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DOG Update

A NESTLÉ PURINA PUBLICATION DEDICATED TO DOG ENTHUSIASTS

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BREEDING HEALTHY DOGS

A New Era: Dog10K Consortium

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BREEDING SELECTION

IS THE FIRST STEP TO PRODUCING HEALTHY DOGS

Breeding healthy dogs that are good examples of their breed begins during the selection process when considering the right stud dog for a brood bitch. A pre-breeding examination, medical history and screening for breed-specific genetic diseases in both prospective parents are tools that can help ensure breeding mates are likely to produce a healthy litter.

It also helps to consider genetic diversity. "Dogs from the breadth of the gene pool should be used for breeding as long as they represent health and quality," says Jerold Bell, DVM, adjunct professor of genetics at the Cummings School of Veterinary Medicine at Tufts University

and a genetics advisor to national parent breed clubs.

"The most common genetic diseases seen by veterinarians are due to ancient liability genes that originated in ancestors that preceded the separation of breeds," Dr. Bell explains. "These diseases, which include allergies, hip dysplasia, heart disease, cruciate ligament disease, slipping kneecaps, cataracts, hereditary cancers, and others, occur in both purebred and mixed-breed dogs."

More recent mutations impact breed-specific genetic disorders. "An increase of breed-related diseases is due to homozygosity of deleterious recessive or additive



Pointer dam and puppies



Skye Terrier

liability genes,” Dr. Bell explains. “In a nutshell, breed-specific genetic diseases result from the expression of specific deleterious genes, not a result of increased homozygosity. Restricted genetic diversity is not an issue in purebred dogs, unless there is no alternative direction to go for health and quality.”

Deleterious mutated genes, which primarily are recessive genes, can accumulate in the background of a breed’s gene pool. “These deleterious genes accumulate primarily because they are not expressed by the carriers in the heterozygous state,” Dr. Bell says. “An unaffected carrier can perpetuate the spread of deleterious genes, which can increase in frequency if linked to positively selected genes, or through genetic drift, which is the random accumulation of disease liability genes in the absence of selection.”

For disorders with a direct DNA test, genetic counselors like Dr. Bell

advise breeders to breed quality carriers to non-carrier dogs and replace the carrier parent with a quality non-carrier offspring. “In this way breeding lines — and breed genetic diversity — are not abandoned, and testable disease liability genes can be lost in one generation,” he says.

“Dogs with hereditary diseases should be selected against for breeding. For many genetic disorders, validated genetic tests are available to identify carriers. For other disorders, genetic screening and medical history help to differentiate normal from affected dogs,” Dr. Bell says. “When planning a breeding, the selection of healthy parents is key to the health of the offspring.”

A pre-breeding veterinary examination should include:

- Phenotypic examination of a dog’s musculoskeletal, cardiac, ophthalmologic, gastrointestinal, pulmonary, and dermatologic

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DOG10K: A DEEP DIVE INTO CANINE GENETICS

The International Consortium of Canine Genome Sequencing, called the Dog10K Consortium, aims to generate, and ultimately share, whole-genome sequence data over the next five years from 10,000 canids, including breed and village dogs, wolves, foxes, coyotes, dingoes, and other canids.

Dog10K will allow for a better understanding of the impact that sequence variations have on individual breeds and subspecies of dogs. The breadth of sequencing data the project will generate include DNA, RNA and mobile genetic elements that can move around in a genome.

"A big part of what distinguishes Dog10K is the extensive sample collection that will cover all established breeds worldwide as well as village dogs, wild canids and niche or non-registered dog populations that fall outside the formal definition of a recognized breeds," says Elaine Ostrander, PhD, Chief of the Cancer Genetics and Comparative Genomics Branch of the National Human Genome Research Institute. "We plan to address research questions related to the genetic underpinnings of canine domestication, breed formation, aging, and behavior and breed morphologic variation.

Advancing understanding of human and canine health is paramount."

