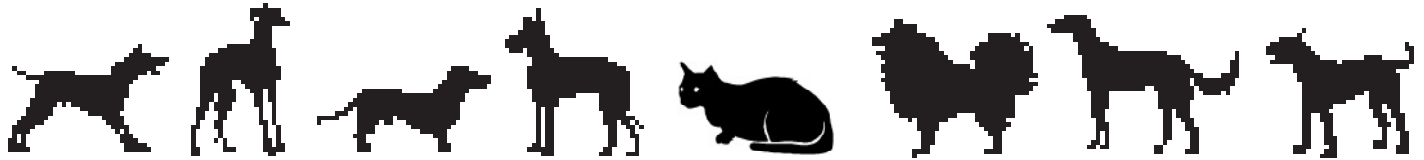

The ADVOCATE



News from the Orthopedic Foundation for Animals Inc., a not-for-profit organization

Volume 1, Issue 2

For Love and Commitment to Animal Wellness

OFA Carries 33 Years of Progress into a New Century

John Olin was a well-known industrialist, philanthropist and sportsman who had a deep love for the sporting dog breeds. His commitment to the welfare of dogs was first evidenced in his founding of Nilo Kennels in East Alton, Illinois, where he bred, trained and campaigned outstanding examples of the sporting breeds.

Olin recognized that hip dysplasia was a common

and debilitating orthopedic disease in canines and in the fall of 1964 gathered a group of individuals to discuss means of limiting hip dysplasia. This initial meeting, which included representatives of the Golden Retriever Club of America, German Shepherd Dog Club of America and the veterinary community, led to the organization of the Orthopedic Foundation for Animals (OFA).

OFA was incorporated as a not-for-profit corporation by the state of Illinois on July 7, 1966. The original purpose of the organization was providing radiographic evaluation, database maintenance and genetic counseling for canine hip dysplasia.

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Four Members Join OFA Board **Page 7**

For More Information

Applications or more information on OFA registries and databases are available by calling (573) 442-0418, faxing (573) 875-5073 or writing the Orthopedic Foundation for Animals, 2300 Nifong Boulevard, Columbia, Mo. 65201-3856.

Information also is available at the OFA website, <http://www.offa.org>.

The Advocate

Published by the Orthopedic Foundation for Animals Inc. to inform and educate veterinarians, veterinary technologists, breeders and owners on advances in animal health and the services of OFA.

Editor

G. Gregory Keller, D.V.M., M.S., Dipl. ACVR

Broadening Horizons

Over the past 10 to 15 years the OFA board has recognized that a variety of heritable diseases impact animal health. It has been estimated that at least 25 percent of the health problems facing veterinarians and breeders have genetic roots. Following scientific advancements that have enhanced the ability to diagnose heritable diseases, OFA has supported development of diagnostic criteria and databases for other genetic diseases.

Each database is a comprehensive list of individuals who have been submitted for certification that they are free of a specified trait. For example, the canine hip registry is a comprehensive database of all dogs that have been submitted for canine hip dysplasia certification. From this database we can summarize the presence of hip dysplasia seen in specified breeds and aid breeders in making informed decisions about their breeding programs.

The OFA Databases

The following databases have been developed by the OFA to date:

Hip Dysplasia arises from a number of malformations of the hip socket and femur and is a cause of debilitating orthopedic problems in many breeds. It is evaluated

OFA Databases Help Breeders Make Informed Decisions

(continued from page 1)

through a standard pelvic radiograph that is taken by a veterinarian. Three veterinary radiologists independently examine the radiograph to evaluate the hip status using standard criteria.

Elbow Dysplasia is a degenerative joint disease that is evaluated through a lateral radiographic view taken by a veterinarian of each elbow in extreme flexion. Three veterinary radiologists independently examine the radiograph to evaluate elbow status using standard criteria.

Luxation of the Patella is a deformity of the hind leg that permits the kneecaps to dislocate, leading to lameness. A physical examination by a veterinarian evaluates patellar conformation.

