Dog Show. A dynamic show dog and the most successful Colored Bull Terrier of all time, Rufus went on to become a therapy dog and breed ambassador.

Preceding the passing of these Westminster champions, “James” (CH Felicity’s Diamond Jim), the English Springer Spaniel who won the Garden in 2008, died in May 2011 at 11 years old. Owned by Teresa and Allen Patton of Fairfax Station, Va., and handled by Kellie Fitzgerald of Bear, Del., James later visited children at cancer centers and Ronald McDonald houses with Teresa Patton. He became the only canine celebrity to be recognized by the Alzheimer’s Association as a Champion for Alzheimer Awareness. J.R., Stump, Rufus and James, along with “Uno,” 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.

### Purina-Sponsored Sporting Events* | November to December 2012

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<td>Kentucky Open Shooting Dog Championship</td>
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<td>English Springer Spaniel National Open Championship</td>
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<td>UKC Battle of the Breeds</td>
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* This table lists some, but not all, upcoming sporting events sponsored by Purina.