Presenting on the Dog10K Consortium to about 200 research scientists at the 10th International Conference on Canine and Feline Genetics and Genomics in May at Bern, Switzerland, Dr. Ostrander, who was recently elected to the National Academy of Sciences, has long played a key role in dog genetics having initiated the canine genome project in 1993. This led to the sequencing of the dog genome in 2003.

A healthy Boxer named "Tasha" was used for the sequencing due to her being highly homozygous. This was key at the time when DNA sequencing was in its infancy because it made the sequencing effort

easier. Tasha's genetic sequence still is the standard template used today to study genetic mutations.

Reflecting on why the dog was chosen over other species for sequencing, Dr. Ostrander says, "The domestic dog was chosen due to its similarities with humans in terms of health and biology, and the shared genomic structure. A complete canine sequence will help scientists better understand human health and biology. We have the support of the general dog community as a genome sequence of the dog promises a better understanding of canine health issues."

The first meeting of canine genetics and genomics researchers from around the world who would take part in Dog10K was at the Academic Summit of Dog Genomes in 2016 in Beijing. The consortium began planning how to collect and select samples, sequencing technology, bioinformatics, analysis, and logistics. A second meeting was held at the Bern conference.

"The idea is to improve the usefulness of the canine model system by refining the existing reference genome from the Boxer and to create new reference genomes from additional dogs," says Guo-Dong Wang, PhD, of the Kunming Institute of Zoology.

"We will apply this new database to a myriad of scientific questions. The idea is to sequence each genome to at least 20x coverage, which will provide optimal coverage with minimal error rates."

An article on Dog10K was published in April 2019 in *National Science Review*. Dr. Ostrander, the lead author, explains the broad sample collection. "The wild canids and village dogs will help us understand the demographic history and occurrence of cross breeding at early stages of dog domestication. Niche populations of unrecognized dog breeds will tell us about natural selection events that occurred when dogs traveled alongside humans during early human



Purina has sponsored the International Conference on Canine and Feline Genetics and Genomics since its beginning in 2002. The 10th meeting of the group of research scientists was held in May 2019 in Bern, Switzerland.

CANINE GENETIC RESEARCHERS REQUEST DNA SAMPLES*		
Sample Type	Research Focus	Investigator
German Shorthaired Pointer, Vizsla, Braque de Bourbonnais	Exfoliative cutaneous lupus erythematosus (ECLE)	Tosso Leeb, University of Bern, Switzerland, tosso.leeb@vetsuisse.unibe.ch
All Breeds	Xanthine stones, early onset (<3 years old) calcium oxalate stones	Eva Furrow, University of Minnesota, furro004@umn.edu
Saint Bernard	Laryngeal paralysis, osteosarcoma	Katie Minor, University of Minnesota, minork@umn.edu
Border Collie, Australian Shepherd, Shetland Sheepdog	Exercise-induced collapse (EIC)	Katie Minor, University of Minnesota, minork@umn.edu
All Breeds	Diabetes mellitus, insulinoma	Lucy Davison, Royal Veterinary College, United Kingdom, ldavison@rvc.ac.uk
Giant Schnauzer	Congenital hypothyroidism, pituitary type	John Fyfe, Michigan State University, fyfe@msu.edu
All Breeds	Ehlers-Danlos syndrome	Jared Jaffey, Midwestern University, jjaffee@midwestern.edu
Bull Terrier	Congenital hypoparathyroidism	Claire Wade, University of Sydney, Australia, claire.wade@sydney.edu.au
Dutch Partridge Dog	Idiopathic epilepsy	Evy Beckers, University of Gent, Belgium, evy.beckers@ugent.be

*This request for DNA samples was compiled from canine genetic researchers attending the 10th International Conference on Canine and Feline Genetics and Genomics. These requests are independent of the Dog10K Consortium.

development, and established breeds will advance studies of breed morphology, behavior and disease susceptibility."

Importantly, a catalog of reference sequence data on all breeds will provide the scientific community with a way to perform matched WGS-based case-control analysis, either directly or through imputation, says Dr. Wang. "This large data set will allow the study of diseases and be an important link between canine and human health," he says.