Autoimmune Thyroiditis is evaluated by laboratory analysis of blood samples to detect the presence or lack of autoimmune thyroid factors. The thyroid gland produces thyroxin, a hormone involved in many aspects of healthy metabolism. Thyroid disease is believed to be the most common inherited disease of dogs.

Congenital Heart Disease can produce a number of cardiac abnormalities. A qualified veterinarian with advanced cardiology training and experience diagnoses the presence or absence of these abnormalities through an examination.

Cranio-mandibular Osteopathy is an inherited bone disease that produces proliferation of bone tissue along the mandible, interfering with jaw mobility. The disease is most commonly found in West Highland Terriers and Scottish Terriers but may occur in other breeds.

DNA Databases

The DNA databases are based on tests that determine the presence of genetic indicators for specific inherited abnormalities. These genetic tests are breed-specific. New databases are developed as tests become available for each disease and breed.

Von Willebrand's Disease is an inherited disorder that leaves dogs susceptible to abnormal bleeding. This registry serves the Scottish Terrier, Manchester Terrier, Doberman Pinscher, Shetland Sheepdog, Poodle and Pembroke Welsh Corgi.

Progressive Retinal Atrophy is an eye disease that leads to blindness. This registry serves the Irish Setter and Portuguese Water Dog.

Copper Toxicosis is a disease that permits copper to accumulate in the body, eventually causing liver disease. This database serves the Bedlington Terrier.



It has been estimated that at least 25 percent of the health problems facing veterinarians and breeders have genetic roots.

Cystinuria is a metabolic disorder that results in the development of recurrent stones in the urinary system. The Newfoundland is served by this database.

Phosphofructokinase Deficiency is a genetic disorder that prevents the metabolism of glucose into energy, leading to muscle disease and exercise intolerance. This database lists the English Springer Spaniel and Cocker Spaniel.

Congenital Stationary Night Blindness is a hereditary disease in the French Briard. It causes blindness due to photoreceptor degenerative changes in the retina.

Pyruvate Kinase Deficiency is a disease that leads to anemia, low exercise tolerance and possibly reduced fertility. It is caused by a lack of pyruvate kinase, an enzyme normally found in red blood cells. This database serves the Basenji.

Service to Breeders

These databases provide information about the genetic characteristics evaluated so the breeder can make conscientious decisions when selecting mating pairs.

With the information provided by the database, breeders can minimize or eliminate detrimental characteristics that could be carried in their breeding stock.

(continued on page 3)



Dr. Laura Hardin and Dr. Janet Rettenmaier Join OFA Staff

Dr. Laura E. Hardin, D.V.M., M.S., and Dr. Janet L. Rettenmaier, D.V.M., M.S., have joined the Orthopedic Foundation for Animals as associate directors.

Hardin received her doctoral degree from Mississippi State University in 1987. She received a master's degree in veterinary epidemiology from the University of Missouri in 1994 and was a post-doctoral fellow in medical informatics at Missouri. She is a candidate for a Ph.D. in curriculum and instruction from the University of Missouri College of Education.



Dr. Hardin

Before joining OFA, Hardin was a medical education research analyst for the University of Missouri School of Medicine. Prior to that appointment, she was an epidemiology specialist in the bureaus of communicable disease control and veterinary public health for the Missouri Department of Health. Hardin has authored or co-authored 13 articles that have been published in professional veterinary, epidemiological

and educational journals.

Rettenmaier graduated from the Iowa State University College of Veterinary Medicine in 1988. She then completed an internship in small animal surgery and internal medicine and a residency in small animal surgery, both at the University of Missouri. She received a master of science degree in veterinary medicine and surgery at Missouri in 1993.



Dr. Rettenmaier

Before joining OFA, Rettenmaier was a research associate at Missouri's College of Veterinary Medicine and was project coordinator of a cardiology pharmaceutical study. She continues to provide veterinary relief and surgical consultation services to veterinary practices.

