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## Genetic Comparison of Purebred Dogs Yields Surprises

The first detailed genetic comparison of purebred domestic dogs promises to rewrite the textbooks with new information about breed classification and insights that may improve canine health by boosting understanding of the more than 350 inherited disorders, including cancer, heart disease, epilepsy, blindness and deafness, which affect dogs.

In analyzing and carefully comparing the genetic information from dogs representing 85 breeds, the researchers were surprised to discover previously unappreciated relationships between existing breeds and new details that suggest completely unexpected breeds to be among the most ancient descendants of dogs' wolf-like ancestors.

The researchers, led by Elaine A. Ostrander and Howard Hughes Medical Institute researcher Leonid Kruglyak, reported their findings in an article published in the May 21, 2004, issue of the journal *Science*. Kruglyak and Ostrander are at the Fred Hutchinson Cancer Research Center. Other co-authors are from the University of Washington and the University of Missouri.

“In all the research on dogs, the question comes up over and over how modern breeds are related to one another genetically,” said Ostrander, whose research has concentrated on using the power of genetics to understand canine diseases. “The answer to this question has important implications for trying to identify disease genes, because if we know a subset of breeds that share a common lineage, then we know to group them together when we're working on a particular disease. For example, if I'm studying lymphoma, and I know that a subset of Asian breeds shares a common lineage, I could group data from those breeds together, rather than considering them separately, in order to gain more statistical power,” she said.

For their analyses, the researchers obtained the help of the American Kennel Club (AKC) and dog breeders across the country to acquire cheek-swab DNA samples from purebred dogs at dog shows and directly from owners.

“While we only analyzed eighty-five breeds of the hundreds of recognized breeds, those eighty-five included the great majority of popular breeds,” said Ostrander. “Just the top 20 breeds, which include the Labrador Retriever, the German Shepherd and the Dachshund, account for about seventy percent of

all AKC registrations.”

To compare the breeds, the researchers analyzed the DNA samples from the cheek-swabs for subtle differences in genetic signposts, called microsatellite loci, among the dogs. The analysis covered 414 dogs from the 85 breeds studied.

Kruglyak and his colleagues performed detailed statistical analyses of the data to detect patterns that would reveal genetic differences among the breeds. The researchers also sought to determine whether the genetic differences they found would yield any general genetic classifications of dog breeds.

“The first major finding was that the different breeds are quite genetically distinct,” said Kruglyak. “The dogs of a particular breed are much more similar to one another than they are to dogs of different breeds. These differences are so distinct that we could just feed a dog's genetic pattern into the database, and the computer could match it to a breed.

“This finding was a bit surprising because most of the breeds are quite recent and were formally genetically isolated only in the nineteenth century, with the advent of breed clubs and breed standards,” said Kruglyak. “It's a much more striking difference than is seen among human populations that evolved on different continents,” he said.

The genetic comparisons also enabled the researchers to cluster many breeds according to shared lineages. The researchers found four such clusters, in particular the separation of breeds that are more ancient from those that probably dated from the 19<sup>th</sup> century at the time when breeds were formally established.

The researchers said they were surprised that the cluster containing the more ancient breeds of Asian and African origin included such a diversity of breeds—such as the Basenji, Saluki, Afghan, Lhasa Apso, Pekingese, Sharpei, Shih Tzu, Akita, Alaskan Malamute, Siberian Husky and Samoyed. All of these breeds showed the closest genetic relationship to the wolf ancestors of dogs, said the researchers.

Noticeably absent from this ancient cluster were several breeds long regarded as the most ancient by breeders, including the Pharaoh Hound and the Ibizan Hound—depicted on Egyptian tomb walls. The researchers said their analysis indicated that the modern representatives of these breeds were recreated in more recent times from combinations of other breeds. The researchers also found genetic evidence for a recent origin of the Norwegian Elkhound, believed to be of ancient Scandinavian origin.

Another group of breeds that clustered genetically included the mastiff-type dogs such as the Bull Mastiff, Bulldog and the Rottweiler. A third group included the herding dogs, and a fourth included the terriers and scent hounds.

Further studies will include more detailed analyses to focus on differences within breeds and between related breeds. Such insights may enable even deeper insights into the origins of inherited diseases to which those breeds are susceptible, said the researchers.