"The Dog10K Consortium will generate a comprehensive data set of unparalleled complexity and power," Dr. Ostrander says. "This will result in a resource that will prove invaluable to a wide range of fields, including comparative genomics, veterinary science, evolutionary biology, medical research, and conservation genetics.

Hosted by the University of Bern and sponsored by Purina since it began in 2002, the International Conference on Canine and Feline Genetics and Genomics provides an important forum for canine genetic researchers worldwide to discuss their work and collaborations.

Purina Senior Research Scientist Rondo Middleton, PhD, a member of the conference's scientific organizing committee, says, "Supporting this event is an important way of helping to advance canine genetic research. The genetic link to nutrition is very valuable. Genetics tell us a great deal about everything a dog could be, but it is the interactions between genetic potential and environmental input, such as nutrition, that ultimately defines what the animal actually becomes."

When breeders include health data from a sire and dam in their selection criteria, they are making a more informed decision and hopefully applying selective pressure to decrease the number of deleterious disease liability genes and improve the probability of healthy genes.



Bulldog

Continued from page 3

- systems, as well as screening for behavioral abnormalities
- Medical history for inherited diseases that cannot be identified during an examination, such as allergies, seizures, bloat, bladder stones, cruciate ligament disease, etc.

To learn about breed-specific genetic testing requirements determined by parent breed clubs, sources include:

- [Orthopedic Foundation for Animals' Canine Health Information Center](#)
- [AKC Bred with H.E.A.R.T. program](#)

Parent clubs can designate required tests and optional tests for the Canine Health Information Center (CHIC) program. Required tests mean a dog must have them to qualify for a CHIC number. Optional tests are not required to earn a CHIC number, but parent clubs encourage the additional testing due to the importance of these conditions in the breed.

"CHIC is not about normalcy," says Eddie Dziuk, OFA Chief Operating officer. "It is about encouraging health screening in accordance with a parent club's testing protocol, sharing the test results in the public domain, and increasing health awareness. The idea is to improve the overall health of the breed and allow breeders to make informed breeding decisions."

"Before breeding, I always search the OFA's database for sires," says Chimera Bulldog breeder Dan Bandy of Shawnee, Oklahoma. "It is so important for owners of bitches to find a healthy male to which to breed, and this can be difficult because owners often do not make health test results public. I often have had to do a lot of legwork myself by reaching out to owners for more information. Some owners are concerned they will sacrifice breed type if they focus on health testing. This simply is not true."