Rettenmaier has written research papers on canine hip dysplasia, cervical spondylomyelopathy and pelvic osteotomy plates. She currently is involved in research projects studying atrial defibrillation and an apparatus for an improved method of sternal closure. She also is a member of the board of directors of the Central Missouri Humane Society.

Databases can help minimize or eliminate detrimental traits

(continued from page 2)

When several generations have been submitted to the registry, breeders have the advantage of knowing the characteristics of related animals, thus providing a clearer picture of inheritance in polygenic traits such as hip dysplasia.

Research Resources

The OFA databases are available for selected research studies. When a proposal is accepted by OFA, data can be provided to researchers in a confidential format that does not divulge the identity of individual dogs or owners.

Following John Olin's original intentions to promote animal wellness, the OFA also supports research studies through financial contributions. Funds are distributed to researchers through the Morris Animal Foundation or the Canine Health Foundation. Occasionally, OFA will directly fund a research project when breed clubs provide matching funds.

The following pages of this issue of the Advocate will focus on currently supported research.

Through its support of such projects, OFA hopes

to provide resources for further understanding and, ultimately, the prevention of genetic diseases.

CHIC Provides New Resource

The Canine Health Information Center has been formed at the Orthopedic Foundation for Animals to provide a new information resource to assist owners, breeders and scientists in breeding healthy dogs. The center, formally initiated in October 1999, is a joint effort of OFA, the Canine Health Foundation and parent breed clubs.

The combined efforts of these organizations will allow breed clubs to identify genetic diseases that impact their breeds. The CHIC will maintain data, provide professional advice and determine testing priorities.

An 18- to 24-month pilot effort will determine the most effective methods for meeting the goals of the CHIC. Six breeds will be involved in the pilot phase: Dalmatian, Basenji, Newfoundland, Mastiff, Golden Retriever and Irish Setter. After the pilot period, the information center will develop programs with any interested breed club.

Research Projects Supported by OFA Will Lead to Prevention of Genetic Diseases

The Orthopedic Foundation for Animals currently supports nine research projects funded through the Morris Animal Foundation and Canine Health Foundation. Summaries of these projects follow.

Feasibility of Genetic Mapping to Identify a Hip Dysplasia Locus in Basenjis

*Principal Investigator: Gary Johnson, D.V.M.
College of Veterinary Medicine
University of Missouri*

Canine hip dysplasia in most breeds is believed to result from a combination of an unknown number of genes. The combination may vary from breed to breed and even among individuals within a breed. As a result, it is a formidable task to identify DNA markers that would aid dog breeders in avoiding dysplastic puppies.

The Basenji, however, offers a unique opportunity to identify a single pair of genes that may be responsible for hip dysplasia. Most Basenjis in North America stem from a very limited number of founders imported to England from Africa, and hip dysplasia in the breed is limited to a restricted subfamily of closely-related dogs.

Preliminary study of pedigree information is consistent with Mendelian inheritance, indicating that a single pair of genes may be responsible for the trait in Basenjis. This study will determine the feasibility of locating a hip dysplasia gene in the Basenji and then determining whether that gene also contributes to hip dysplasia in other breeds.

Development of a Multi-Generational DNA Bank and Registry for Tibetan Terriers

*Principal Investigator: Gary Johnson, D.V.M.
College of Veterinary Medicine
University of Missouri*

The Tibetan Terrier breed has four well-documented genetic diseases — progressive retinal atrophy, lens luxation, cataracts and ceroid lipofuscinosis, a neurodegenera-

tive eye disorder. Many dogs are bred before these conditions become apparent, allowing the diseases to be passed to succeeding generations of dogs. Earlier identification of the diseases would enable breeders to make better decisions within their breeding programs.

Stuart F. Eckmann and Linda W. Bell of the Tibetan Terrier Breed Club sought research grants from the American Kennel Club Canine Health Foundation and OFA to isolate DNA from the blood of a large number of Tibetan Terriers. The samples will be available to scientists studying diseases found in the breed and provide reference samples for future research efforts.

The University of Missouri is serving as the center of this research project, which includes the distribution of blood sample collection kits and DNA processing and storage.

The project goal of more than 250 DNA samples could be sufficient to search for DNA markers for at least one of the heritable diseases recognized in the breed.

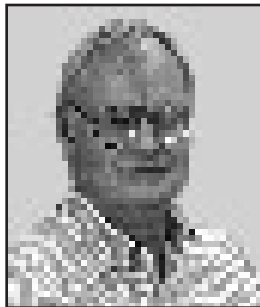
Canine Chromosome Mapping

*Principal Investigator: George J. Brewer, D.V.M.
Department of Human Genetics and Internal Medicine
University of Michigan*

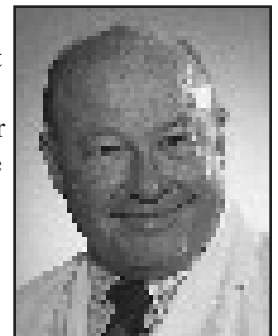
This project seeks to identify specific genetic causes of important diseases and to develop DNA tests that will allow breeders to reduce or eliminate diseases through selective breeding. Examples of diseases to be studied include canine hip dysplasia, progressive rod-cone degeneration (PRCD), cataracts, epilepsy and renal dysplasia.

The underlying premises of studying hip dysplasia are hypotheses that one to four major genes cause canine hip dysplasia and that one major gene is likely responsible within a single breed. Genetic analysis is undertaken on a number of breeds to increase the chances of identifying specific genes related to disease.

Part of the work examines “candidate genes” identified in other species as being related to the biochemical makeup of joints and therefore possible contributors to hip dysplasia.



Dr. Johnson



Dr. Brewer



Cytogenetics of Canine Cancer

Principal Investigator: Susan LaRue, D.V.M., Ph.D.
*College of Veterinary Medicine and Biomedical Sciences
Colorado State University*

Cancer is a leading cause of death in dogs. Research strongly suggests that development of cancer stems from cellular genetic mutations.

The genetics of cancer may be more important in dogs than in humans due to selective breeding, but little is known about the genetics of canine cancers. A major obstacle in the study of canine chromosomes has been the inability to identify chromosomes using techniques commonly applied to the study of humans.

Research supported by OFA, through the Morris Animal Foundation, is helping to overcome these obstacles through a new method allowing direct identification of canine chromosomes. This method, Comparative Genomic Hybridization, allows an entire set of chromosomes to be scrutinized in a single assay.

The method is being used to identify recurring chromosomal aberrations that may be useful in predicting treatment responses and eventually identifying the gene that causes a tumor.



Dr. LaRue

Immunotherapy of Canine Melanoma

Principal Investigator: Jaime F. Modiano, V.M.D., Ph.D.
*College of Veterinary Medicine
Texas A&M University*

Malignant melanoma, a cancer of the skin, is a devastating cancer that often is incurable in dogs. Existing therapies for metastatic melanoma (cancer spreading to other body tissues) produce poor chances of long-term survival and, often, a poor quality of life.

New cancer therapies target specific molecules or genes whose aberrant function is responsible for the development of cancer. These studies propose to define a genetic approach that, when combined with intensive modulation of the canine immune system, may improve the therapeutic outcomes and the quality of life for dogs with metastatic tumors.



Dr. Modiano

It is hoped that this research will lead to new therapies for the treatment of other metastatic cancers as well as malignant melanomas.

Pathogenesis of Canine Osteosarcoma

Principal Investigator: Roy Levine, Ph.D.
*College of Veterinary Medicine
Cornell University*

Osteosarcoma is the most common bone cancer that occurs in dogs. It is difficult to manage due to its aggressive growth and the high incidence of metastasis to other tissues. However, little is known about the origins of osteosarcoma in dogs, resulting in limited diagnosis and treatment options.