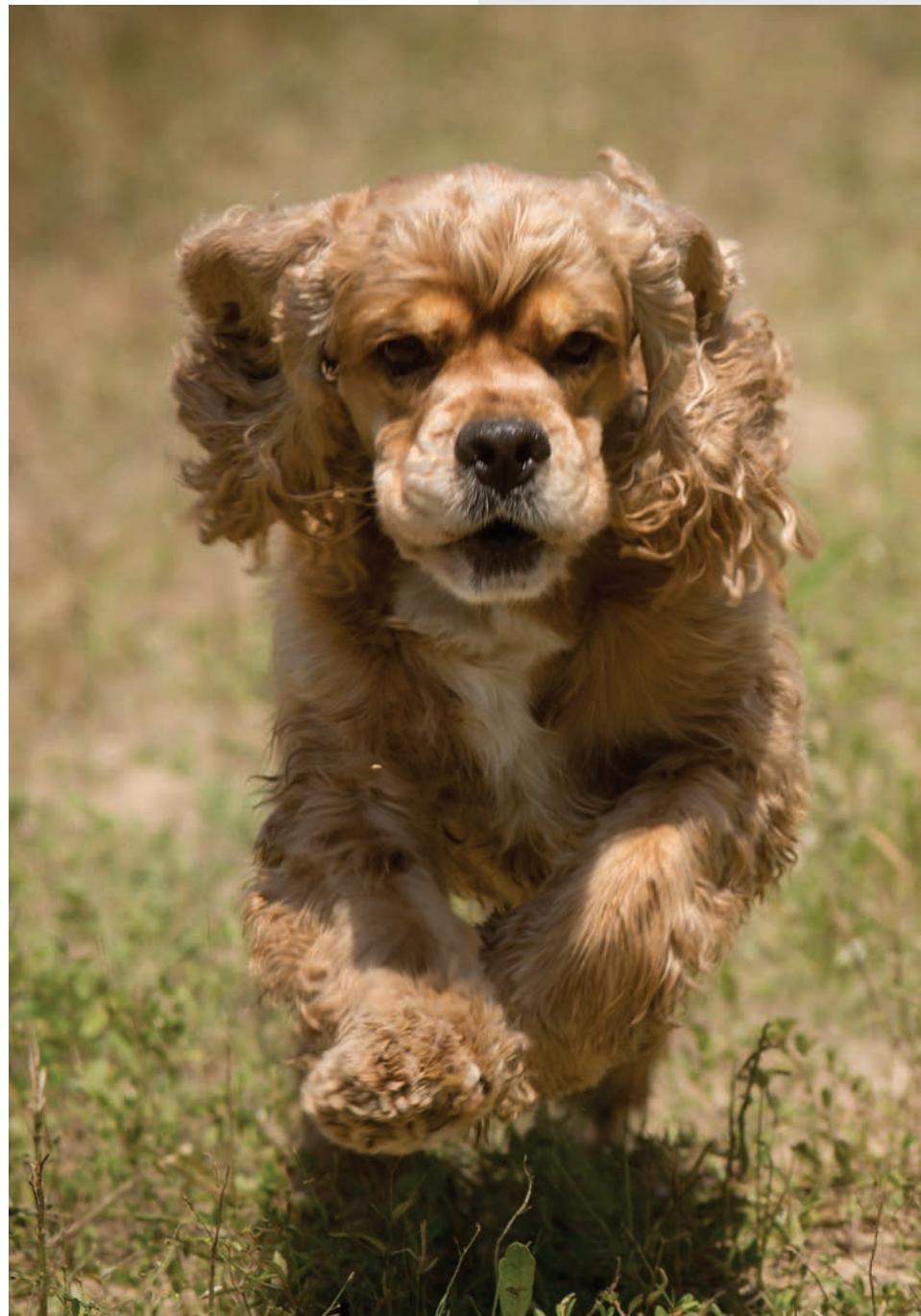
OFA along with the AKC Canine Health Foundation launched CHIC in 2001 as a centralized database to store health test results with individual dogs. Since then, over 130,000 dogs have been issued CHIC numbers for being health tested according to their breed-specific health testing requirements.

CHIC is a valuable resource for dog breeders. When breeders include health data from a sire and dam in their selection criteria, they are making a more informed decision and hopefully applying selective pressure to decrease the number of deleterious disease liability genes and improve the probability of healthy genes.

Similarly, AKC Bred with H.E.A.R.T. designates breeders who practice health, education, accountability, responsibility, and tradition in their breeding program. This means they health test their breeding stock in accordance with the recommendations of the breed parent club and that they keep up with breed education including advances in canine health. Those who are accepted into the program work hard to ensure they are breeding happy, healthy purebred dogs.

Simply put, breeding healthy dogs begins during the selection process. There are many tools today to help breeders make decisions about the best dogs to breed. Staying informed, using genetic health tests and screening breeding stock are important ways to put breeders on track to produce a healthy litter.

"It's so important to be aware of diseases that affect your breed," Brandy says. "It also is great to know that as a breeder when you practice health testing and put in time researching the best breeding partners, you are helping to move your breed forward toward improved health and longevity." ■



Cocker Spaniel

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*Data was collected by Relevance Research via an online survey from August 15-19, 2018. A total of 826 nationally-representative dog owners qualified and completed the survey. Qualified participants were men and women age 18 and older, owned one or more adult dogs, were household members most responsible for taking the dog(s) to a veterinarian, and had taken the dog(s) to a veterinarian in the past 12 months.

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