This project has isolated five canine osteosarcoma cell lines and begun to isolate the molecular defects responsible for the cancers. The identification of the genes that are abnormally expressed in canine osteosarcoma will facilitate the development of diagnostic tests for early detection of tumors and potentially provide targets for therapeutic intervention.



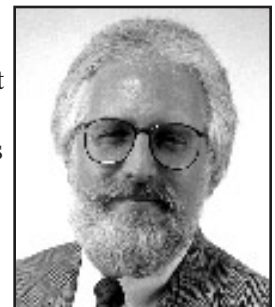
Dr. Levine

Pathogenesis and Therapy of Acquired Megaesophagus

Principal Investigator: Robert J. Washabau, V.M.D., Ph.D.
*School of Veterinary Medicine
University of Pennsylvania*

The esophagus carries food and water from the mouth to the stomach. Idiopathic megaesophagus — the dilation of this muscular passageway — is the most common cause of regurgitation in older dogs. The incidence of serious illness and death of dogs with megaesophagus is high, as the condition leads to chronic malnutrition and recurrent pneumonia.

Myasthenia gravis, or muscle weakness, has been identified as a cause of about 25 percent of the cases of acquired megaesophagus. This study seeks to determine causes for the abnormal muscle contractions in the remainder of the cases and to identify potential therapies.



Dr. Washabau

Research Supported by OFA Addresses a Variety of Inherited Diseases (continued from page 5)

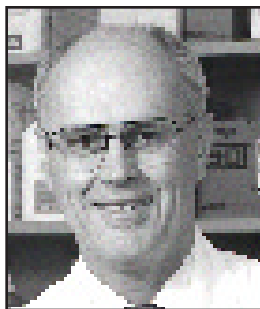
Inheritance of Autoimmune Thyroiditis

*Principal Investigator: Ray Nachreiner, D.V.M.
College of Veterinary Medicine
Michigan State University*

Hypothyroidism is a metabolic disease leading to a variety of clinical signs in dogs. Some of these include lethargy, obesity and chronic skin lesions. One of the causes of hypothyroidism, autoimmune thyroiditis, is known to be heritable.

Autoimmune thyroiditis is the most common cause of primary hypothyroidism in dogs and can be detected by laboratory tests that are currently available.

In support of further knowledge about autoimmune thyroiditis, the Animal Health Diagnostic Laboratory at Michigan State University's College of Veterinary Medicine has conducted a retrospective evaluation of more than 50,000 blood samples. This study will evaluate trends in the occurrence of autoimmune thyroiditis and its relationship to thyroid function.



Dr. Nachreiner

Inheritance of a Forelimb Anomaly in Newfoundlands

*Principal Investigators: George Padgett, D.V.M.,
and Ulreh Mostosky, D.V.M.
College of Veterinary Medicine
Michigan State University*

An increasing number of reports worldwide have heightened interest in the forelimb anomaly of Newfoundland Dogs. This abnormality causes lameness due to bowing of the bones of the front legs and initially was thought to be a form of dwarfism or achondroplasia (failure of bone growth). The condition is diagnosed in adult dogs through radiographs of the radius and ulna.



Dr. Mostosky

Genetic studies indicate that parents of affected progeny are phenotypically normal, ruling out a dominant mode of inheritance. Sex-linked inheritance also is ruled out because males and females appear to be affected in equal numbers.

This proposal has been funded to determine if this trait is autosomal recessive or polygenic. To accomplish this, two affected individuals will be mated and their offspring will be evaluated. If all offspring are affected, autosomal recessive inheritance will be confirmed.

The puppies from this litter will be studied further to document the pathogenesis of the disease and possibly to identify key factors affecting its progression.



OFA Hip Dysplasia Video Is Now Available

Hip dysplasia is the most common inherited orthopedic disease affecting dogs. A 12-minute video, "CDH: The Hidden Disease," describing canine hip dysplasia and OFA's procedures is now available. An optional \$10 donation covers the cost of production and handling.

To request a copy of this video, please call OFA at (573) 442-0418 or write the foundation at 2300 E. Nifong Boulevard, Columbia, Mo. 65201-3856.

Visit Us on the Web!

The web site of the Orthopedic Foundation for Animals, <http://www.offa.org>, is being redesigned so that we may better serve our clients.

The new site will be more user-friendly and will include more detailed information about each of the foundation's disease databases.





Four Members Added to OFA Board of Directors

The Orthopedic Foundation for Animals Inc. board was expanded with the election of four new directors at the board's October meeting. The new directors are:

Richard C. (Dick) Fox of Cortland, N.Y., is a retired commercial banker who has bred and exhibited English Setters under the Foxtract prefix since 1968. He produced the fourth-rated all-breed dog in the U.S. in 1988 and the third-ranked all-breed dog in Canada in 1996.



Fox

Fox, now a computer consultant, is a former ESAA director and was a founder of the Iroquois English Setter Club and served several terms as its president. He recently was licensed to judge English Setters by the American Kennel Club. He founded the ESAA Brainstem Auditory Evoked Response database and new Health Trust Fund.

Susan LaCroix Hamil of Laguna Beach, Calif., is a veterinary technician and veterinary hospital manager. She has bred Bloodhounds since 1970. Her Quiet Creek line has produced nearly 45 champions. Hamil was named the top breeder and owner at the 1990 national specialty



Hamil



The OFA Board

Members of the OFA board of directors attending their summer meeting in Columbia, Mo., were (seated, from left), Edward L. Kozicky of Godfrey, Ill.; Dr. Fran Smith of Lonsdale, Minn.; Constance Josse of St. Louis, Mo.; and Dr. U.V. Mostosky of Haslett, Mich. Standing (from left) were Jack Newton of Woodland Hills, Calif.; William J. Feeny of Cotati, Calif.; Marshall Simonds of Carlisle, Mass.; Dr. Ray Weitkamp of Arcadia, Calif.; and Dr. Eric Jimenez of New Haven, Conn.

and campaigned nationally-ranked Bloodhounds in 1994, 1995 and 1999.

Hamil is licensed by AKC to judge Bloodhounds and Greyhounds and has judged in the U.S. and Europe. She is a past president and current AKC delegate of the American Bloodhound Club and has been a director of the California Federation of Dog Clubs and past president of the California Veterinary Medical Association Auxiliary.

Hamil is a director of the AKC Canine Health Foundation and is chairman of the Blue Bell Foundation for Cats. She has written columns on canine and feline issues for her local newspaper, AKC Gazette and Dog Fancy. She was a founder of Bloodhound West's rescue and welfare program in 1978.



Hovan

Rhonda Hovan of Akron, Ohio, has exhibited Golden Retrievers in conformation for nearly 30 years. She has bred 50 champions, including the current number-one Golden Retriever, under the "Faera" prefix.

Hovan is a member of the board of directors of the Golden Retriever Club of America and is special features editor of GRNews. She is a regular columnist in GRNews and has written articles on health and genetics for other publications such as the AKC Gazette and Canine Health Foundation newsletters. Hovan is licensed by the AKC to judge several sporting and herding breeds.

W. Terry Stacy of Huntington Beach, Calif., is national show and breeder services manager for Kal Kan Foods. His program supports 98 of the largest U.S. dog shows sponsored by Kal Kan and Pedigree Dog Food and supports more than 20,000 breeders. He also publishes Breeders Forum magazine.



Stacy

Stacy has been involved with purebred dogs for more than 45 years and has bred champion Cocker Spaniels.

Stacy was granted an AKC All-Breed Professional Handler's License in 1960. From 1964 to 1979 he operated Charter Kennels and served as a professional all-breed handler. He retired from the AKC as senior vice president of events in 1996 after serving the club for 13

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A Review of OFA Databases and Research

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